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Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea (Review)

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[Intervention Review]

Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea

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ABSTRACT

Background

Obstructive sleep apnoea (OSA) is a syndrome characterised by episodes of apnoea (complete cessation of breathing) or hypopnoea (insufficient breathing) during sleep. Classical symptoms of the disease — such as snoring, unsatisfactory rest and daytime sleepiness — are experienced mainly by men; women report more unspecific symptoms such as low energy or fatigue, tiredness, initial insomnia and morning headaches. OSA is associated with an increased risk of occupational injuries, metabolic diseases, cardiovascular diseases, mortality, and being involved in traffic accidents.

Continuous positive airway pressure (CPAP) - delivered by a machine which uses a hose and mask or nosepiece to deliver constant and steady air pressure- is considered the first treatment option for most people with OSA. However, adherence to treatment is often suboptimal. Myofunctional therapy could be an alternative for many patients. Myofunctional therapy consists of combinations of oropharyngeal exercises - i.e. mouth and throat exercises. These combinations typically include both isotonic and isometric exercises involving several muscles and areas of the mouth, pharynx and upper respiratory tract, to work on functions such as speaking, breathing, blowing, sucking, chewing and swallowing.

Objectives

To evaluate the benefits and harms of myofunctional therapy (oropharyngeal exercises) for the treatment of obstructive sleep apnoea.

Search methods

We identified randomised controlled trials (RCTs) from the Cochrane Airways Trials Register (date of last search 1 May 2020). We found other trials at web-based clinical trials registers.

Selection criteria

We included RCTs that recruited adults and children with a diagnosis of OSA.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. We assessed our confidence in the evidence by using GRADE recommendations. Primary outcomes were daytime sleepiness, morbidity and mortality.

Main results

We found nine studies eligible for inclusion in this review and nine ongoing studies. The nine included RCTs analysed a total of 347 participants, 69 of them women and 13 children. The adults' mean ages ranged from 46 to 51, daytime sleepiness scores from eight to 14, and severity of the condition from mild to severe OSA. The studies' duration ranged from two to four months.

None of the studies assessed accidents, cardiovascular diseases or mortality outcomes. We sought data about adverse events, but none of the included studies reported these.

In adults, compared to sham therapy, myofunctional therapy: probably reduces daytime sleepiness (Epworth Sleepiness Scale (ESS), MD (mean difference) -4.52 points, 95% Confidence Interval (CI) -6.67 to -2.36; two studies, 82 participants; moderate-certainty evidence); may increase sleep quality (MD -3.90 points, 95% CI -6.31 to -1.49; one study, 31 participants; low-certainty evidence); may result in a large reduction in Apnoea-Hypopnoea Index (AHI, MD -13.20 points, 95% CI -18.48 to -7.93; two studies, 82 participants; low-certainty evidence); may have little to no effect in reduction of snoring frequency but the evidence is very uncertain (Standardised Mean Difference (SMD) -0.53 points, 95% CI -1.03 to -0.03; two studies, 67 participants; very low-certainty evidence); and probably reduces subjective snoring intensity slightly (MD -1.9 points, 95% CI -3.69 to -0.11 one study, 51 participants; moderate-certainty evidence).

Compared to waiting list, myofunctional therapy may: reduce daytime sleepiness (ESS, change from baseline MD -3.00 points, 95% CI -5.47 to -0.53; one study, 25 participants; low-certainty evidence); result in little to no difference in sleep quality (MD -0.70 points, 95% CI -2.01 to 0.61; one study, 25 participants; low-certainty evidence); and reduce AHI (MD -6.20 points, 95% CI -11.94 to -0.46; one study, 25 participants; low-certainty evidence).

Compared to CPAP, myofunctional therapy may result in little to no difference in daytime sleepiness (MD 0.30 points, 95% CI -1.65 to 2.25; one study, 54 participants; low-certainty evidence); and may increase AHI (MD 9.60 points, 95% CI 2.46 to 16.74; one study, 54 participants; low-certainty evidence).

Compared to CPAP plus myofunctional therapy, myofunctional therapy alone may result in little to no difference in daytime sleepiness (MD 0.20 points, 95% CI -2.56 to 2.96; one study, 49 participants; low-certainty evidence) and may increase AHI (MD 10.50 points, 95% CI 3.43 to 17.57; one study, 49 participants; low-certainty evidence).

Compared to respiratory exercises plus nasal dilator strip, myofunctional therapy may result in little to no difference in daytime sleepiness (MD 0.20 points, 95% CI -2.46 to 2.86; one study, 58 participants; low-certainty evidence); probably increases sleep quality slightly (-1.94 points, 95% CI -3.17 to -0.72; two studies, 97 participants; moderate-certainty evidence); and may result in little to no difference in AHI (MD -3.80 points, 95% CI -9.05 to 1.45; one study, 58 participants; low-certainty evidence).

Compared to standard medical treatment, myofunctional therapy may reduce daytime sleepiness (MD -6.40 points, 95% CI -9.82 to -2.98; one study, 26 participants; low-certainty evidence) and may increase sleep quality (MD -3.10 points, 95% CI -5.12 to -1.08; one study, 26 participants; low-certainty evidence).

In children, compared to nasal washing alone, myofunctional therapy and nasal washing may result in little to no difference in AHI (MD 3.00, 95% CI -0.26 to 6.26; one study, 13 participants; low-certainty evidence).

Authors' conclusions

Compared to sham therapy, myofunctional therapy probably reduces daytime sleepiness and may increase sleep quality in the short term. The certainty of the evidence for all comparisons ranges from moderate to very low, mainly due to lack of blinding of the assessors of subjective outcomes, incomplete outcome data and imprecision. More studies are needed. In future studies, outcome assessors should be blinded. New trials should recruit more participants, including more women and children, and have longer treatment and follow-up periods.

PLAIN LANGUAGE SUMMARY

Myofunctional therapy (oropharyngeal - mouth and throat - exercises) for people with obstructive sleep apnoea

Background

Obstructive sleep apnoea (OSA) is a sleeping disorder. People with OSA have periods where their breathing stops during the night. OSA can cause snoring, unsatisfactory rest, daytime sleepiness, low energy or fatigue, tiredness, initial insomnia and morning headaches.

Continuous positive airway pressure (CPAP) is considered the first treatment option for most people with OSA. However, adherence to CPAP is often poor. A CPAP machine uses a hose and mask or nosepiece to deliver constant and steady air pressure. People who use CPAP often say that using the machine is uncomfortable, causes nasal congestion and abdominal bloating. They can feel claustrophobic and the machine is noisy. The noise can disturb bed partners.

Myofunctional therapy teaches people to do daily exercises to strengthen their tongue and throat muscles. Myofunctional therapy may reduce the intensity of the OSA symptoms and reduce daytime sleepiness on its own, or combined with CPAP.

Key results

We found nine RCT studies that analysed a total of 347 participants, 69 of them women, and 13 children.

In adults, compared to sham therapy, myofunctional therapy probably reduces daytime sleepiness, may increase sleep quality, may result in a large reduction in Apnoea-Hypopnoea Index (the number of apneas or hypopnoeas recorded during the polysomnography study per hour of sleep), may have little to no effect in reduction of snoring frequency and probably reduces subjective snoring intensity slightly.

Compared to waiting list, myofunctional therapy may reduce daytime sleepiness, may result in little to no difference in sleep quality and may reduce AHI.

Compared to CPAP, myofunctional therapy may result in little to no difference in daytime sleepiness and may increase AHI.

Compared to CPAP plus myofunctional therapy, myofunctional therapy alone may result in little to no difference in daytime sleepiness and may increase AHI.

Compared to respiratory exercises plus nasal dilator strip, myofunctional therapy may result in little to no difference in daytime sleepiness, probably increases sleep quality slightly and may result in little to no difference in AHI.

Compared to standard medical treatment, myofunctional therapy may reduce daytime sleepiness and may increase sleep quality.

In children, compared to nasal washing alone, adding myofunctional therapy to nasal washing may result in little to no difference in AHI.

Certainty of the evidence

Our level of certainty about the results of the studies ranges from moderate to very low for all comparisons, mainly due to problems related to risk of bias (for inadequate blinding of participants and incomplete outcome data in some studies) and imprecision.

Most of the participants in the studies were men and we could not undertake separate analyses for women.

Conclusions

Compared to sham therapy, myofunctional therapy probably reduces daytime sleepiness and may increase sleep quality in the short term in patients with obstructive sleep apnoea. New blinded studies, with more participants and longer times of treatment and follow-up, are needed.

The review is current to May 2020.

SUMMARY OF FINDINGS

Summary of findings 1. Myofunctional therapy compared to sham therapy for obstructive sleep apnoea

Myofunctional therapy compared to sham therapy for obstructive sleep apnoea

Patient or population: obstructive sleep apnoea

Setting: Outpatient

Intervention: Myofunctional therapy

Comparison: Sham therapy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with sham therapy	Risk with Myofunctional therapy				
Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months.	The mean ESS endpoint score was 12.1	MD 4.52 lower (6.67 lower to 2.36 lower)	-	82 (2 RCTs)	⊕⊕⊕⊕ MODERATE ¹	Probably reduces day time sleepiness. Scores from 0 to 24. Lower scores denote lower daytime sleepiness. MCID 3 points.
Sleep quality (PSQI): endpoint score. Follow-up: 3 months.	The mean PSQI endpoint score was 10.8	MD 3.9 lower (6.31 lower to 1.49 lower)	-	31 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May increase sleep quality. Scores from 0 to 21. Lower scores denote a healthier sleep quality. MCID 3 points.
Apnoea Hypopnoea Index: endpoint score. Follow-up: 3 months.	The mean AHI endpoint score was 28.8 events/hour	MD 13.2 events/hour lower (18.48 lower to 7.93 lower)	-	82 (2 RCTs)	⊕⊕⊕⊕ LOW ^{1 2}	May result in a large reduction of AHI events per hour. Lower scores better. MCID 5 points.
Snoring frequency: change from baseline. Follow-up: 3 months.	The mean snoring frequency change from baselines was -6.2	MD 43.07 lower (84.63 lower to 1.51 lower)	-	16 (1 RCT)	⊕⊕⊕⊕ VERY LOW ^{2 3 4}	May have little to no effect in reduction of snoring frequency but the evidence is very uncertain. Subjective snoring frequency, endpoint analysis: MD 2.2 lower (3.96 lower to 0.44 lower; one study, 51 participants). Lower scores better. MCID: not available.
Snoring intensity: endpoint score. Follow-up: 3 months.	The mean snoring intensity endpoint score was 6.2	MD 1.9 lower (3.69 lower to 0.11 lower)	-	51 (1 RCT)	⊕⊕⊕⊕ MODERATE ¹	Probably reduces subjective snoring intensity slightly. Subjective VAS. Lower scores better. MCID: not available.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AHI: apnoea hypopnoea index; **CI:** Confidence interval; **ESS:** Epworth sleepiness scale; **MD:** mean difference; **MCID:** Minimal Clinically Important Difference; **PSQI:** Pittsburgh Sleep Quality Index; **VAS:** Visual Analog Scale

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

- 1 Downgraded one point for Incomplete outcome data
- 2 Downgraded one point for imprecision
- 3 Downgraded one point for unblinded
- 4 Downgraded one point for concealment not done

Summary of findings 2. Myofunctional therapy compared to waiting list for obstructive sleep apnoea

Myofunctional therapy compared to waiting list for obstructive sleep apnoea

Patient or population: obstructive sleep apnoea

Setting: Outpatient

Intervention: Myofunctional therapy

Comparison: Waiting list

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with waiting list	Risk with Myofunctional therapy				
Daytime sleepiness (ESS): change from baseline. Follow-up: 4 months.	The mean ESS change from baseline was -1.4	MD 3 lower (5.47 lower to 0.53 lower)	-	25 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May reduce daytime sleepiness. Scores from 0 to 24. Lower scores denote lower daytime sleepiness. MCID 3 points. Endpoint analysis: MD 2.2 lower (5.94 lower to 1.54 higher).
Sleep quality (PSQI): change from baseline. Follow-up: 4 months.	The mean PSQI change from baseline was -0.2	MD 0.7 lower (2.01 lower to 0.61 higher)	-	25 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in sleep quality. Scores from 0 to 21. Lower scores denote a healthier sleep quality. MCID 3 points.

AHI: change from baseline. Follow-up: 4 months.	The mean AHI change from baseline was -4.5 events/hour	MD 6.2 events/hour lower (11.94 lower to 0.46 lower)	-	25 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	<p>Endpoint analysis: MD 1.3 lower (3.24 lower to 0.64 higher).</p> <p>May reduce AHI.</p> <p>Events per hour. Lower scores better. MCID 5 points.</p> <p>Endpoint analysis: MD 3.8 events/hour lower (10.98 lower to 3.38 higher).</p>
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***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AHI: apnoea hypopnoea index; **CI:** Confidence interval; **ESS:** Epworth sleepiness scale; **MD:** mean difference; **MCID:** Minimal Clinically Important Difference; **PSQI:** Pittsburgh Sleep Quality Index

GRADE Working Group grades of evidence

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Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

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Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded one point for unblinded

² Downgraded one point for imprecision

Summary of findings 3. Myofunctional therapy compared to CPAP for obstructive sleep apnoea

Myofunctional therapy compared to CPAP for obstructive sleep apnoea

Patient or population: obstructive sleep apnoea

Setting: Outpatient

Intervention: Myofunctional therapy

Comparison: CPAP

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N ^o of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CPAP	Risk with Myofunctional therapy				
Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months.	The mean ESS endpoint score was 7.2	MD 0.3 higher (1.65 lower to 2.25 higher)	-	54 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in daytime sleepiness.

						Scores from 0 to 24. Lower scores denote lower daytime sleepiness. MCID 3 points.
AHI: endpoint score. Follow-up: 3 months.	The mean AHI endpoint score was 4.3 events/hour	MD 9.6 events/hour higher (2.46 higher to 16.74 higher)	-	54 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May increase AHI. Events per hour. Lower scores better. MCID 5 points.
Snoring frequency: endpoint score. Follow-up: 3 months.	The mean snoring frequency endpoint score was 3.1	MD 1.8 higher (0.16 lower to 3.76 higher)	-	54 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in snoring frequency. Subjective VAS. Lower scores better. MCID: not available.
Snoring intensity: endpoint score. Follow-up: 3 months.	The mean snoring intensity endpoint score was 2.6	MD 1.7 higher (0.02 lower to 3.42 higher)	-	54 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in snoring intensity. Subjective VAS. Lower scores better. MCID: not available.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AHI: apnoea hypopnoea index; **CI:** Confidence interval; **ESS:** Epworth sleepiness scale; **MD:** mean difference; **MCID:** Minimal Clinically Important Difference; **PSQI:** Pittsburgh Sleep Quality Index; **VAS:** Visual Analog Scale

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded one point for incomplete outcome data

² Downgraded one point for imprecision

Summary of findings 4. Myofunctional therapy compared to CPAP + Myofunctional therapy for obstructive sleep apnoea

Myofunctional therapy compared to CPAP + Myofunctional therapy for obstructive sleep apnoea

Patient or population: obstructive sleep apnoea

Setting: Outpatient

Intervention: Myofunctional therapy

Comparison: CPAP + Myofunctional therapy

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CPAP + Myofunctional therapy	Risk with Myofunctional therapy				
Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months.	The mean ESS endpoint score was 7.3	MD 0.2 higher (2.56 lower to 2.96 higher)	-	49 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in daytime sleepiness. Scores from 0 to 24. Lower scores denote lower daytime sleepiness. MCID 3 points.
AHI: endpoint score. Follow-up: 3 months.	The mean AHI endpoint score was 3.4 events/hour	MD 10.5 events/hour higher (3.43 higher to 17.57 higher)	-	49 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May increase AHI. Events per hour. Lower scores better. MCID 5 points.
Snoring frequency: endpoint score. Follow-up: 3 months.	The mean snoring frequency endpoint score was 3.9	MD 1 higher (1.13 lower to 3.13 higher)	-	49 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in snoring frequency. Subjective VAS. Lower scores better. MCID: not available.
Snoring intensity: endpoint score. Follow-up: 3 months.	The mean snoring intensity endpoint score was 3.1	MD 1.2 higher (0.5 lower to 2.9 higher)	-	49 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in snoring intensity. Subjective VAS. Lower scores better. MCID: not available.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AHI: apnoea hypopnoea index; **CI:** Confidence interval; **ESS:** Epworth sleepiness scale; **MD:** mean difference; **MCID:** Minimal Clinically Important Difference; **PSQI:** Pittsburgh Sleep Quality Index

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded one point for incomplete outcome data

² Downgraded one point for imprecision

Summary of findings 5. Myofunctional therapy compared to respiratory exercises + nasal dilator strip for obstructive sleep apnoea

Myofunctional therapy compared to respiratory exercises + nasal dilator strip for obstructive sleep apnoea

Patient or population: Obstructive sleep apnoea

Setting: Outpatient

Intervention: Myofunctional therapy

Comparison: Respiratory exercises + nasal dilator strip

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N° of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with respiratory exercises + nasal dilator strip	Risk with Myofunctional therapy				
Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months.	The mean ESS endpoint score was 8.7	MD 0.2 higher (2.46 lower to 2.86 higher)	-	58 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in daytime sleepiness. Scores from 0 to 24. Lower scores denote lower daytime sleepiness. MCID 3 points.
Sleep quality (PSQI): endpoint score. Follow-up: 3 months.	The mean PSQI endpoint score was 6.2	MD 1.94 lower (3.17 lower to 0.72 lower)	-	97 (2 RCTs)	⊕⊕⊕⊕ MODERATE ¹	Probably increases sleep quality slightly. Scores from 0 to 21. Lower scores denote a healthier sleep quality. MCID 3 points.
AHI: endpoint score. Follow-up: 3 months.	The mean AHI endpoint score was 18.8 events/hour	MD 3.8 events/hour lower (9.05 lower to 1.45 higher)	-	58 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in AHI. Events per hour. Lower scores better. MCID 5 points.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AHI: apnoea hypopnoea index; **CI:** Confidence interval; **ESS:** Epworth sleepiness scale; **MD:** mean difference; **MCID:** Minimal Clinically Important Difference; **PSQI:** Pittsburgh Sleep Quality Index

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded one point for unblinded
² Downgraded one point for imprecision

Summary of findings 6. Myofunctional therapy plus nasal washing compared to Nasal washing alone for obstructive sleep apnoea

Myofunctional therapy plus nasal washing compared to nasal washing alone for obstructive sleep apnoea

Patient or population: Obstructive sleep apnoea
Setting: Outpatient
Intervention: Myofunctional therapy plus nasal washing
Comparison: Nasal washing alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Nasal washing alone	Risk with Myofunctional therapy plus nasal washing				
AHI score reduction to below 5 points. Follow-up: 2 months.	Study population		OR 12.50 (0.84 to 186.30)	13 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in AHI. Events per hour. Lower scores better. MCID 5 points.
	167 per 1000	714 per 1000 (144 to 974)				
AHI score change. Follow-up: 2 months.	The mean AHI score change was 1.32	MD 3 higher (0.26 lower to 6.26 higher)	-	13 (1 RCT)	⊕⊕⊕⊕ LOW ^{1 2}	May result in little to no difference in AHI. Events per hour. Lower scores better. MCID 5 points. Endpoint analysis: MD 3.54 lower (7.72 lower to 0.64 higher).

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AHI: apnoea hypopnoea index; **CI:** Confidence interval; **ESS:** Epworth sleepiness scale; **MD:** mean difference; **MCID:** Minimal Clinically Important Difference; **OR:** odds ratio; **PSQI:** Pittsburgh Sleep Quality Index

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

¹ Downgraded one point for unblinded

² Downgraded one point for imprecision

Summary of findings 7. Myofunctional therapy compared to Standard medical treatment for obstructive sleep apnoea

Myofunctional therapy compared to standard medical treatment for obstructive sleep apnoea

Patient or population: obstructive sleep apnoea

Setting: Outpatient

Intervention: Myofunctional therapy

Comparison: Standard medical treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Standard medical treatment	Risk with Myofunctional therapy				
Daytime sleepiness (ESS): change from baseline. Follow-up: 3 months.	The mean daytime sleepiness (ESS): change from baseline. Follow-up: 3 months was 0.2	MD 6.4 lower (9.82 lower to 2.98 lower)	-	26 (1 RCT)	⊕⊕○○ LOW ^{1 2}	May reduce daytime sleepiness. Scores from 0 to 24. Lower scores denote lower daytime sleepiness. MCID 3 points.
Sleep quality (PSQI): change from baseline. Follow-up: 3 months.	The mean sleep quality (Pittsburgh Sleep Quality Index): change from baseline. Follow-up: 3 months was -1.5	MD 3.1 lower (5.12 lower to 1.08 lower)	-	26 (1 RCT)	⊕⊕○○ LOW ^{1 2}	May increase sleep quality. Scores from 0 to 21. Lower scores denote a healthier sleep quality. MCID 3 points.
Snoring frequency: change from baseline. Follow-up: 3 months.	The mean snoring frequency: change from baseline. Follow-up: 3 months was 0.1	MD 2.4 lower (2.8 lower to 2 lower)	-	26 (1 RCT)	⊕⊕○○ LOW ^{1 2}	May reduce snoring frequency slightly. Lower scores better. MCID: not available.
Snoring intensity: change from baseline. Follow-up: 3 months.	The mean snoring intensity: change from baseline was 0. Follow-up: 3 months	MD and CI not estimable	-	26 (1 RCT)	⊕⊕○○ LOW ^{1 2}	May reduce snoring intensity. Reduction of 3.2 points in the myofunctional therapy group and no change in any patient in the standard medical treatment group. Lower scores better. MCID: not available.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

AHI: apnoea hypopnoea index; **CI:** Confidence interval; **ESS:** Epworth sleepiness scale; **MD:** mean difference; **MCID:** Minimal Clinically Important Difference; **PSQI:** Pittsburgh Sleep Quality Index

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

- ¹ Downgraded one point for unblinded
- ² Downgraded one point for imprecision

BACKGROUND

Description of the condition

Obstructive sleep apnoea (OSA) is a syndrome characterised by episodes of apnoea (complete cessation of ventilation) or hypopnoea (insufficient breathing) during sleep. Classical symptoms of the disease — such as snoring, unsatisfactory rest and daytime sleepiness — are experienced mainly by men; women report more unspecific symptoms such as low energy or fatigue, tiredness, initial insomnia and morning headaches (Evans 2014; Fietze 2018; Nigro 2018; Theorell-Haglöw 2018). OSA is associated with an increased risk of occupational injuries (Hirsch Allen 2016), metabolic diseases (Patinkin 2017), cardiovascular diseases (Hou 2018; Sarkar 2018), mortality (Butler 2019; Marshall 2008), and being involved in traffic accidents (Gottlieb 2018; Tregear 2009).

Obesity is probably the single most important risk factor for OSA in adults (Carneiro 2018; Hnin 2018) and children (Andersen 2019). It is estimated that over 70% of people with OSA are obese, and the prevalence of OSA among obese people may be as high as 45% (Romero-Corral 2010). Obesity is a growing problem all over the world and the incidence and prevalence of OSA is predicted to increase in parallel with it (Blüher 2019; Garvey 2015). Socioeconomic status could be a risk factor for OSA and, coupled with obesity and disparities in health care, could influence the association between OSA and ethnic minorities (Guglielmi 2019). Other factors that seem to play a relevant role in the genesis of OSA include an anatomically narrow or highly collapsible upper airway or problems related with muscle responsiveness, loop gain and pharyngeal dilator muscle activity (Carberry 2016; Eckert 2013).

Diagnosis of OSA includes polysomnography - a sleep study that includes overnight continuous monitoring of the patient, usually done in hospital - or home sleep apnoea testing in people presenting with a combination of symptoms, including excessive daytime sleepiness, loud snoring, witnessed apnoea episodes, or non-dipping nocturnal hypertension (Crinion 2019; Kapur 2017; Randerath 2018).

Published reviews have found wide variation in the reported prevalence of OSA. This is caused in part by substantial methodological heterogeneity in population prevalence studies, including differences in the diagnostic threshold used to define the cut-off level for the Apnea-Hypopnea Index (AHI) or the inclusion (or not) of excessive daytime sleepiness as a necessary diagnostic criterion (Lozo 2016; Senaratna 2017). In adults, the prevalence of OSA with excessive daytime sleepiness could range from between 3% and 18% of men, and 1% and 17% of women (Franklin 2015; Jonas 2017; Mirrakhimov 2013; Sunwoo 2018; van der Spuy 2018). However, OSA in women is probably under-diagnosed, given the widespread belief that OSA is rare in women and that the symptomatology in women differs from classical symptoms of snoring and daytime somnolence (Garvey 2015). In children, prevalence could range from 1% to 6% (Bixler 2009; Katidis 2017; Li 2010; Tsukada 2018).

Description of the intervention

Myofunctional therapy for OSA is usually a multi-component intervention including several combinations of oropharyngeal exercises (Camacho 2017). Current proposals vary regarding the time frame of the treatment; the type and intensity of exercises to

be included; and the delivery of the interventions (e.g. whether they should be delivered by a professional, such as a speech pathologist, or self-administered by the patient using an app).

Therapy can include isotonic and isometric exercises involving several muscles and areas of the mouth, pharynx and upper respiratory tract, working on functions such as speaking, breathing, blowing, sucking, chewing or swallowing (de Felicio 2018; Guimaraes 2009).

How the intervention might work

Myofunctional therapy aims to improve the functioning of upper airway dilator muscles that are essential to maintain pharyngeal patency (Folha 2015; Guimaraes 2009; Osman 2018). Muscular endurance exercises aim to improve the tone, tension and mobility of oropharyngeal muscles and soft tissues, in order to reduce airway closures during sleep (Diaféria 2017b). The therapy also targets parapharyngeal fat pads, such as tongue fat, which are increased in people with OSA (Kim 2014).

A similar approach to that described above is purported to be useful for children with OSA (Guilleminault 2013).

Why it is important to do this review

Continuous positive airway pressure (CPAP) is considered the first treatment option for most people with OSA. However, adherence to treatment is often suboptimal (Bakker 2019; Mehrtash 2019; Rotenberg 2016). Poor compliance with CPAP is probably due to the side effects of the treatment, which include discomfort, nasal congestion, abdominal bloating, mask leaks, claustrophobia and inconvenience of regular usage (Wozniak 2014). A Cochrane Review published in 2014 evaluated the efficacy of different interventions aimed at improving adherence in CPAP-naïve people (people who have never undergone CPAP treatment) with severe sleep apnoea. It estimated that basal adherence to CPAP (four or more hours per night) could range from 28% to 59% in randomised controlled trials (RCTs), and found that some interventions could result in additional increases in adherence rates ranging from 14% to 26% (Wozniak 2014). However, significant numbers of patients would still remain non-adherent.

Although there are other possible treatment options for some patients with OSA, including oral appliances or surgery (Carvalho 2016; Jen 2018; Werz 2017), myofunctional therapy is noninvasive, inexpensive, and has no major risks. It could be a safe and acceptable option for many patients with OSA, and economically accessible for people and countries with lower incomes.

There are some published reviews on myofunctional therapy for OSA or snoring but they include in their analysis the results of observational studies which are not as reliable as randomised clinical trials for assessing the efficacy or safety of the compared interventions. Also, those reviews do not include evidence from new studies published recently (Camacho 2017; de Felicio 2018; Kayamori 2017).

It is necessary to have a reliable summary of available evidence from RCTs assessing the effects of myofunctional therapy on people with OSA to guide decision-making for patients, professionals and funding agencies.

OBJECTIVES

To evaluate the benefits and harms of myofunctional therapy (oropharyngeal exercises) for the treatment of obstructive sleep apnoea.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs). We included studies reported in full text, those published as an abstract only and unpublished data.

Types of participants

We included adults and children (below 18 years old) with a diagnosis of obstructive sleep apnoea, defined as five or more episodes of apnoea or hypopnoea per hour of sleep by polysomnography (PSG) or portable monitoring (Type I to Type III sleep monitors).

We excluded studies where the included participants experience other types of sleep-disordered breathing, such as central sleep apnoea, or where obstructive sleep apnoea has developed after a stroke.

Types of interventions

We included studies comparing myofunctional therapy (oropharyngeal exercises) with one of the following control groups.

- Sham therapy or no intervention
- Continuous positive airway pressure (CPAP)
- Any other active intervention
- Combination therapy: myofunctional therapy added to CPAP versus CPAP alone or CPAP plus sham myofunctional therapy
- Waiting list

We did not include studies in which myofunctional therapy is part of a multi-component intervention and there is no possibility to assess the separate effect of myofunctional therapy.

We included the following co-interventions, provided they are not part of the randomised treatment: exercise for weight loss and diet and sleep recommendations.

Comparisons.

- Myofunctional therapy versus sham therapy
- Myofunctional therapy versus no intervention or waiting list
- Myofunctional therapy versus CPAP
- Myofunctional therapy plus CPAP versus CPAP alone.
- Myofunctional therapy compared to respiratory exercises plus nasal dilator strip for obstructive sleep apnoea
- Myofunctional therapy plus nasal washing compared to nasal washing alone for obstructive sleep apnoea
- Myofunctional therapy compared to standard medical treatment for obstructive sleep apnoea

Types of outcome measures

Primary outcomes

- Daytime sleepiness, measured by a validated scale or questionnaire (e.g. the Epworth Sleepiness Scale (ESS); [Johns 1991](#))
- Morbidity (including accidents and cardiovascular diseases) and mortality

Secondary outcomes

- Quality of life, measured by a validated scale or questionnaire (e.g. the SF-36; [Ware 1993](#))
- Sleep quality, measured by a validated scale or questionnaire (e.g. the Pittsburgh Sleep Quality Index (PSQI); [Buysse 1989](#))
- Adverse events and side effects
- Apnoea-Hypopnoea Index (AHI), defined as the number of episodes of apnoea or hypopnoea per hour of sleep, measured objectively by polysomnography
- Snoring

If data permitted, we pooled data for the short, medium and long term, defined as follows.

- Short term: up to three months
- Medium term: from three months to two years
- Long term: more than two years

Search methods for identification of studies

Electronic searches

We identified studies from searches of the following databases and trial registries.

- Cochrane Airways Trials Register ([Cochrane Airways 2019](#)), via the Cochrane Register of Studies (all years to 1 May 2020)
- Cochrane Central Register of Controlled Trials (CENTRAL), via the Cochrane Register of Studies (all years to 1 May 2020)
- MEDLINE Ovid SP (1946 to 1 May 2020)
- Embase Ovid SP (1974 to 1 May 2020)
- US National Institutes of Health Ongoing Trials Register ([clinicaltrials.gov](#))
- World Health Organization International Clinical Trials Registry Platform ([apps.who.int/trialsearch/](#))

The database search strategies are listed in [Appendix 1](#). The Cochrane Airways Information Specialist developed the search strategy in collaboration with the review authors. Another Cochrane Information Specialist peer-reviewed this search strategy by using the Peer Review of Electronic Search Strategies (PRESS) checklist ([McGowan 2016](#)). The Airways Information Specialist designed the initial strategy in MEDLINE and adapted it for use in the other databases. We searched all databases and trial registries from their inception up to 1 May 2020, with no restriction on language or type of publication. We searched for conference abstracts and grey literature through the Cochrane Airways Trials Register and the CENTRAL database.

Searching other resources

We checked the reference lists of all primary studies and review articles for additional references. We searched relevant manufacturers' websites for study information.

On 22 June 2020, we searched on [PubMed](#) for errata or retractions from included studies published in full text.

Data collection and analysis

Selection of studies

We used Cochrane's Screen4Me workflow to help assess the search results. Screen4Me comprises three components: known assessments – a service that matches records in the search results to records that have already been screened in Cochrane Crowd and been labelled as 'RCT' or as 'Not an RCT'; the RCT classifier – a machine learning model that distinguishes RCTs from non-RCTs; and Cochrane Crowd (<http://crowd.cochrane.org>) – Cochrane's

citizen science platform where the Crowd helps to identify and describe health evidence. More detailed information about the Screen4Me components can be found in the following publications: [Marshall 2018](#), [McDonald 2017](#), [Noel-Storr 2018](#), [Thomas 2017](#).

Following this initial assessment, three review authors (IM-A, JV and MR-E) independently screened the titles and abstracts of the search results and coded them as 'retrieve' (eligible or potentially eligible or unclear) or 'do not retrieve'. We retrieved the full-text reports of all potentially eligible studies, and three review authors (IM-A, JV and MR-E) independently screened them for inclusion, recording the reasons for exclusion of ineligible studies. We resolved any disagreement through discussion or, if required, consulted another review author (J-RR). We identified and excluded duplicates and collated multiple reports of the same study so that each study, rather than each report, is the unit of interest in the review. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram [Figure 1](#) and [Characteristics of excluded studies](#) table ([Moher 2009](#)).

Figure 1. Study flow diagram.

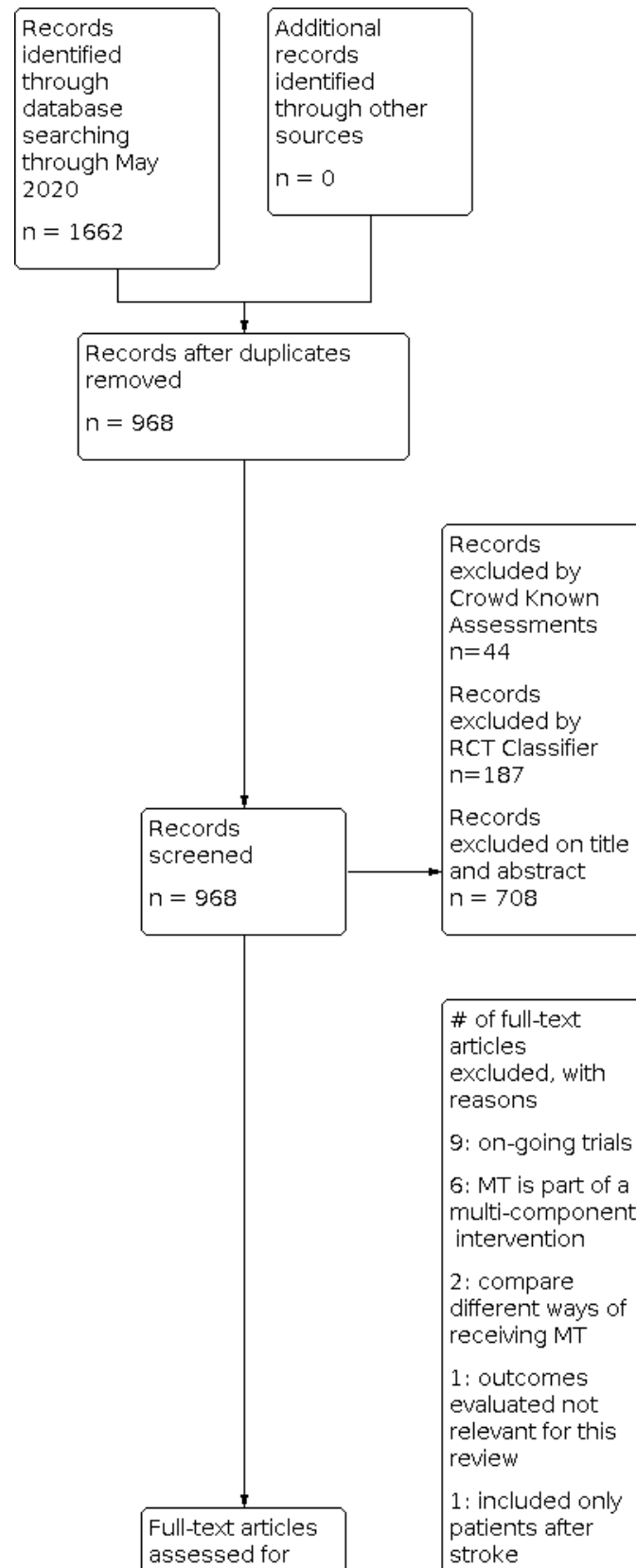
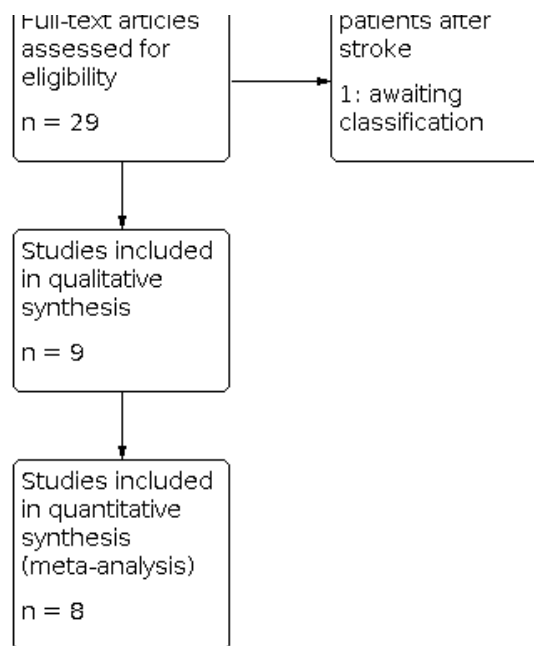


Figure 1. (Continued)



Data extraction and management

We used a data collection form for study characteristics and outcome data and which had been piloted on one study in the review. Two review authors (IM-A and MR-E) independently extracted the following characteristics from the included studies.

- Methods: study design, total duration of study, details of any 'run-in' period, number of study centres and their locations, study setting, withdrawals and date of study.
- Participants: number (N), mean age, age range, gender, severity of condition, previous history of CPAP use, diagnostic criteria, baseline lung function, smoking history, inclusion criteria and exclusion criteria.
- Interventions: intervention, comparison, concomitant interventions and excluded co-interventions.
- Outcomes: primary and secondary outcomes specified and collected, and time points reported.
- Notes: funding for studies and notable conflicts of interest of trial authors.

Two review authors (MR-E and IM-A) independently extracted outcome data from included studies. We noted in the [Characteristics of included studies](#) tables if outcome data were not reported in a usable way. We resolved disagreements by consensus or by involving a third review author (J-RR or JV). One review author (MR-E) transferred data into the Review Manager file ([RevMan 2014](#)). We double-checked that data were entered correctly by comparing the data presented in this systematic review with the study reports. Another review author (J-RR) spot-checked study characteristics for accuracy against the study report.

Assessment of risk of bias in included studies

Two review authors (IM-A and MR-E) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)).

We resolved any disagreements by discussion or by involving another review author (JV or J-RR). We assessed the risk of bias according to the following domains.

- Random sequence generation
- Allocation concealment
- Blinding of participants and personnel
- Blinding of outcome assessment
- Incomplete outcome data
- Selective outcome reporting
- Other bias

We judged each study as being at high, low or unclear risk of bias for each domain. We provided a quote from the study report, together with a justification for our judgement, in the 'Risk of bias' table. We summarized the 'Risk of bias' judgements across different studies for each of the domains listed. We considered blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different than for a patient-reported pain scale). Where information on risk of bias relates to unpublished data or correspondence with a trialist, we noted this in the 'Risk of bias' table.

When considering treatment effects, we took into account the risk of bias for the studies that contribute to that outcome.

Assessment of bias in conducting the systematic review

We conducted the review according to the published protocol and we have justified any deviations from it in the 'Differences between protocol and review' section of this review.

Measures of treatment effect

We analysed dichotomous data as odds ratios (ORs) and continuous data as the mean difference (MD) or standardized mean difference (SMD). If data from rating scales were combined in a

meta-analysis, we ensured they were entered with a consistent direction of effect (e.g. lower scores always indicate improvement).

We undertook meta-analyses only where they were meaningful; that is, if the treatments, participants and the underlying clinical question were similar enough for pooling to make sense. We described skewed data narratively (for example, as medians and interquartile ranges for each group).

Where multiple trial arms were reported in a single study, we included only the relevant arms. If two comparisons (e.g. drug A versus placebo and drug B versus placebo) were combined in the same meta-analysis, we either combined the active arms or halved the control group to avoid double-counting.

If adjusted analyses were available (ANOVA or ANCOVA), we used these as a preference in our meta-analyses. If both change-from-baseline and endpoint scores were available for continuous data, we used change-from-baseline unless there was low correlation between measurements in individuals. If a study reported outcomes at multiple time points, we used the last one.

We used intention-to-treat (ITT) or 'full analysis set' analyses where they were reported (i.e. those where data had been imputed for participants who were randomly assigned but did not complete the study), instead of completer or per-protocol analyses.

Unit of analysis issues

For dichotomous outcomes, we used participants, rather than events, as the unit of analysis (i.e. number of children admitted to hospital, rather than number of admissions per child). However, if rate ratios were reported in a study, we analysed them on this basis. We only meta-analysed data from cluster-RCTs if the available data had been adjusted, or could be adjusted, to account for the clustering.

Dealing with missing data

We contacted investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study was identified as an abstract only). Where this was not possible, and we considered the missing data to introduce serious bias, we took this into consideration in the GRADE rating for affected outcomes.

Assessment of heterogeneity

We used the I^2 statistic to measure heterogeneity among the studies in each analysis. If we identified substantial heterogeneity, we reported it and explored the possible causes using prespecified subgroup analyses.

Assessment of reporting biases

If we were able to pool more than 10 studies, we created and examined a funnel plot to explore possible small-study and publication biases.

Data synthesis

We used a random-effects model and performed a sensitivity analysis with a fixed-effect model.

Subgroup analysis and investigation of heterogeneity

A lack of data meant it was not possible to carry out planned subgroup analyses for the following factors.

- Gender (women versus men)
- Age (18 years and younger versus older than 18 years)
- Severity of OSA (mild versus moderate to severe)

We planned to use the following outcomes in subgroup analyses.

- Daytime sleepiness
- Morbidity (including accidents and cardiovascular diseases) and mortality
- Serious adverse events

We used the formal test for subgroup interactions in Review Manager 5 (RevMan 2014).

Sensitivity analysis

We compared the results from a fixed-effect model with those using a random-effects model without changes in the conclusions.

We undertook a further sensitivity analysis comparing choice of summary statistic (odds ratio (OR) or risk ratio (RR)) and found no changes in the conclusions.

The small number of studies for each comparison meant it was not possible to carry out planned sensitivity analyses for the primary outcomes, in which we would have removed: studies with a high risk of bias for key sources of potential bias (e.g. randomisation, allocation concealment, blinding); studies with missing data; or both.

Summary of findings and assessment of the certainty of the evidence

We created a 'Summary of findings' table using the following outcomes: daytime sleepiness, morbidity (including accidents and cardiovascular diseases) and mortality, quality of life, sleep quality, adverse events, AHI and snoring. We reported outcomes separately for short, medium and long term when data are available. We used the five GRADE considerations (risk of bias, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of evidence from the studies that contributed data for the prespecified outcomes. We used the methods and recommendations described in Chapters 14 and 15 (Schünemann 2020 a; Schünemann 2020 b) of the *Cochrane Handbook for Systematic Reviews of Interventions*, using GRADEpro GDT software (GRADEpro GDT). We justified all decisions to downgrade the quality of studies using footnotes and we made comments to aid readers' understanding of the review where necessary.

RESULTS

Description of studies

Results of the search

See Figure 1 for the study flow diagram.

Our searches (conducted first on 9 October 2019 and updated 1 May 2020) found 1662 references. After excluding duplicate publications

and irrelevant reports, we identified nine studies for inclusion in the review. We also identified nine ongoing studies (see [Characteristics of ongoing studies](#)).

Included studies

We included nine randomised, parallel group studies. The studies randomised a total of 425 participants, 69 of them women and 13 children. Results were analysed in 347 participants.

Three studies compared myofunctional therapy with sham therapy (98 participants) ([Diaferia 2017](#); [Goswami 2019](#); [Guimaraes 2009](#)); one study compared myofunctional therapy with CPAP (54 participants) ([Diaferia 2017](#)); one study compared myofunctional therapy with CPAP plus myofunctional therapy (49 participants) ([Diaferia 2017](#)); one study compared myofunctional therapy with waiting list (25 participants) ([Puhan 2006](#)); two studies compared myofunctional therapy with respiratory exercises plus nasal dilator strip (97 participants) ([Ieto 2015](#); [Kayamori 2015](#)); one study compared myofunctional therapy with standard medical therapy (26 participants) ([Bellur 2012](#)); one study compared myofunctional therapy with standard medical therapy and with inspiratory muscle training (41 participants) ([Erturk 2013](#)); one study compared nasal washing alone with nasal washing and myofunctional therapy (13 children) ([Villa 2015](#)).

Four trials were conducted in Brazil, two in Turkey, one in the USA, one in Switzerland and one in Italy.

Regarding funding, three studies did not report any funding ([Bellur 2012](#); [Erturk 2013](#); [Villa 2015](#)); five studies reported public funding ([Diaferia 2017](#); [Guimaraes 2009](#); [Goswami 2019](#); [Ieto 2015](#); [Kayamori 2015](#)); and one study reported funding from a non-profit organisation ([Puhan 2006](#)).

An overview of the characteristics of the included studies is given in [Table 1](#).

Excluded studies

We excluded ten studies for the following reasons: six studies evaluated multi-component interventions, which precluded isolating the effect of oropharyngeal exercises ([Atilgan 2019](#); [Bague 2014](#); [Kaur 2019](#); [Kittivoravithkul 2018](#); [Neumannova 2018](#); [Torres-Castro 2016](#)); one study compared different ways of receiving myofunctional therapy ([O'Connor-Reina 2018](#)); one study included only participants with post-stroke OSA ([Ye 2018](#)); one study compared myofunctional therapy support program based on self-efficacy theory compared to no support during myofunctional therapy ([Kim 2019](#)); and one did not evaluate any of this review's outcomes of interest ([Villa 2017](#)).

See [Excluded studies](#).

Risk of bias in included studies

See [Figure 2](#) for risk of bias summary.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias): All outcomes	Blinding of outcome assessment (detection bias): All outcomes	Incomplete outcome data (attrition bias): All outcomes	Selective reporting (reporting bias)	Other bias
Bellur 2012	+	+	-	-	+	+	+
Diaferia 2017	?	?	+	+	-	+	+
Erturk 2013	+	+	-	-	+	+	+
Goswami 2019	+	-	-	-	+	+	+
Guimaraes 2009	+	+	+	+	-	+	+
Ieto 2015	+	+	-	-	+	+	+
Kayamori 2015	+	+	-	-	+	+	+
Puhan 2006	+	+	-	-	+	+	+
Villa 2015	?	?	-	+	+	+	+

Allocation

Of the nine included studies, in two studies, the sequence generation was unclear ([Diaferia 2017](#); [Villa 2015](#)); in one study, allocation concealment was not done ([Goswami 2019](#)) and for three, it was unclear ([Diaferia 2017](#); [Ieto 2015](#); [Villa 2015](#)).

Blinding

Participants were blinded in only two studies ([Diaferia 2017](#); [Guimaraes 2009](#)), and unblinded in the rest.

Evaluators were blinded only in three studies ([Diaferia 2017](#); [Guimaraes 2009](#); [Villa 2015](#)), and unblinded in the rest.

Incomplete outcome data

We considered [Diaferia 2017](#) and [Guimaraes 2009](#) at high risk of bias in this domain.

Selective reporting

None of the studies presented reporting bias risk.

Other potential sources of bias

We did not find any other potential sources of bias in the included studies.

Effects of interventions

See: [Summary of findings 1](#) Myofunctional therapy compared to sham therapy for obstructive sleep apnoea; [Summary of findings 2](#) Myofunctional therapy compared to waiting list for obstructive sleep apnoea; [Summary of findings 3](#) Myofunctional therapy compared to CPAP for obstructive sleep apnoea; [Summary of findings 4](#) Myofunctional therapy compared to CPAP + Myofunctional therapy for obstructive sleep apnoea; [Summary of findings 5](#) Myofunctional therapy compared to respiratory exercises + nasal dilator strip for obstructive sleep apnoea; [Summary of findings 6](#) Myofunctional therapy plus nasal washing compared to Nasal washing alone for obstructive sleep apnoea; [Summary of findings 7](#) Myofunctional therapy compared to Standard medical treatment for obstructive sleep apnoea

Myofunctional therapy versus sham therapy

Three studies analysed this comparison ([Diaferia 2017](#); [Goswami 2019](#); [Guimaraes 2009](#)), for a total of 98 participants: 82 men and 16 women. Average participant age in the studies ranged between 43 and 51 years.

Primary outcomes

Daytime sleepiness

Two studies ([Diaferia 2017](#); [Guimaraes 2009](#)) provided data on this outcome, measured by endpoint scores of the Epworth Sleepiness Scale (ESS). Pooled results showed that, compared to sham therapy, myofunctional therapy probably reduces daytime sleepiness (Mean difference (MD) -4.52 points, 95% CI -6.67 to -2.36; two studies, 82 participants; moderate-certainty evidence; [Analysis 1.1](#); [Summary of findings 1](#)).

Morbidity (including accidents and cardiovascular diseases) and mortality

None of the three studies analysed this outcome.

Secondary outcomes

Quality of life

None of the three studies analysed this outcome.

Sleep quality

Only one study evaluated the effect of the interventions on sleep quality ([Guimaraes 2009](#)), measured by endpoint scores of the Pittsburgh Sleep Quality Index (PSQI). Results showed that, compared to sham therapy, myofunctional therapy may increase sleep quality (MD -3.90 points, 95% CI -6.31 to -1.49; one study, 31 participants; low-certainty evidence; [Analysis 1.2](#); [Summary of findings 1](#))

Adverse events and side effects

None of the studies reported on adverse events or side effects.

Apnoea-Hypopnoea Index (AHI)

Two studies ([Diaferia 2017](#); [Guimaraes 2009](#)) provided data on this outcome, measured by endpoint scores. Pooled results showed that, compared to sham therapy, myofunctional therapy may result in a large reduction of AHI events per hour (MD -13.20 points, 95% CI -18.48 to -7.93; two studies, 82 participants; low-certainty evidence; [Analysis 1.3](#); [Summary of findings 1](#)).

Snoring frequency

Two studies provided data on this outcome but used different instruments to measure snoring frequency ([Diaferia 2017](#); [Goswami 2019](#)).

[Goswami 2019](#) measured snoring frequency in an objective way by recording sounds, and defined snoring rate as number of snores higher than 60 dBA per hour of sleep. They assessed changes from baseline and found that, compared to sham therapy, myofunctional therapy may have little to no effect in reduction of snoring frequency but the evidence is very uncertain (MD -43.07 points, 95% CI -84.63 to -1.51; one study, 16 participants; very low-certainty evidence; [Analysis 1.4](#); [Summary of findings 1](#)).

[Diaferia 2017](#) assessed snoring frequency in a subjective way, using an analogue scale, for which they did not explain the range of possible values. They found that, compared to sham therapy, myofunctional therapy may result in a reduction of snoring frequency (MD -2.20 points, 95% CI -3.96 to -0.44; one study, 51 participants; low-certainty evidence; [Analysis 1.5](#)).

Snoring intensity

[Diaferia 2017](#) assessed endpoint scores in a subjective way, using an analogue scale, and found that, compared to sham therapy, myofunctional therapy probably reduces subjective snoring intensity slightly (MD -1.90 points, 95% CI -3.69 to -0.11; one study, 51 participants; moderate-certainty evidence; [Analysis 1.6](#); [Summary of findings 1](#)).

Myofunctional therapy versus waiting list

Only one study analysed this comparison ([Puhan 2006](#)). It included 25 participants in the analysis, of whom 21 were men, with an average age of 49 years.

Primary outcomes

Daytime sleepiness

The study assessed Epworth Sleepiness Scale (ESS) change from baseline and found that, compared to waiting list, myofunctional therapy may reduce daytime sleepiness (MD -3.00 points, 95% CI -5.47 to -0.53; one study, 25 participants; low-certainty evidence; [Analysis 2.1](#); [Summary of findings 2](#)).

The study assessed Epworth Sleepiness Scale (ESS) endpoint scores and found that, compared to waiting list, myofunctional therapy may result in little to no difference (MD -2.20 points, 95% CI -5.94 to 1.54; one study, 25 participants; low-certainty evidence; [Analysis 2.2](#)).

Morbidity (including accidents and cardiovascular diseases) and mortality

The study did not analyse this outcome.

Secondary outcomes

Quality of life

The study did not analyse this outcome.

Sleep quality

For Pittsburgh Sleep Quality Index (PSQI) change from baseline, the study found that, compared to waiting list, myofunctional therapy may result in little to no difference (MD -0.70 points, 95% CI -2.01 to 0.61; one study, 25 participants; low-certainty evidence; [Analysis 2.3](#); [Summary of findings 2](#)).

For Pittsburgh Sleep Quality Index (PSQI) endpoint scores, the study found that, compared to waiting list, myofunctional therapy may result in little to no difference (MD -1.30 points, 95% CI -3.24 to 0.64; one study, 25 participants; low-certainty evidence; [Analysis 2.4](#)).

Adverse events and side effects

The study did not report on adverse events or side effects.

Apnoea-Hypopnoea Index (AHI)

The study assessed Apnoea-Hypopnoea Index change from baseline and found that, compared to waiting list, myofunctional therapy may reduce AHI (MD -6.20 points, 95% CI -11.94 to -0.46; one study, 25 participants; low-certainty evidence; [Analysis 2.5](#); [Summary of findings 2](#)).

Regarding Apnoea-Hypopnoea Index endpoint scores, compared to waiting list, myofunctional therapy may result in little to no difference (MD -3.80 points, 95% CI -10.98 to 3.38; one study, 25 participants; low-certainty evidence; [Analysis 2.6](#)).

Snoring frequency

The study did not analyse this outcome.

Snoring intensity

The study did not analyse this outcome.

Myofunctional therapy versus CPAP

Only one study analysed this comparison ([Diaferia 2017](#)). It included 54 participants in the analysis, all men, with an average age of 48 years.

Primary outcomes

Daytime sleepiness

[Diaferia 2017](#) assessed Epworth Sleepiness Scale endpoint scores and found that, compared to CPAP, myofunctional therapy may result in little to no difference in daytime sleepiness (MD 0.30 points, 95% CI -1.65 to 2.25; one study, 54 participants; low-certainty evidence; [Analysis 3.1](#); [Summary of findings 3](#)).

Morbidity (including accidents and cardiovascular diseases) and mortality

The study did not analyse this outcome.

Secondary outcomes

Quality of life

The study did not analyse this outcome.

Sleep quality

The study did not analyse this outcome.

Adverse events and side effects

The study did not report on adverse events or side effects.

Apnoea-Hypopnoea Index (AHI)

Regarding *endpoint scores*, the study results showed that, compared to CPAP, myofunctional therapy may increase AHI (MD 9.60 points, 95% CI 2.46 to 16.74; one study, 54 participants; low-certainty evidence; [Analysis 3.2](#); [Summary of findings 3](#)).

Snoring frequency

Regarding *endpoint scores* of snoring frequency, the study results showed that, compared to CPAP, myofunctional therapy may result in little to no difference (MD 1.80 points, 95% CI -0.16 to 3.76; one study, 54 participants; low-certainty evidence; [Analysis 3.3](#); [Summary of findings 3](#)).

Snoring intensity

Regarding *endpoint scores* of snoring intensity, the study results showed that, compared to CPAP, myofunctional therapy may result in little to no difference (MD 1.70 points, 95% CI -0.02 to 3.42; one study, 54 participants; low-certainty evidence; [Analysis 3.4](#); [Summary of findings 3](#)).

Myofunctional therapy versus CPAP and myofunctional therapy

Only one study analysed this comparison ([Diaferia 2017](#)). It included 49 participants in the analysis, all men, with an average age of 48 years.

Primary outcomes

Daytime sleepiness

[Diaferia 2017](#) assessed Epworth Sleepiness Scale *endpoint scores* and found that, compared to CPAP combined with myofunctional therapy, myofunctional therapy alone may result in little to no

difference in daytime sleepiness (MD 0.20 points, 95% CI -2.56 to 2.96; one study, 49 participants; low-certainty evidence; [Analysis 4.1](#); [Summary of findings 4](#)).

Morbidity (including accidents and cardiovascular diseases) and mortality

The study did not analyse this outcome.

Secondary outcomes

Quality of life

The study did not analyse this outcome.

Sleep quality

The study did not analyse this outcome.

Adverse events and side effects

The study did not report on adverse events or side effects.

Apnoea-Hypopnoea Index (AHI)

Study results found that, compared to CPAP combined with myofunctional therapy, myofunctional therapy alone may increase AHI (MD 10.50 points, 95% CI 3.43 to 17.57; one study, 49 participants; low-certainty evidence; [Analysis 4.2](#); [Summary of findings 4](#)).

Snoring frequency

Regarding *endpoint scores* of snoring frequency, the study found that, compared to CPAP combined with myofunctional therapy, myofunctional therapy alone may result in little to no difference in snoring frequency (MD 1.00 points, 95% CI -1.13 to 3.13; one study, 49 participants; low-certainty evidence; [Analysis 4.3](#); [Summary of findings 4](#)).

Snoring intensity

Regarding *endpoint scores* of snoring intensity, the study found that, compared to CPAP combined with myofunctional therapy, myofunctional therapy alone may result in little to no difference in snoring intensity (MD 1.20 points, 95% CI -0.50 to 2.90; one study, 49 participants; low-certainty evidence; [Analysis 4.4](#); [Summary of findings 4](#)).

Myofunctional therapy versus respiratory exercises plus nasal dilator strip

Two studies analysed this comparison ([Ieto 2015](#); [Kayamori 2015](#)), for a total of 97 participants: 56 men and 41 women. Average participant age in the studies ranged between 45 and 48 years.

Primary outcomes

Daytime sleepiness

Only one study ([Kayamori 2015](#)) evaluated endpoint scores of the Epworth Sleepiness Scale (ESS) and found that, compared to respiratory exercises combined with nasal dilator strip, myofunctional therapy may result in little to no difference in daytime sleepiness (MD 0.20 points, 95% CI -2.46 to 2.86; one study, 58 participants; low-certainty evidence; [Analysis 5.1](#); [Summary of findings 5](#)).

Morbidity (including accidents and cardiovascular diseases) and mortality

Neither of the studies provided data for this outcome.

Secondary outcomes

Quality of life

Neither of the studies provided data for this outcome.

Sleep quality

Both studies provided data on this outcome ([Ieto 2015](#); [Kayamori 2015](#)), measured by endpoint scores of the Pittsburgh Sleep Quality Index (PSQI). Pooled together, their results showed that, compared to respiratory exercises combined with nasal dilator strip, myofunctional therapy probably increases sleep quality slightly (MD -1.94 points, 95% CI -3.17 to -0.72; two studies, 97 participants; moderate-certainty evidence; [Analysis 5.2](#); [Summary of findings 5](#)).

Adverse events and side effects

Neither of the studies reported on this outcome.

Apnoea-Hypopnoea Index (AHI)

Only [Kayamori 2015](#) measured endpoint scores of AHI and found that, compared to respiratory exercises combined with nasal dilator strip, myofunctional therapy may result in little to no difference in AHI (MD -3.80 points, 95% CI -9.05 to 1.45; one study, 58 participants; low-certainty evidence; [Analysis 5.3](#); [Summary of findings 5](#)).

Snoring frequency

Neither of the studies provided data for this outcome.

Snoring intensity

Neither of the studies provided data for this outcome.

Myofunctional therapy plus nasal washing versus nasal washing alone

Only one study analysed this comparison ([Villa 2015](#)). The study randomised 30 children with residual apnoea after adenotonsillectomy and analysed results for 27 children. Participants' mean age was 5 years; 24 were boys and three were girls. Fourteen children had AHI values below five and the other 13 children had AHI values between 5 and 12.

Primary outcomes

Daytime sleepiness

The study did not analyse this outcome.

Morbidity (including accidents and cardiovascular diseases) and mortality

The study did not analyse this outcome.

Secondary outcomes

Quality of life

The study did not analyse this outcome.

Sleep quality

The study did not analyse this outcome.

Adverse events and side effects

The study did not report on adverse events or side effects.

Apnoea-Hypopnoea Index (AHI)

The authors did not present separate statistical analysis for the 13 children with AHI above 4 at the baseline. We have done our own calculations based on visual information provided in a graph.

Regarding the participants that reached AHI levels below 5 after treatments, the study found that compared to nasal washing alone, myofunctional therapy plus nasal washing may result in little to no difference in AHI (OR 12.50, 95% CI 0.84 to 186.30; one study, 13 participants; low-certainty evidence; [Analysis 6.1](#); [Summary of findings 6](#)).

Regarding AHI score change before and after treatments, the study found that, compared to nasal washing alone, myofunctional therapy plus nasal washing may result in little to no difference in AHI (MD 3.00, 95% CI -0.26 to 6.26; one study, 13 participants; low-certainty evidence; [Analysis 6.2](#); [Summary of findings 6](#)).

Regarding AHI score after treatments, the study found that, compared to nasal washing alone, myofunctional therapy plus nasal washing may result in little to no difference in AHI (MD -3.54, 95% CI -7.72 to 0.64; one study, 13 participants; low-certainty evidence; [Analysis 6.3](#); [Summary of findings 6](#)).

Snoring frequency

The study did not analyse this outcome.

Snoring intensity

The study did not analyse this outcome.

Myofunctional therapy versus standard medical treatment

Only one study analysed this comparison ([Bellur 2012](#)). It included 26 participants in the analysis, with an average age of 51 years.

Primary outcomes

Daytime sleepiness

The study evaluated the effect of the interventions on this outcome, measured by change from baseline of the Epworth Sleepiness Scale. Study results showed that, compared to standard medical treatment, myofunctional therapy may reduce daytime sleepiness (MD -6.40 points, 95% CI -9.82 to -2.98; one study, 26 participants; low-certainty evidence; [Analysis 7.1](#); [Summary of findings 7](#)).

Morbidity (including accidents and cardiovascular diseases) and mortality

The study did not analyse this outcome.

Secondary outcomes

Quality of life

The study did not analyse this outcome.

Sleep quality

The study evaluated the effect of the interventions on this outcome, measured by change from baseline of the Pittsburgh Sleep Quality Index (PSQI).

Study results showed that, compared to standard medical treatment, myofunctional therapy may increase sleep quality (MD -3.10 points, 95% CI -5.12 to -1.08; one study, 26 participants; low-certainty evidence; [Analysis 7.2](#); [Summary of findings 7](#)).

Adverse events and side effects

The study did not report on adverse events or side effects.

Apnoea-Hypopnoea Index (AHI)

The study did not analyse this outcome.

Snoring frequency

The study evaluated the effect of the interventions on this outcome, measured by change from baseline. Study results showed that compared to standard medical treatment myofunctional therapy may reduce snoring frequency slightly (MD -2.40 points, 95% CI -2.80 to -2.00; one study, 26 participants; low-certainty evidence; [Analysis 7.3](#); [Summary of findings 7](#)).

Snoring intensity

The study evaluated the effect of the interventions on this outcome, measured by change from baseline. The study found that, compared to standard medical treatment, myofunctional therapy may reduce snoring intensity. They found an average reduction of 3.2 points in the myofunctional therapy group and no change in any patient in the standard medical treatment group (MD and 95% CI not estimable; one study, 26 participants; low-certainty evidence; [Analysis 7.4](#); [Summary of findings 7](#)).

Myofunctional therapy versus inspiratory muscle training

Only one study analysed this comparison ([Erturk 2013](#)). It included 29 participants in the analysis.

Primary outcomes

Daytime sleepiness

The study did not analyse this outcome.

Morbidity (including accidents and cardiovascular diseases) and mortality

The study did not analyse this outcome.

Secondary outcomes

Quality of life

They reported that they assessed quality of life using the Functional Outcomes of Sleep Questionnaire (FOSQ) but they did not provide detailed numeric data of results on each treatment group.

Sleep quality

The study did not analyse this outcome.

Adverse events and side effects

The study did not report on adverse events or side effects.

Apnoea-Hypopnoea Index (AHI)

The study did not analyse this outcome.

Snoring frequency

The study did not analyse this outcome.

Snoring intensity

The study did not analyse this outcome.

DISCUSSION

Summary of main results

In this review, we compared the efficacy of myofunctional therapy as a treatment for obstructive sleep apnoea with other treatment options. We included nine studies that randomised a total of 425 participants and analysed 347 participants.

Three studies with 98 participants compared myofunctional therapy with sham therapy. One study with 54 participants compared myofunctional therapy with CPAP. One study with 49 participants compared myofunctional therapy with CPAP plus myofunctional therapy. One study with 25 participants compared myofunctional therapy with waiting list. Two studies with 97 participants compared myofunctional therapy with respiratory exercises plus nasal dilator strip. One study with 26 participants compared myofunctional therapy and standard medical therapy. One study with 13 children compared myofunctional therapy added to nasal washing and nasal washing alone.

The review revealed that, for adults:

- compared to sham therapy, myofunctional therapy probably reduces daytime sleepiness, may increase sleep quality, may result in a large reduction in Apnoea-Hypopnoea Index (AHI), may have little to no effect in reduction of snoring frequency but the evidence is very uncertain and probably reduces subjective snoring intensity slightly.
- compared to waiting list, myofunctional therapy may reduce daytime sleepiness, may result in little to no difference in sleep quality and may reduce AHI.
- compared to CPAP, myofunctional therapy may result in little to no difference in daytime sleepiness, may increase AHI and may result in little to no difference in snoring frequency and snoring intensity.
- compared to CPAP plus myofunctional therapy, myofunctional therapy alone may result in little to no difference in daytime sleepiness, may increase AHI and may result in little to no difference in snoring frequency and snoring intensity.
- compared to respiratory exercises plus nasal dilator strip, myofunctional therapy may result in little to no difference in daytime sleepiness, probably increases sleep quality slightly and may result in little to no difference in AHI.
- compared to standard medical treatment, myofunctional therapy may reduce daytime sleepiness, may increase sleep quality and may reduce snoring frequency slightly and may reduce snoring intensity.

In children, compared to nasal washing alone, adding myofunctional therapy may result in little to no difference in AHI.

None of the studies looked at morbidity (including accidents and cardiovascular diseases) and mortality, or quality of life.

Overall completeness and applicability of evidence

For all the comparisons addressed in this review, we found few studies and small sample sizes.

The length of the interventions and follow-up periods of the included studies were short (less than four months). Therefore, it is not clear whether potential beneficial effects of the treatment will endure in the medium and long term, and whether compliance with the treatment will persist.

The included studies did not provide separate information to make subgroup analyses possible. For example, none of the studies disaggregated results by sex to allow for separate analyses for men and women.

None of the studies reported any adverse events. However, we believe that myofunctional therapy would be unlikely to cause adverse effects because of the type of intervention it represents, and therefore we do not believe that investigators have overlooked that problem.

For numerical outcomes, we have considered as minimum clinically important differences (MCID) the following ones: for daytime sleepiness, three points if measured by the ESS ([Patel 2017](#); [Weaver 2001](#)); for sleep quality, three points if measured by the PSQI ([Hughes 2009](#)); for AHI five points ([Kim 2017](#)).

Quality of the evidence

The certainty of the evidence for all comparisons ranges from moderate to very low, mainly due to lack of blinding of the assessors of subjective outcomes, incomplete outcome data and imprecision.

Potential biases in the review process

Our search design confronted the problem that indexing of studies in this area is poor. We used a combination of text words and index terms in our search strategy to mitigate this, however we cannot rule out having missed studies on this topic due to differences in the terminology used to describe the interventions.

In addition, for some comparisons - such as the comparison with sham therapy - we have pooled results from studies that differ in the components and doses of the interventions. It is difficult to pinpoint to what extent differences in results are related to differences in interventions components. However, results from all the studies pointed in the same direction: i.e. myofunctional therapy produces a better effect compared to sham therapy.

Agreements and disagreements with other studies or reviews

Four reviews on OSA and myofunctional therapy have been published previously ([Camacho 2017](#); [de Felicio 2018](#); [Hsu 2020](#); [Kayamori 2017](#)). Three reviews concluded that myofunctional therapy produces positive results ([Camacho 2017](#); [de Felicio 2018](#); [Kayamori 2017](#)), more beneficial than the results we have found. We believe the reason for this difference is that study eligibility criteria were different. Our review included only RCTs, whereas these reviews included in their analyses the results of observational studies, which can be biased and provide a lower level of certainty of the evidence.

A recently published review highlights respiratory muscle therapy as an adjunct management for OSA ([Hsu 2020](#)). Like our review, [Hsu 2020](#) concludes that further studies are needed. Like us, [Hsu 2020](#) highlights research limitations in this area, including the

nature and small number of extant studies, the heterogeneity of the interventions, and the low certainty of evidence.

AUTHORS' CONCLUSIONS

Implications for practice

Compared to sham therapy, waiting list or standard medical treatment, in adults, myofunctional therapy may improve daytime sleepiness and sleep quality in the short term. However, certainty of the evidence is moderate to low.

Compared to CPAP, myofunctional therapy may result in little to no difference in daytime sleepiness, may increase AHI and may result in little to no difference in snoring frequency and snoring intensity.

Compared to CPAP plus myofunctional therapy, myofunctional therapy alone may result in little to no difference in daytime sleepiness, may increase AHI and may result in little to no difference in snoring frequency and snoring intensity.

Compared to respiratory exercises plus nasal dilator strip, myofunctional therapy may result in little to no difference in daytime sleepiness, probably increases sleep quality slightly and may result in little to no difference in AHI.

In children, compared to nasal washing alone, adding myofunctional therapy may result in little to no difference in AHI.

Implications for research

More studies are needed. Given that most of the studies included in this review suffered from lack of blinding of outcome assessors, in future studies, outcome assessors should be blinded.

New trials should: recruit more participants; include more women and children; and have longer treatment and follow-up periods.

Future studies should also include enough participants with different levels of severity of OSA (mild, moderate and severe) to permit adequate assessment of the impact of myofunctional therapy in each of those subgroups.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Bellur 2012

Study characteristics

Methods	<p>Study design: parallel, RCT.</p> <p>Recruitment period: November 2010 – June 2012.</p> <p>Duration of study: study start date: November 2010. Actual study completion date: June 2012.</p> <p>Study setting: outpatient. Hacettepe University Faculty of Physical Therapy and Rehabilitation Cardiopulmonary Rehabilitation Department. Ankara, Turkey.</p>
Participants	<p>Key inclusion criteria: mild, moderate and severe patients with OSA who did not use CPAP, aged 19-75 years.</p> <p>Key exclusion criteria: participants with a history of stroke, neurological disease, severe obstructive nasal disease and infection history in the last month, or BMI was 40 kg/m² or more.</p> <p>Age (years): mean (SD): 53.7 (7.1) in oropharyngeal exercises group and 47.3 (7.3) in standard medical treatment control group.</p> <p>Gender: for participants that ended the study: therapy group: 11 men and 3 women; control group: 10 men and 2 women.</p> <p>Comorbidities: not stated.</p> <p>BMI: mean (SD): 31.4 (3.8) in oropharyngeal exercises group and 32.1 (3.7) in standard medical treatment control group.</p> <p>AHI (events/hour): not available.</p> <p>ESS: mean (SD): 8.1 (6.3) in oropharyngeal exercises group and 9.7 (5.9) in control group.</p> <p>PSQI: mean (SD): not available.</p> <p>N randomised: 36, 18 to each group.</p> <p>N analysed: 26.</p> <p>Dropouts: 4 in oropharyngeal exercises group and 6 in standard medical treatment control group.</p>
Interventions	<p>Intervention: oropharyngeal exercises.</p> <p>Same set of oropharyngeal exercises used by Guimaraes (see NCT00660777 Guimaraes 2009). 5 days a week for 3 months supervised by physical therapist. Used mirror for visual feedback.</p> <p>Comparator: standard medical treatment.</p> <p>Concomitant interventions: none.</p>
Outcomes	<p>Prespecified outcomes: protocol not available.</p> <p>Reported outcomes:</p> <ul style="list-style-type: none"> • Neck circumference.

Bellur 2012 (Continued)

- Snoring frequency.
- Snoring intensity.
- Daytime sleepiness (ESS).
- Sleep quality score (PSQI).

Time points of measurement: 3 months.

Notes

Publication: abstract from conference proceedings only. Additional information requested and received from authors on allocation procedures.

Funding for trial: not reported.

Conflicts of interest: none.

Registered: not reported.

Sample size calculations: not reported.

Data sharing statement: none.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation with closed envelopes.
Allocation concealment (selection bias)	Low risk	Randomisation with closed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Similar percentages of losses to follow-up in both groups.
Selective reporting (reporting bias)	Low risk	Protocol not available.
Other bias	Low risk	The study appears to be free of other sources of bias.

Diaferia 2017
Study characteristics

Methods

Study design: parallel, RCT.

Recruitment period: not specified.

Duration of study: study start date: October 2010. Actual primary completion date: December 2011.

Diaferia 2017 (Continued)

Study setting: outpatient. Universidade Federal de São Paulo, São Paulo, Brazil.

Participants

Key inclusion criteria: men, age 25 to 65 years, BMI lower than 35 kg/m², and with OSA diagnosis confirmed by clinical and polysomnographic criteria.

Key exclusion criteria: women; participants who were uncooperative, illiterate, or who had a low education level that prevented the completion of questionnaires and the understanding of the guidelines about the use of CPAP and practice of exercises that have been written to be practiced at home; patients with other sleep disorders or with previous treatment for OSA (i.e., CPAP, intraoral device, or surgery); patients with serious or decompensated clinical or psychiatric medical illnesses, such as congestive heart failure, cardiomyopathy, COPD, chronic active hepatitis, liver cirrhosis with severe symptoms, myasthenia gravis, demyelinating disease, motor neuron disease, depression, schizophrenia, obsessive compulsive disorder, disorder anxiety, bipolar disorder, eating disorder, attention deficit disorder, and hyperactivity; patients who used alcohol, stimulants or sedatives; and patients with grade III or IV palatine tonsils, grade II or III septal deviation, or evident micrognathia.

Gender: all men.

Age: mean (SD): participants that completed the study: 48.1 (11.2) years old. Participants that did not complete the study: 39.4 (10.1).

BMI: mean (SD): participants that completed the study: 27.4 (4.9) kg/m². Participants that did not complete the study: 28.1 (3.0) kg/m².

AHI (events/hour): mean (SD) in participants that completed the study: 30.9 (20.6). Participants that did not complete the study: 30.4 (20.2).

ESS: mean (SD): participants that completed the study: 12.7 (3.0). Participants that did not complete the study: 12.1 (1.8).

N randomised: 140 participants: 35 placebo, 35 myofunctional therapy, 35 CPAP, and 35 combined therapy.

N analysed: 100.

Dropouts: 40 participants: 11 in placebo group for "reported worsening of OSA and snoring"; 8 in myofunctional therapy group "quit speech therapy exercises"; 8 in CPAP group "quit use of CPAP"; and 13 in combined therapy group "performed exercises but did not use CPAP".

Interventions

Intervention: oropharyngeal exercises.

The participants were instructed by one speech pathologist to perform the following tasks:

- Soft palate: elevation of the soft palate and uvula while pronouncing an oral vowel intermittently /a/ (isotonic exercise) and continuously (isometric exercise). The palatopharyngeal, palatoglossus, uvula, tensor veli palatini, and levator veli palatini muscle are recruited in this exercise. The isotonic exercise also recruits pharyngeus lateral wall. These exercises had to be repeated daily, three times a day, for 3 minutes and were performed once a week under supervision to ensure adequate effort.
- Tongue: brushing the superior and lateral surfaces of the tongue while the tongue is positioned in the floor of the mouth (5 times each movement, 3 times a day); pushing the tip of the tongue against the hard palate and sliding the tongue backward (20 times, 3 times a day); sucking the tongue upward against the palate, pressing the entire tongue against the palate (20 times); and rotating the tongue in the oral vestibule 10 times right and left side. Forcing the back of the tongue against the floor of the mouth while keeping the tip of the tongue in contact with the inferior incisors (20 times, 3 times a day).

Stomatognathic functions:

- Suction: sucking yogurt with a narrow straw.
- Breathing and speech: forced nasal inspiration and oral expiration in conjunction with phonation of open vowels, while sitting; and balloon inflation with prolonged nasal inspiration and then forced blowing, repeated 5 times without taking the balloon out of the mouth.

Diaferia 2017 (Continued)

- Swallowing and chewing: alternate bilateral chewing and deglutition, using the tongue in the palate, closed teeth, without perioral contraction, whenever feeding. This exercise aims for the correct position of the tongue while eating and targets the appropriate functionality and movement of the tongue and jaw. The patients were instructed to incorporate this mastication pattern whenever they were eating.

Comparators:

- Placebo.

The patients were instructed by one speech pathologist to perform exercises without therapeutic function (relaxation and stretching of the neck muscles).

- CPAP.

All participants from the CPAP and combined groups underwent a full night, attended PSG to manually determine the optimum pressure of CPAP. The CPAP titration was performed according to the protocol proposed by the American Academy of Sleep Medicine.

- Combined therapy: CPAP plus oropharyngeal exercises.

Placebo exercises and oropharyngeal exercises were performed at home for 3 months with 3 daily exercise sessions of 20 minutes each.

Concomitant interventions: None.

Outcomes

Prespecified outcomes

Primary Outcome Measures:

- Objective sleep pattern: sleep stages, arousals, apnoea-hypopnoea index, oxyhaemoglobin saturation evaluated by polysomnography.

Secondary Outcome Measures:

- Daytime sleepiness (ESS).
- Quality of life (WHOQOL-BREF and FOSQ questionnaires).
- Cognition.
- Evaluations of psychomotor vigilance test.

Time points of measurement: before treatment and 90 days after and 3 weeks later (“washout”) for all outcomes.

Reported outcomes:

Results on quality of life, cognition and psychomotor vigilance test were not reported.

Notes

Quote in NCT01289405: “target number of participants that the researchers need for the study: 80”. But 140 participants were included. No information provided on reasons for the increase in final participants.

Additional information on allocation procedures requested from authors, but no answer received.

Funding for trial: Associação Fundo de Incentivo à Pesquisa—AFIP Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Conflicts of interest: the authors declare that they have no conflict of interest.

Registered: ClinicalTrials.gov NCT01289405.

Sample size calculations: quote: “The G*Power 3.1.10 program was used to calculate sample sizes. With an expected difference in the hours of CPAP used between the CPAP group and the combined

Diaferia 2017 (Continued)

group (0.40), α of 0.05 and sample size of 54 patients (27 patients in CPAP and 27 combined group), a power of 0.85 was found. The significance level was set at 5%."

Data sharing statement: none.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Prior to treatment, the patients were divided randomly into four groups". Comment: no description of the randomisation process.
Allocation concealment (selection bias)	Unclear risk	Not reported. Method of allocation concealment not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote in NCT01289405: "Double blinding (Participant, Investigator)".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote in NCT01289405: "Double blinding (Participant, Investigator)".
Incomplete outcome data (attrition bias) All outcomes	High risk	Figure 2 . The flow chart of patient selection during this study started with 140 participants, 35 randomised to each of the four groups. Dropouts: 11 in placebo group for "reported worsening of OSA and snoring"; 8 in myofunctional therapy group "quit speech therapy exercises"; 8 in CPAP group "quit use of CPAP"; and 13 in combined therapy group "performed exercises but did not use CPAP". 140 patients with 40 patients failing to complete the study. However, differences in dropout rates are not statistically significant.
Selective reporting (reporting bias)	Low risk	Prespecified relevant outcomes in clinicaltrials.gov were reported.
Other bias	Low risk	The study appears to be free of other sources of bias.

Erturk 2013
Study characteristics

Methods	<p>Study design: parallel, RCT.</p> <p>Recruitment period: not available.</p> <p>Duration of study: not available.</p> <p>Study setting: outpatient. Hacettepe University Faculty of Physical Therapy and Rehabilitation Cardiopulmonary Rehabilitation Department, Turkey.</p>
Participants	<p>Key inclusion criteria: participants with mild, moderate and severe OSA who did not use CPAP, aged 19-75 years.</p> <p>Key exclusion criteria: participants with a history of stroke, neurological disease, severe obstructive nasal disease and infection history in the last month, or BMI was 40 kg/m² or more.</p>

Erturk 2013 (Continued)

Age (years): not available.

Gender: not available.

Comorbidities: not available.

BMI: not available.

AHI (events/hour): not available.

ESS: not available.

PSQI: not available.

N randomised: 41: 15 in the IMT group, 14 in oropharyngeal exercises (OE) group and 12 in the control group.

N analysed: 41.

Dropouts: not reported.

Interventions

Intervention: oropharyngeal exercises.

- Same set of oropharyngeal exercises used by Guimaraes (see NCT00660777 [Guimaraes 2009](#)). 5 days a week for 3 months supervised by physical therapist. Used mirror for visual feedback.

Comparators:

- Inspiratory muscle training. Not detailed.
- Standard medical treatment.

Concomitant interventions: none

Outcomes

Prespecified outcomes: protocol not available.

Reported outcomes:

- Anthropometric measurements (neck and abdominal circumference).
- Respiratory muscle strength (MIP, MEP).
- Exercise capacity (six minute walk test).
- Polysomnography recordings.
- Quality of life (FOSQ).
- Fatigue severity (FSS).

Time points of measurement: before and 12 weeks after the treatment.

Notes

Publication: abstract from conference proceedings only. Additional information requested and received from authors on allocation procedures.

Funding for trial: not reported.

Conflicts of interest: none.

Registered: not reported.

Sample size calculations: not reported.

Data sharing statement: none.

Risk of bias

Bias	Authors' judgement	Support for judgement
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Erturk 2013 (Continued)

Random sequence generation (selection bias)	Low risk	Randomisation with closed envelopes.
Allocation concealment (selection bias)	Low risk	Randomisation with closed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	None declared.
Selective reporting (reporting bias)	Low risk	Protocol not available but they published outcome measurements relevant for the objectives of the study.
Other bias	Low risk	The study appears to be free of other sources of bias.

Goswami 2019
Study characteristics

Methods	<p>Study design: parallel, RCT.</p> <p>Recruitment period: not available.</p> <p>Duration of study: study start date: 15 December 2016. Actual study completion date: 18 May 2017.</p> <p>Study setting: outpatient. University of Minnesota Medical Center sleep clinic.</p>
Participants	<p>Key inclusion criteria: between 20 and 65 years of age, fluent in English, and with a BMI equal or lower than 32 kg/m²; participants had to be habitual snorers (self-reported or bed partner reported snoring three or more nights a week) with a PSG or HST within the past year that showed objective snoring with no more than mild obstructive sleep apnoea (AHI 0–14). For both PSG and HST, apneas were defined as a drop equal or higher than 90% in peak signal excursion of the apnoea sensor for 10 seconds or more while hypopnoeas were defined as a drop equal or higher than 30% from peak signal excursion of the airflow sensor associated with oxygen desaturation equal or higher than 4% from pre-event baseline. AHI was calculated in accordance with the AASM rules, terminology, and technical specifications.</p> <p>Key exclusion criteria: anyone with comorbid sleep disorders (significant insomnia, uncontrolled restless legs syndrome, chronic insufficient sleep intake, or pathological excessive daytime sleepiness, i.e., ESS higher than 11), significant medical comorbidities including decompensated cardiopulmonary disease and chronic rhinitis, self-reported average of three or more alcoholic drinks per day, or significant daily opioid use. Those currently using CPAP were excluded. To minimize variation in OSA risk factors, authors excluded anyone with higher than 5% weight change since their sleep apnoea evaluation. Given data collection procedures, they excluded participants with a less than 10 megabytes per second WiFi connection where they sleep, inability to sleep in a quiet environment, or a loud snorer as a bed partner.</p> <p>Age (years): mean (SD): 51 (11) in intervention group and 51 (10) in control group.</p> <p>Gender: 6 women, 10 men.</p>

Goswami 2019 (Continued)

Comorbidities: not detailed.

BMI: mean (SD): 27.5 (3.4) in intervention group and 27.4 (3.8) in control group.

AHI (events/hour): mean (SD): 9.2 (4.0) in intervention group and 8.2 (3.2) in control group.

ESS: mean (SD): 8 (3.5) in intervention group and 7 (4.0) in control group.

PSQI: not measured.

N randomised: 32.

N analysed: 16, 8 in each comparison group.

Dropouts: 16, 8 in each comparison group.

Interventions

Intervention: oropharyngeal exercises.

Smartphone application that requires users to articulate phonemes to achieve voice-controlled on-screen objectives.

The exercise routine comprises three different games of 5 minutes each, played consecutively for a total of 15 minutes daily. These games focus on improving endurance, strength, and coordination of upper airway muscles by moving the user's tongue base forwards and backwards repeatedly. Game 1 prompts the user to repeatedly enunciate the /i/ sound to perform the on-screen objective, with the aim of building endurance by holding the tongue forward. Game 2 is designed to improve strength by inducing pulsing of the tongue in forward and backward motion through vocalization of /i/ and /a/ to control the on-screen object. Game 3 prompts articulation of /i/, /u/, and /a/ to improve coordination by navigating the tongue through different zones.

Duration of treatment, up to 12 weeks.

Comparator: a daily 'check-in' on a mobile application but without exercises.

Concomitant interventions: participants using mandibular advancement device and nasal dilator strips routinely were restricted from using these on the nights of sleep recording for the study duration.

Outcomes

Prespecified outcomes:

Primary Outcome Measures:

- Snoring intensity (snoring sounds higher than 60 dBA per hour of sleep).
- Snoring rate (snoring sounds/hour of sleep).

Secondary Outcome Measures:

- Sleep quality: self-reported on Likert scale (0 to 5).
- Bed partner sleep quality: reported on Likert scale (0 to 5).
- Daytime sleepiness (ESS)

Time points of measurement: before and 12 weeks after the treatment.

Reported outcomes: they did not report results on sleep quality, nor on sleepiness.

Notes

Additional information requested and received from authors on allocation procedures.

Funding for trial: NIH Research Evaluation and Commercialization Hub (MN-REACH) Grant no. 5U01HL127479-03.

Conflicts of interest: quote: "Umesh Goswami: holds equity in the entity aimed at commercialisation of the technology described in this manuscript; Adam Black: holds the provisional patent of the technology described in this manuscript and holds equity in the entity aimed at commercialisation of the technology; Brian Krohn: holds the provisional patent of the technology described in this manuscript and holds equity in the entity aimed at commercialisation of the technology."

Goswami 2019 (Continued)

Registered: ClinicalTrials.gov: NCT03264963.

Sample size calculations: not reported.

Data sharing statement: none.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "we randomly assigned participants". Additional information from authors: "1:1 randomisation using computer generated random numbers."
Allocation concealment (selection bias)	High risk	Not done.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quotes: "The participants were not blinded to their assignment of the study arm." "Masking: None (Open Label)".
Blinding of outcome assessment (detection bias) All outcomes	High risk	Participants not blinded. High risk for participant-assessed outcomes such as daytime sleepiness or sleep quality. Low risk for snoring measurements. Quote: "A non-contact microphone ... was positioned 30 cm above the participant's mouth during sleep to optimise signal quality and patient comfort ... to record sound levels. Data were collected and stored in de-identified form, assigned to a unique participant ID."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Equal percentages of losses in both compared groups. Quotes: "Despite instructions to record their sleep environment sounds twice weekly, participants' recording frequency varied. Over the study period, 16 participants (8 intervention group, 8 control group) met the requirement of recording 12 nights of sleep for 5 h or longer. Data from these 16 participants were analysed." "In the control group 2 participants withdrew after randomisation before activity and 6 did not complete the minimum of 12 nighttime recordings of at least 5 hours in length." "Participants were considered to have completed the protocol if they produced at least 12 recordings of ≥ 5 h each (primary end point)."
Selective reporting (reporting bias)	Low risk	Pre-specified relevant outcomes in clinicaltrials.gov were reported.
Other bias	Low risk	The study appears to be free of other sources of bias.

Guimaraes 2009
Study characteristics

Methods

Study design: parallel, RCT.

Recruitment period: February 2004 to October 2007.

Duration of study: study start date: February 2004. Actual primary completion date: October 2007. Actual study completion date: April 2008.

Guimaraes 2009 (Continued)

Study setting: outpatient. Universidade Federal de São Paulo, São Paulo, Brazil.

Participants

Key inclusion criteria: participants aged between 25 and 65 years old with a recent diagnosis of moderate obstructive sleep apnoea.

Key exclusion criteria: BMI higher than 40 kg/m²; facial malformations; regular use of hypnotic medications; hypothyroidism; previous stroke; neuromuscular disease; heart failure; coronary disease; severe obstructive nasal disease.

Age (years)*: mean (SD): 47.7(9.8) in myofunctional therapy group and 51.5 (6.8) in control group.

Gender*: 10 women, 21 men.

Comorbidities*: 26/31 hypertension; 2/31 diabetes.

BMI*: mean (SD): 29.6 (3.8) in myofunctional therapy group and 31.0 (2.8) in control group.

AHI (events/hour)*: mean (SD): 22.4 (4.8) in myofunctional therapy group and 22.4 (5.4) in control group.

ESS*: mean (SD): 14 (5) in myofunctional therapy group and 14 (7) in control group.

PSQI*: mean (SD): 10 (4) in myofunctional therapy group and 11 (4) in control group.

* Data from the 31 included in analysis.

N randomised: 39.

N analysed: 31, 16 myofunctional therapy and 15 control.

Dropouts: 8 participants, 3 in the myofunctional therapy and 5 in control group.

Interventions

Intervention: oropharyngeal exercises.

The participants were instructed by one speech pathologist to perform the following tasks:

- Soft palate. Pronounce an oral vowel intermittently (isotonic exercise) and continuously (isometric exercise). The palatopharyngeus, palatoglossus, uvula, tensor veli palatini, and levator veli palatini muscles are recruited in this exercise. The isotonic exercise also recruits pharyngeus lateral wall. These exercises had to be repeated daily for 3 minutes and were performed once a week under supervision to ensure adequate effort.
- Tongue. Brushing the superior and lateral surfaces of the tongue while the tongue is positioned in the floor of the mouth (five times each movement, three times a day). Placing the tip of the tongue against the front of the palate and sliding the tongue backward (a total of 3 minutes throughout the day). Forced tongue sucking upward against the palate, pressing the entire tongue against the palate (a total of 3 minutes throughout the day). Forcing the back of the tongue against the floor of the mouth while keeping the tip of the tongue in contact with the inferior incisors (a total of 3 minutes throughout the day).
- Facial. The exercises of the facial musculature use facial mimicking to recruit the orbicularis oris, buccinator, major zygomaticus, minor zygomaticus, levator labii superioris, levator anguli oris, lateral pterygoid, and medial pterygoid muscles. The exercises include: orbicularis oris muscle pressure with mouth closed (isometric exercise); recruited to close with pressure for 30 seconds, and right after, requested to realize the posterior exercise; suction movements contracting only the buccinator. These exercises were performed with repetitions (isotonic) and holding position (isometric). Recruitment of the buccinator muscle against the finger that is introduced in the oral cavity, pressing the buccinator muscle outward. Alternated elevation of the mouth angle muscle (isometric exercise) and after, with repetitions (isotonic exercise). Patients were requested to complete 10 intermittent elevations 3 times. Lateral jaw movements with alternating elevation of the mouth angle muscle (isometric exercise).

Stomatognathics functions:

Guimaraes 2009 (Continued)

- Breathing and Speech. Forced nasal inspiration and oral expiration in conjunction with phonation of open vowels, while sitting; balloon inflation with prolonged nasal inspiration and then forced blowing, repeated five times without taking the balloon out of the mouth.
- Swallowing and Chewing. Alternate bilateral chewing and deglutition, using the tongue in the palate, closed teeth, without perioral contraction, whenever feeding. The supervised exercise consisted of alternate bread mastication. This exercise aims for the correct position of the tongue while eating and targets the appropriate functionality and movement of the tongue and jaw. The patients were instructed to incorporate this mastication pattern whenever they were eating.

The same schedule and set of instructions applied to the control group were given to participants with the substitution of deep breathing by effective therapy.

Comparator: sham therapy

A weekly, supervised session (30 minutes) of deep breathing through the nose while sitting. The patients were also instructed to perform the same procedure at home once a day (30 minutes), plus nasal lavage with application of 10 mL of saline in each nostril three times a day. At study entry, bilateral chewing was recommended when eating meals.

Concomitant interventions: none.

Outcomes
Prespecified outcomes:

Primary outcome:

- AHI.

Secondary outcomes:

- Lowest oxygen saturation.
- Daytime sleepiness (ESS).
- Sleep quality (PSQI).
- Snoring frequency.
- Snoring intensity.

Time points of measurement: 3 months.

Reported outcomes: all prespecified outcomes.

Notes

Additional information requested and received from authors on allocation procedures. Three of the RCTs included in this review were led by the same researcher and allocation procedure were similar (Guimaraes 2009, Ieto 2015 and Kayamori 2015).

Funding for trial: supported by Fundacao de Amparo a Pesquisa do Estado de Sao Paulo, Conselho Nacional de Desenvolvimento Científico e Tecnológico, and the E. J. Zerbini Foundation.

Conflicts of Interest: quote: "None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript."

Registered: ClinicalTrials.gov NCT00660777.

Sample size calculations: not reported.

Data sharing statement: none.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "We typed equal number of (1 or 2), corresponding to control or treatment and put all the small papers (A or B) in a sealed envelope. One paper was

Guimaraes 2009 (Continued)

		picked up for each patient in the moment of randomisation by someone that was not involved in the study.”
Allocation concealment (selection bias)	Low risk	See random sequence generation above.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Masking: Single (Participant)”.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: “Masking: Single (Participant)”.
Incomplete outcome data (attrition bias) All outcomes	High risk	Relevant percentages of losses in follow-up. Quotes: “we recruited 39 patients. Eight patients (3 in the active treatment arm) were excluded due to low adherence”. “Patients who failed to return for three consecutive weeks or failed to comply with the exercises at home (performing 85% of the exercises) were excluded from the study.” Per protocol analysis “31 patients included in the final analysis”.
Selective reporting (reporting bias)	Low risk	Prespecified outcomes in clinicaltrials.gov were reported.
Other bias	Low risk	The study appears to be free of other sources of bias.

Ieto 2015
Study characteristics

Methods	<p>Study design: parallel, RCT.</p> <p>Recruitment period: November 2011 to November 2013.</p> <p>Duration of study: study start date: December 2011. Estimated primary completion date: December 2015.</p> <p>Study setting: outpatient. Universidade Federal de São Paulo, São Paulo, Brazil.</p>
Participants	<p>Key inclusion criteria: participants with primary snore, mild and moderate obstructive sleep apnoea, 25 years to 65 years.</p> <p>Key exclusion criteria: BMI equal or higher than 40, craniofacial malformations, smokers, pregnant women, edentulous, total dental prostheses, use of hypnotic medications, stroke, neuromuscular dystrophy, coronary artery disease, CHF, COPD, severe nasal obstructive disease, pharyngeal surgery, already had some kind of treatment for OSA.</p> <p>Age (years): mean (SD): 48(14) in therapy group and in 45 (13) control group.</p> <p>Gender: 17 women, 22 men.</p> <p>BMI: mean (SD) 28.2 (3.1) kg/m².</p> <p>AHI (events/hour): mean (SD): 15.3 (9.3).</p> <p>ESS: mean (SD): 9.2 (4.9).</p>

Ieto 2015 (Continued)

PSQI: mean (SD): 6.4 (3.3).

N randomised: 39, 19 to therapy group and 20 to control group.

N analysed: 39.

Dropouts: 2, 1 in each group.

Interventions

Intervention: oropharyngeal exercises

Participants were instructed to perform nasal washing 3 times a day followed by oropharyngeal exercises for approximately 8 minutes. The oropharyngeal exercises were simplified and included: push the tip of the tongue against the hard palate and slide the tongue backward (20 times); suck the tongue upward against the palate, pressing the entire tongue against the palate (20 times); force the back of the tongue against the floor of the mouth while keeping the tip of the tongue in contact with the inferior incisive teeth (20 times); elevation of the soft palate and uvula while intermittently saying the vowel "A" (20 times). After gaining control and coordination of movement (typically after 3-5 weeks), elevation of the soft palate and uvula was performed without vocalization for 5 seconds; recruitment of the buccinator muscle against the finger that is introduced in the oral cavity, pressing the buccinator muscle outward (10 times each side); alternate bilateral chewing and deglutition using the tongue in the palate, without perioral contraction, whenever feeding. The participants were instructed to incorporate this mastication pattern whenever they were eating.

Comparator: nasal dilator strips during sleep.

Participants were instructed to use nasal dilator strips during sleep, to perform nasal washing with saline solution 3 times a day and to perform deep breathing exercises through the nose while sitting.

Concomitant interventions: none.

Outcomes

Prespecified outcomes:

Primary outcome measures:

- Upper airway collapsibility.
- Images from magnetic resonance.
- Negative expiratory pressure.
- Snore.

Secondary outcome measures:

- Sleep related questionnaires.

Time points of measurement: before and 12 weeks after the treatment.

Reported outcomes: all prespecified outcomes.

Notes

Additional information from PhD thesis. Additional information requested and received from authors on allocation procedures. Three of the RCTs included in this review were led by the same researcher and allocation procedure were similar (Guimaraes 2009, Ieto 2015 and Kayamori 2015).

Funding for trial: supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Conflicts of interest: the authors reported no potential conflicts of interest.

Registered: ClinicalTrials.gov: NCT01636856.

Sample size calculations: quote: "We anticipated a 50% reduction in objective snoring in patients randomised to oropharyngeal exercises based on our previous research. We included 38 patients ($\beta=80\%$, $\alpha=95\%$)."

Data sharing statement: none.

leto 2015 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "patients were randomised for 3 months to either Control or Therapy group." In PhD thesis: "A randomização foi feita por blocos de quatro e estratificada de acordo com a gravidade da AOS (ronco primário, AOS leve e AOS moderada)."
Allocation concealment (selection bias)	Low risk	Additional information from authors: "We typed equal number of (1 or 2), corresponding to control or treatment and put all the small papers (A or B) in a sealed envelope. One paper was picked up for each patient in the moment of randomization by someone that was not involved in the study."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Masking: None (Open Label)".
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Masking: None (Open Label)".
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "One patient in each group withdrew from the study after randomisation." Quote: "Comparisons were performed by intention-to-treat analysis. Missing data at study termination were repeated from baseline according to Last Observation Carried Forward methods."
Selective reporting (reporting bias)	Low risk	Prespecified outcomes in clinicaltrials.gov were reported.
Other bias	Low risk	The study appears to be free of other sources of bias.

Kayamori 2015
Study characteristics

Methods	<p>Study design: parallel, RCT.</p> <p>Recruitment period: not available.</p> <p>Duration of study: not available.</p> <p>Study setting: outpatient. Sleep Laboratory of the Department of Pulmonology, Heart Institute, Hospital das Clínicas, School of Medicine, University of São Paulo, Brazil.</p>
Participants	<p>Key inclusion criteria: participants of both sexes, aged between 20 and 65 years old, recently diagnosed with primary snore, mild, moderate or severe OSA, who refused to use CPAP were included.</p> <p>Key exclusion criteria: participants with BMI equal or higher than 35 kg/m², craniofacial deformities, edentulous, regular use of hypnotic medication, severe nasal obstruction, patients undergoing other treatments for OSA and patients with unavailability to comply with the protocol.</p> <p>Age (years): mean (SD): 46.3 (18.8) in therapy group and 45.5 (11.7) in control group.</p> <p>Gender: 34 men, 24 women.</p> <p>BMI: mean (SD): 28.9 (3.5) in therapy group and 28.7 (3.4) in control group.</p>

Kayamori 2015 (Continued)

AHI (events/hour): mean (SD): 19.5 (14.2) in therapy group and 17.2 (10.94) in control group.

ESS: mean (SD): 9.9 (5.0) in therapy group and 10.3(5.2) in control group.

PSQI: mean (SD): 6.3 (3.5) in therapy group and 6.9 (3.3) in control group.

N randomised: 60, 30 to therapy group and 30 to control group.

N analysed: 58.

Dropouts: 2 in control group.

Interventions

Intervention: oropharyngeal exercises.

As follows:

- Tongue. Sweep: tip of tongue placed in the incisive papillae and slid in an anteroposterior direction against the hard palate. Initially without lingual (isotonic) pressure and then with lingual (isometric) pressure, without tightening the teeth, 20 times. Target musculature: Genioglossus and hipoglossus musculature. If it was not possible to perform this exercise, the patient was guided to push the hard palate: squeeze the anterior third of the tongue against the alveolar region of the hard palate maintaining the lip seal and without squeezing the teeth, 5 seconds, 20 times. Target musculature: suprahyoids (milohioid, genioid and digastric anterior belly). Coupling: initially isotonic tongue clicks, 20 times. Then stick the tongue against the palate isomerically maintaining the lingual coupling for 5 seconds, 20 times. Target musculature: Genioglossus, palatoglossus, hipoglossus and suprahyoids (milohioid, genioid and anterior ventral digastric). Lowering the back of the tongue: with the aid of a spatula or finger, stimulate the lowering reflex of the lingual back by 5 rapid touches in the region of the back of the tongue, 20 times. After the musculature necessary to perform the lowering is perceived, the lingual dorsum is asked to be lowered and relaxed isotonically 20 times; then the lingual dorsum is kept low, isomerically for 5 seconds, 20 times. Target musculature: hyoglossus and suprahyoid musculature.
- Buccinator and orbicular muscles of the mouth. Finger on the cheek: finger on the internal mucosa of the cheek, parallel to dental occlusion. The patient must press the finger with the cheek against the teeth. Initially performing isotonic exercises, 10 times each side. Afterwards isometric exercises are performed 10 seconds and 10 times each side. Target musculature: work mainly horizontal strap (buccinator mainly and orbicular mouth).
- Palate lift muscles, palate tensor and uvula muscle. Elevation of soft palate and uvula: intermittent vowel "A" production (isotonic exercises) 10 times, for 1 to 2 weeks. After the patient perceives the movement of the musculature, the vowel "A" is removed, performing only the intermittent elevation of the musculature of the palate, 20 times. After the gain of control and coordination of movement, the contraction of the musculature was maintained (isometric exercise), recruiting even the uvula muscle in the final phase, 5 seconds, 20 times. Target musculature: palatoglossus, palatopharyngeal, palate tensor, palate elevator and uvula. In the final stage, the soft palate lifting exercise, palate tensor and uvula is performed for the back of the tongue, i.e. support the apex of the tongue on the incisors lower and lower the lingual dorsum while raising the soft palate and uvula, 5 seconds, 20 times. Target musculature: palatoglossus, palatopharyngeal, tensor of the palate, palate elevator and uvula. And in the last stage, also hyoglossus musculature and suprahyoids.
- Alternating bilateral chewing. For maintenance of tongue and facial musculature.

12 weekly sessions lasting approximately 30 minutes.

Comparator: nasal dilator strips during sleep.

Participants were instructed to use nasal dilator strips during sleep and to perform breathing exercises 3 times a day daily, increasing the time of inspiration and expiration during sessions using diaphragmatic expansion.

12 weekly sessions lasting approximately 30 minutes.

Concomitant interventions: all patients from both groups were instructed to wash with 10 mL of saline solution in both nostrils 3 times a day.

Outcomes

Prespecified outcomes: protocol not available.

Kayamori 2015 (Continued)

Reported outcomes:

Primary outcome measures:

- Apnea Hypopnea Index.
- Sleep quality (PSQI).
- Daytime sleepiness (ESS).

Secondary outcome measures:

- Specific speech therapy evaluation for OSA.
- Upper airway anatomy assessed by magnetic resonance imaging.

Time points of measurement: before and 13 weeks after the treatment.

Notes

Information from PhD thesis. Additional information requested and received from authors on allocation procedures, Three of the RCTs included in this review were leaded by the same researcher and allocation procedure were similar (Guimaraes 2009, Ieto 2015 and Kayamori 2015).

Funding for trial: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) e Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).

Conflicts of interest: not reported.

Registered: not reported.

Sample size calculations: "The sample calculation was based on the assumption of a reduction of approximately 1.5 cm H₂O in the Pcrit with previous knowledge of a drop of approximately 40% in the AHI in the Therapy group and a reduction of 5% in the Control group in a previous study. We calculated a total number of 34 patients, considering a significance value of p=0.05 and standard deviation of 1.3 and power of 90%. Considering possible withdrawals and other events the total number of 40 patients."

Data sharing statement: none.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "We typed equal number of (1 or 2), corresponding to control or treatment and put all the small papers (A or B) in a sealed envelope. One paper was picked up for each patient in the moment of randomisation by someone that was not involved in the study."
Allocation concealment (selection bias)	Low risk	See random sequence generation above.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded study.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 patients lost in the control group. No imputation methods reported for their results.

Kayamori 2015 (Continued)

Selective reporting (reporting bias)	Low risk	Provided information on results for the outcomes considered relevant for the study Protocol of the study not available.
Other bias	Low risk	The study appears to be free of other sources of bias.

Puhan 2006
Study characteristics

Methods	<p>Study design: parallel, RCT.</p> <p>Recruitment period: not available.</p> <p>Duration of study: study start date: 1 August 2004. Actual study completion date: 1 April 2005.</p> <p>Study setting: outpatient. Zuercher Hoehen-klinik Wald, Wald, Switzerland and one private practice in Zurich.</p>
Participants	<p>Key inclusion criteria: german speaking participants aged above 18 years with self-reported snoring and an apnoea-hypopnoea index of 15-30 (determined by a specialist in sleep medicine within the past year).</p> <p>Key exclusion criteria: current CPAP, use of drugs that act on the CNS (such as benzodiazepines), current or planned intervention for weight reduction, consumption of 14 alcoholic drinks or more a week or 2 or more a day, and obesity (body mass index equal or higher than 30 kg/m²).</p> <p>Age (years): mean (SD): 49.9 (6.7) in didgeridoo playing group and 47.0 (8.9) in control group.</p> <p>Gender: 4 women, 21 men.</p> <p>Comorbidities: not detailed.</p> <p>BMI: mean (SD): 25.8 (4.0) in didgeridoo playing group and 25.9 (2.4) in control group.</p> <p>AHI (events/hour): mean (SD): 22.3 (5.0) in didgeridoo playing group and 19.9 (4.7) in control group.</p> <p>ESS: mean (SD): 11.8 (3.5) in didgeridoo playing group and 11.1 (6.4) in control group.</p> <p>PSQI: mean (SD): 5.2 (1.7) in didgeridoo playing group and 5.8 (2.8) in control group.</p> <p>N randomised: 25, 14 to didgeridoo playing and 11 to waiting list.</p> <p>N analysed: 25.</p> <p>Dropouts: none.</p>
Interventions	<p>Intervention: playing didgeridoo.</p> <p>For a period of 4 months, at least 5 times a week. Regular instruction by professional didgeridoo teacher.</p> <p>In the first lesson (week 1), participants learned the lip technique to produce and hold the keynote for 20-30 seconds. In the second lesson (week 2), the instructor explained the concept and technique of circular breathing. Circular breathing is a technique that enables the wind instrumentalist to maintain a sound for long periods of time by inhaling through the nose while maintaining airflow through the instrument, using the cheeks as bellows. In the third lesson (week 4), the instructor taught the participants his technique to further optimise the complex interaction between the lips, the vocal tract, and circular breathing so that the vibrations in the upper airway are more readily transmitted to the lower airways. In the fourth lesson, 8 weeks after randomisation, the instructor and the participants repeated the basics of didgeridoo playing and made corrections when necessary. Participants had to practice</p>

Puhan 2006 (Continued)

at home for at least 20 minutes on at least five days a week and recorded the days with practice and the practice time (answer options for 0, 20, or 30 minutes).

Participants received a standardised acrylic plastic didgeridoo that was developed by the instructor in collaboration with Creacryl GmbH (Ebmingen, Zurich, Switzerland)

Comparator: waiting list.

Participants in the control group remained on a waiting list to start their didgeridoo training after 4 months. They were not allowed to start didgeridoo playing during these 4 months.

Concomitant interventions: none.

Outcomes	<p>Prespecified outcomes:</p> <p>Primary outcome measures:</p> <ul style="list-style-type: none"> • Daytime sleepiness (ESS). • Sleep quality (PSQI). • Quality of life (SF-36). • Proxy evaluation. • Apnea Hypopnea Index. <p>Secondary outcome measures:</p> <p>No secondary outcome measures.</p> <p>Time points of measurement: before and 13 weeks after the treatment.</p> <p>Reported outcomes: All prespecified outcomes.</p>	
Notes	<p>Funding for trial: Zurich Lung Association, Zuercher Hoehenklinik Wald.</p> <p>Conflicts of interest: one of the authors “is a professional didgeridoo instructor and teaches tai chi and qid gong.”</p> <p>Registered: retrospectively, at ISRCTN31571714.</p> <p>Sample size calculations: not reported.</p> <p>Data sharing statement: none.</p>	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “We used STATA software (STATA 8.2, College Station, Tx) to generate the randomisation list (ralloc command) with stratification for disease severity (apnoea-hypopnoea index 15-21 or 22-30 and Epworth score lower than 12 or equal or higher than 12).”
Allocation concealment (selection bias)	Low risk	Quote: “The randomisation list was concealed from the recruiting physicians and the didgeridoo instructor in an administrative office otherwise not involved in the study. We used a central telephone service, which the didgeridoo instructor used to obtain group allocation.”
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants not blinded. High risk for patient-assessed outcomes. Quote: “we blinded outcomes assessors when possible (sleep studies)”. Low risk for IAH measurements.

Puhan 2006 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	High risk	Participants not blinded. High risk for patient-assessed outcomes. Quote: "we blinded outcomes assessors when possible (sleep studies)". Low risk for IAH measurements.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no losses to follow-up. Quote: "We analysed all data on an intention to treat basis."
Selective reporting (reporting bias)	Low risk	Prespecified outcomes in ISRCTN31571714 were reported.
Other bias	Low risk	The study appears to be free of other sources of bias.

Villa 2015
Study characteristics

Methods	<p>Study design: parallel, RCT.</p> <p>Recruitment period: not reported.</p> <p>Duration of study: study start date: not reported. Actual study completion date: not reported.</p> <p>Study setting: outpatient. Pediatric Sleep Center (S. Andrea Hospital) Rome, Italy.</p>
Participants	<p>Key inclusion criteria: children 4 or more years old, with adenotonsillar hypertrophy and OSA (clinical cutoff value of AHI higher than 5 for moderate-severe OSA) treated with adenotonsillectomy (AT), but in which residual OSA persist (residual OSA defined as an AHI index higher than 1 event/hour after AT and persistence of respiratory symptoms (snoring, oral breathing, and sleep apnoea).</p> <p>Key exclusion criteria: positive history for recurrent laryngospasm, allergy, asthma, acute or chronic cardiorespiratory or neuromuscular diseases, chronic inflammatory diseases, major craniofacial abnormalities, chromosomal syndromes, or epilepsy.</p> <p>Age (years): mean (SD): 6.01 (1.55) in intervention group and 5.76 (0.82) in control group.</p> <p>Gender: 24 boys, 3 girls.</p> <p>Comorbidities: not detailed.</p> <p>BMI: centile Mean (SD): 81.85 (29.94) in intervention group and 68.22 (28.68) in control group.</p> <p>AHI (events/hour): mean (SD): 4.82 (1.36). 4.87 (2.96) in intervention group and 4.56 (3.22) in control group.</p> <p>ESS: not assessed.</p> <p>PSQI: not assessed.</p> <p>N randomised: 30.</p> <p>N analysed: 27.</p> <p>Dropouts: 3, 2 from group 1 who did not comply with the exercises they were required to perform, and 1 from group 2 who not only did nasal washes but also nasal steroids for 3 months.</p>
Interventions	<p>Intervention: oropharyngeal exercises.</p>

Villa 2015 (Continued)

"Oropharyngeal exercises were divided into three categories, i.e., nasal breathing rehabilitation, labial seal and lip tone exercises, and tongue posture exercises... Children were required to perform the exercises every day at home, at least three times a day, doing 10–20 repetitions each time. Children underwent three monthly meetings with a therapist. In the first meeting (T1), the therapist carried out a morphofunctional evaluation and taught the patients and their parents nasal breathing rehabilitation exercises and exercises designed to restore competence and lip tone, which children were required to perform daily at home for 2 months. All the patients were also required to fill in a diary in which their compliance to exercises was recorded. The aim of the second meeting was to ensure that the home exercises were being executed correctly. In the third meeting (T2), underwent the second morphofunctional evaluation."

Duration of treatment 2 months.

Comparator: control group (treated with nasal washing alone).

Concomitant interventions: nasal washing was performed using the Neti Pot filled with 2.5 % saline hypertonic solution. All the participants performed nasal washing 2 times, in the morning and evening, for 2 months.

Outcomes	<p>Prespecified outcomes: protocol not available.</p> <p>Reported outcomes:</p> <ul style="list-style-type: none"> • Apnea Hypopnea Index. • ADHD-RS. • Morphofunctional evaluation form that assessed respiratory pattern (nasal or oral), labial seal (competent or not), and lip tone (normal or not). • Glatzel and Rosenthal tests, which assess nasal patency. <p>Time points of measurement: 2 months after the treatment.</p>
Notes	<p>Additional information on allocation procedures requested from authors, but no answer received.</p> <p>Funding for trial: none reported.</p> <p>Conflicts of interest: "The authors declare that they have no conflict of interest."</p> <p>Sample size calculations: not reported.</p> <p>Registered: not reported.</p> <p>Data sharing statement: none.</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients with residual OSA were randomised in two groups ". Comment: no description of the randomisation process.
Allocation concealment (selection bias)	Unclear risk	Not reported. Method of allocation concealment not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Low risk for AHl or for morphofunctional evaluations "In order to reduce a possible observer bias, the therapist who performed all the morphofunction-

Villa 2015 (Continued)

		al evaluations in both groups at T1 and T2 was always the same and he was blinded to the group because another therapist had taught the exercises.
		Parents not blinded. High risk for parent-assessed outcomes (ADHD-RS).
Incomplete outcome data (attrition bias) All outcomes	Low risk	No serious imbalance in losses in compared intervention groups. Quotes: excluded “two from group 1 who did not comply with the exercises they were required to perform, and one from group 2 who not only did nasal washes but also nasal steroids for 3 months.” Per protocol analysis done.
Selective reporting (reporting bias)	Low risk	Protocol not available but they published outcome measurements relevant for the objectives of the study.
Other bias	Low risk	The study appears to be free of other sources of bias.

Abbreviations: AASM: American Academy of Sleep Medicine; ADHD-RS: Attention Deficit Hyperactive Disorder Rating Scale; AHI: Apnea-Hypopnea Index; AT: Adenotonsillectomy; BMI: Body Mass Index; CHF: Congestive Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; CPAP: Continuous Positive Airway Pressure; ESS: Epworth Sleepiness Scale; FOSQ: Functional Outcomes of Sleep Questionnaire; FSS: Fatigue Severity Scale; HST: Home Sleep Test; IMT: Inspiratory Muscle Training; MD: Mean Difference; MEP: Maximal Expiratory Pressure; MIP: Maximal Inspiratory Pressure; nCPAP: nasal Continuous Positive Airway Pressure; OSA: Obstructive Sleep Apnea; PSG: Polysomnography; PSQI: Pittsburgh Sleep Quality Index; RCT: Randomised Clinical Trial; SD: Standard Deviation; SMD: Standardised Mean Difference; SF-36: 36-item Short Form health survey; WHOQOL-BREF: World Health Organization Quality of Life

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Atilgan 2019	Active multi-component intervention. Included oropharyngeal exercises and breathing exercises. Not possible to differentiate the separate effect of oropharyngeal exercises.
Bague 2014	Active multi-component intervention. Included oropharyngeal exercises, pulmonary exercises, electrical stimulation and manual therapy. Not possible to differentiate the separate effect of oropharyngeal exercises.
Kaur 2019	Active multi-component intervention. Included oropharyngeal exercises plus pranayama. Not possible to differentiate the separate effect of oropharyngeal exercises.
Kim 2019	Myofunctional therapy support program based on self-efficacy theory compared to no support during myofunctional therapy.
Kittivoravitkul 2018	Active multi-component intervention. Included oropharyngeal exercises plus incentive spirometry. Not possible to differentiate the separate effect of oropharyngeal exercises.
Neumannova 2018	Active multi-component intervention. Included oropharyngeal exercises, breathing retraining, respiratory muscle training with physiotherapist. Not possible to differentiate the separate effect of oropharyngeal exercises.
O'Connor-Reina 2018	Compares two different ways of receiving myofunctional therapy: an app versus diagrams and videos.
Torres-Castro 2016	Active multi-component intervention. Included oropharyngeal exercises, urban walking program, diet and sleep recommendations. Not possible to differentiate the separate effect of oropharyngeal exercises.
Villa 2017	The study does not evaluate any of the outcomes relevant for this review.

Study	Reason for exclusion
Ye 2018	All participants with post-stroke obstructive sleep apnoea syndrome.

Characteristics of studies awaiting classification *[ordered by study ID]*

Ferrara 2019

Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: children with nocturnal enuresis and SDB, from habitual snoring to OSA.</p> <p>Exclusion criteria: not available.</p>
Interventions	<p>Intervention:</p> <ul style="list-style-type: none"> Desmopressin with or without oxybutynin, dietary and lifestyle recommendations and myofunctional therapy. <p>Comparator:</p> <ul style="list-style-type: none"> Desmopressin with or without oxybutynin, and dietary and lifestyle recommendations.
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> Nocturnal enuresis. <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> Modified paediatric sleep questionnaire (PSQ-22).
Notes	Information from abstract. Email sent to authors but no response from them.

OSA: obstructive sleep apnoea; SDB: sleep disordered breathing.

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

Bousata 2016

Study name	Apnelog study: effects of oropharyngeal exercises on maximum anterior and posterior tongue strength and endurance in patients with severe OSA.
Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: severe OSA.</p> <p>Exclusion criteria: not available.</p>
Interventions	<p>Intervention:</p> <ul style="list-style-type: none"> Daily oropharyngeal exercises (therapy) plus CPAP. <p>Comparator:</p> <ul style="list-style-type: none"> CPAP (control).
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> Maximum anterior and posterior tongue strength and endurance.

Bousata 2016 (Continued)

Secondary Outcome Measures:

- Apnea Hypopnea Index.
- Daytime sleepiness (ESS).
- Oxygen Desaturation Index.

Measurements: 4-6 months after treatment.

Starting date	Study Start Date: not available. Estimated/actual Study Completion Date: not available.
Contact information	J. Bousata. Cliniques Universitaires Saint Luc, Brussels, Belgium.
Notes	Study finished but results pending for publication. Information from abstract to congress and from authors.

DRKS00015632

Study name	Prospective controlled and randomised pilot study of the effect of an intensive orofacial exercise therapy in obstructive sleep apnoea patients.
Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: patients from 18 to 80 years old, with a history of low-grade or moderate-grade OSA diagnosed by the history and clinical examination in combination with cardiorespiratory polygraphy; clinical symptoms with bronchopathy (snoring) and/or externally observed respiratory distress and/or daytime fatigue and a polygraphically proven AHI between 10/hour and 30/hour.</p> <p>Exclusion criteria: patients with neurological diseases (especially dementia, Parkinson's disease, multiple sclerosis, state after Apoplex, including all neurodegenerative diseases); patients with a predominantly central form of sleep apnoea; patients with state after palatal, tonsillar, maxillary, mandibular, pharyngeal and laryngeal exacerbations due to a malignancy (state after tonsillectomy or state after tonsillectomy in childhood or adulthood is not an exclusion criterion); patients with state after uvulopharyngopalatoplasty for the treatment of OSA; patients with state after radiotherapy and / or chemotherapy for malignant tumour of the head and neck; patients under current cPAP or aPAP therapy; pregnancy.</p>
Interventions	<p>Intervention:</p> <ul style="list-style-type: none"> • A specially designed exercise therapy for a period of 6 weeks 3 times a week (Mon-Wed-Fri) at the premises of the Speech Therapy Institute / ENT-University Medical Center Mainz for 35 minutes each. <p>Comparator:</p> <ul style="list-style-type: none"> • Participants in the control group should not perform targeted exercise therapy, but should implement a non-specific exercise therapy with chewing gum over one hour daily and increased mouth movement while eating for this 6-week period.
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> • Apnea Hypopnea Index. <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> • Daytime sleepiness (ESS). • Sleep quality (PSQI).

DRKS00015632 (Continued)

Starting date **Study Start Date:** 24 September 2018.
Estimated Study Completion Date: not available. Recruitment ongoing.

Contact information Thomas Brauer. University Medical Center Mainz. Germany.

Notes Information from DRKS - German Clinical Trials Register.

NCT02502942

Study name Effects of Upper Airway Muscle Training on Obstructive Sleep Apnea (OSA).

Methods Parallel, RCT.

Participants **Inclusion criteria:** 18 to 79 years old (adult, older Adult); prior diagnosis of OSA with AHI higher than 10 events/hour; PAP group: subjects who have been on PAP treatment for at least 3 months, with good compliance (at least 4 hours a day and use PAP for longer than 70% of the time).

Untreated group: untreated subjects with generally mild OSA as defined by AHI lower than 20 events/hour and nadir SaO₂ higher than 70%. Additionally, investigators will also recruit OSA subjects of all severities who have previously tried but are not currently using PAP.

Oral appliance treatment group: subjects have residual AHI higher than 10 events/hour with oral appliance therapy.

Exclusion Criteria: in those with untreated sleep apnoea, severe sleepiness with current ESS higher than 18 or history of motor vehicle accident due to obstructive sleep apnoea; taking medications classified as a muscle relaxant; pregnant women; psychiatric disorder, other than mild and controlled depression, e.g. schizophrenia, bipolar disorder, major depression, panic or anxiety disorders; current smokers, alcohol (higher than 3 oz/day) or use of illicit drugs. More than 10 cups of beverages with caffeine (coffee, tea, soda/pop) per day. Unstable cardiac disease (e.g. CHF). Pulmonary disease (apart from well-controlled mild asthma and OSA). Systemic neuromuscular disease. Other systemic disease that affects breathing (e.g. stroke) or those with expected survival lower than 1 year. Poor oral condition, including: active periodontal disease, loose or broken teeth, lack of eight teeth in each arch, active TMJ dysfunction. Known allergy to oral appliance components.

Interventions

Intervention:

- Upper airway muscle exercise for six weeks. The exercises include 4 steps: step 1 is to put on an individualized fitted oral retainer device to guide the exercise; step 2 is to push the tongue towards the hard palate to press the movable part of the oral retainer device for 4 minutes; step 3 is to touch the hard palate using the middle part of the tongue, hold for 10 seconds and repeat it for 4 minutes; step 4 is to remove the retainer device and brush the tongue gently on both sides for 2 minutes. The exercise will take 20 minutes a day (10 minutes in the morning and 10 minutes in the afternoon/evening).

Comparator:

- Sham exercise.

Outcomes

Primary Outcome Measures:

- Apnea Hypopnea Index.

Secondary Outcome Measures:

- Daytime sleepiness (ESS).
- Sleep quality (PSQI).

NCT02502942 (Continued)

- Subjective quality of life (SF-36).
- Neurocognitive function (PVT).
- Upper airway anatomy (acoustic pharyngostomy).
- Tongue strength and endurance (IOPI).

Measurements: 6 weeks after treatment.

Starting date	Study Start Date: August 2015. Actual Study Completion Date: 24 June 2019
Contact information	Atul Malhotra, MD. University of California, San Diego.
Notes	Information from ClinicalTrials.gov.

NCT02568761

Study name	Injection snoreplasty and oropharyngeal exercises: two therapeutic options in the management of snoring and obstructive sleep apnoea syndrome.
Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: 18 years and older; evaluated at the Snoring and Apnea Ambulatory of Hospital de Clinicas de Porto Alegre with clinical complaints related to snoring and sleep apnoea with polysomnography held within 90 days before the inclusion, evidencing index of apnoea/hypopnoea from 0 to 30 events per hour of sleep (snoring, mild and moderate apnoea), without showing desaturation below 90% for time periods longer than 60 minutes; patient without specific prior treatment for snoring and/or apnoea.</p> <p>Exclusion criteria: prior pharyngeal surgery to treat snoring or OSA; BMI higher than 35Kg/m²; nasal or pharyngeal anatomical obstruction higher than 50% of the light; craniofacial deformity; pregnancy; major illnesses associated; ethanol allergy history; absence of a companion to observe the intensity of snoring; patients with no ability to understand the issues (understanding of the proposed procedure and consent form).</p>
Interventions	<p>Intervention: oropharyngeal exercises.</p> <p>Weekly sessions of myofunctional exercises under the supervision of a qualified professional, lasting about 30 minutes each, combined with daily exercises without supervision for a period of 3 months. Myofunctional isometric and isotonic exercises of the soft palate, pharyngeal side walls, face and tongue.</p> <p>Comparator: non-surgical treatment.</p> <p>Non-surgical treatment involving the injection of 1.5 mL of 50% ethanol (1 mL of 99.5% ethanol diluted in 1 mL of 2% xylocaine) into the upper palate. 0.5 mL of the solution will be implemented in three different regions of the submucosal layer of the soft palate, one median and two paramedians.</p>
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> • Snoring Intensity (measured in decibels). • Snoring Index (number of snores per hour of sleep). <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> • Sleep quality (PSQI). • Sleep quality of the participant room partner (PSQI).

NCT02568761 (Continued)

- Daytime sleepiness (ESS).

Measurements: 3 months after treatment.

Starting date	Study Start Date: August 2015. Estimated Study Completion Date: July 2017.
Contact information	Caroline P Royer. Serviço de Otorrinolaringologia do Hospital de Clínicas de Porto Alegre.
Notes	Information from ClinicalTrials.gov.

NCT03061019

Study name	Comparison of Two Oral Myofunctional Reeducation Methods for Children With Obstructive Sleep Apnea Before Adenotonsillectomy: a Randomized Controlled Trial.
Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: 5 to 14 years old; present signs of obstructive sleep apnoea: snoring, apnoea / respiratory pauses audible by the entourage (objectivised by a score, to the hierarchical questionnaire of severity of Spruyt and Gozal, greater than or equal to 2,72; be programmed for adenoidectomy, tonsillectomy or adeno-tonsillectomy within 3 months (or more).</p> <p>Exclusion criteria: present with a craniofacial syndrome or a severe medical condition with complex medical management; present with an abnormality of the neuromuscular tone (such as Duchenne myopathy or cerebral palsy); receive orthodontic therapy during the study; have a class III malocclusion (mandibular prognathic type), for which a propulsion oral appliance is contraindicated because it may aggravate mandibular prominence (maxillary deficiency is not a exclusion criterion); a non-nutritive oral habit such as digital sucking (or pacifier) that persists because it interferes with oral reeducation, and is a contraindication to orthodontic treatments. Children who have recently stopped such a habit may be included in the study.</p>
Interventions	<p>Intervention: daily oral exercises (plus nasal hygiene).</p> <p>Parents and participants of this group will receive instructions for nasal and oral myofunctional exercises, to perform at home each day, for 5 to 10 minutes. A booklet (measure of adherence) and a phone application for Android/Apple with descriptions/videos of those exercises will be given to them. These exercises will include nasal hygiene procedures, nasal cartilage exercises, lingual posture rehabilitation exercises, lip tone enhancement exercises, and swallowing rehabilitation exercises.</p> <p>Comparators:</p> <ul style="list-style-type: none"> • Using of a flexible oral appliance during quiet activities and sleep (plus nasal hygiene). <p>Parents and participants will be instructed in wearing the soft/flexible oral appliance and how to perform nasal hygiene in order to better tolerate the device. The oral appliance comes in several sizes, adapted to the age of the child; it is constructed in a soft elastomer material, in a position of slight propulsion and opening of the mandible to help clear the pharynx. It has a ramp to guide the tongue in a good position, a labial screen to stretch the labial strap and prevent the tongue from protruding between front teeth.</p> <ul style="list-style-type: none"> • Using nasal hygiene alone (control group). <p>Parents and Participants of this group will be reminded of the nasal hygiene procedures (application of saline in each nostril 3 times a day), and given a diary to report daily use.</p>
Outcomes	Primary Outcome Measures:

NCT03061019 (Continued)

- Apnea Hypopnea Index.
- Oxygen Desaturation Index.
- Flow limitation index.

Secondary Outcome Measures:

- Oral muscles strength.
- Nasal resistance.
- Quality of life OSA 18 questionnaire, consisting of an 18-items score and VAS (from 0 to 10), filled by parents.

Measurements: 3 months after treatment.

Starting date	Study Start Date: 1 March 2017. Estimated Study Completion Date: 31 December 2019.
Contact information	Nelly Huynh. CHU Sainte Justine, Université de Montréal.
Notes	Information from ClinicalTrials.gov.

NCT03753633

Study name	Efficiency of speech therapy in resistant hypertensive patients with mild obstructive sleep apnoea syndrome.
Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: patients in follow-up in the Hypertension Program (ProHart) at Hospital Univer-sitário Clementino Fraga Filho - UFRJ at least six months; patients with resistant hypertension and mild obstructive sleep apnoea detected by polysomnography; all participants that give written in-formed consent.</p> <p>Exclusion criteria: age older than 85 years; cognitive deficit that prevents speech therapy; severe clinical events in the last 6 months; refusal of the patient to participate in the study; pregnancy; pri-or and regular use of CPAP; Clinical data suggestive of neurological disease with cognitive and / or motor sequelae, craniofacial malformation, severe upper airway obstruction, neuromuscular dis-ease, users of hypnotic drugs.</p>
Interventions	<p>Intervention: speech therapy group.</p> <p>Patients will be treated with speech therapy, once a week, for 40 minutes for 12 weeks. Oropharyn-geal exercises will be performed under the supervision of a speech therapist. Patients will perform the oropharyngeal exercises at home every day.</p> <p>Comparator: sham comparator control group.</p> <p>Patients will perform inspiratory and expiratory exercises recruiting diaphragmatic muscle.</p>
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> • Daytime sleepiness (ESS). • Quality of life (SF-36). • Sleep quality (PSQI). <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> • Apnea Hypopnea Index.

NCT03753633 (Continued)

Measurements: 12 weeks after treatment.

Starting date	Study Start Date: 1 October 2017. Estimated Study Completion Date: December 2019.
Contact information	Alessandra B de Sousa. Hospital Universitário Clementino Fraga Filho Rio de Janeiro, Brazil.
Notes	Information from ClinicalTrials.com.

NCT04053153

Study name	Effects of upper airway muscle training on obstructive sleep apnoea severity.
Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: 21 to 50 years old with mild to moderate OSA; diagnosed by a physician, based upon interpretation of data recorded on a take home sleep study; BMI lower than 30 kg/m²; mild to moderate OSA; AHI of 5-30.</p> <p>Exclusion criteria: apnoea hypopnoea index on overnight sleep study higher than 30 per hour; currently practices didgeridoo; consumes more than 2 alcoholic beverages per day; history of chronic lung disease (e.g., COPD, asthma); oral maxillofacial issue or craniofacial musculoskeletal conditions; any treatment for OSA (current or past); mobile device use frequency less than once per week; homelessness; no reliable transportation to assessment sessions; planned social/family/employment obligations that would limit participant from engaging in Asate Silent Sleep training during the intervention period; significant upper extremity weakness/paralysis or pain limiting ability to hold the medical didgeridoo; uncorrected low vision or blindness; deafness; no Internet connection/Chrome browser/mobile devices with iOS and Android; no USB port in computer; pregnancy.</p>
Interventions	<p>Intervention:</p> <ul style="list-style-type: none"> • Use of musical instrument based on the medical didgeridoo. <p>Comparator:</p> <ul style="list-style-type: none"> • Sham comparator: use of sham musical instrument.
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> • Apnea Hypopnea Index. <p>Secondary Outcome Measures:</p> <p>None.</p>
Starting date	Study Start Date: 1 October 2019. Estimated Study Completion Date: 31 July 2020.
Contact information	Clete A. Kushida, Division Chief/Medical Director, Stanford University.
Notes	Information from ClinicalTrials.gov.

NCT04169984

Study name	Myofunctional Therapy in Patients With Mild-moderate Sleep Apnea.
Methods	Parallel, RCT.
Participants	<p>Inclusion criteria: patients over 18 and under 80 years old, with AHI from 5 to 29 assessed by a respiratory polygraphy, and absence of daytime sleepiness (ESS lower than 12).</p> <p>Exclusion criteria: refractory high blood pressure (blood pressure that is not controlled with three antihypertensive drugs, including a diuretic); ictus, transient ischaemic attack, neuromuscular diseases, acute coronary syndrome or hospitalisation for worsening heart failure, in the previous 30 days; professional drivers, profession of risk or respiratory failure; previous surgical intervention for the treatment of sleep apnoea (those patients who have refused treatment with CPAP or mandibular advancement devices after 1 month of not using them, could be included).</p>
Interventions	<p>Intervention: myofunctional therapy.</p> <p>Comparator: sham comparator.</p>
Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> • Apnea Hypopnea Index. <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> • Change in snoring. • Change in oximeter parameters. • Degree of therapeutic adherence. • Quality of life (SF-36). • Sleep quality (PQSI). • Daytime sleepiness (ESS).
Starting date	<p>Study Start Date: June 2020.</p> <p>Estimated Study Completion Date: June 2022.</p>
Contact information	Irene M Cano Pumarega. Hospital Universitario Ramón y Cajal, Pneumology Department. Madrid. Spain.
Notes	Information from ClinicalTrials.com.

UMIN000035476

Study name	Myofunctional therapy effective for obstructive sleep apnoea in elderly patients.
Methods	Cross-over, RCT.
Participants	<p>Inclusion criteria: patients 65 years and older who are attending Geriatrics and General medicine at Osaka University, and who were suspected and diagnosed as OSA.</p> <p>Exclusion criteria: patients with cognitive impairment, those under hyperdialysis, those with more CSA than OSA.</p>
Interventions	<p>Intervention:</p> <ul style="list-style-type: none"> • Exercise using 'Fukimodoshi': a Japanese whistle, which is usually used as a toy for children. <p>Comparators:</p>

UMIN000035476 (Continued)

- Exercise using a device for exercise of the tongue, which is used to prevent aspiration pneumonia.
- Pronouncing vowels, elevation of the mouth muscles, suction movements.

Outcomes	<p>Primary Outcome Measures:</p> <ul style="list-style-type: none"> • Portable sleep monitor. • Polysomnography. • Perum miRNA. <p>Secondary Outcome Measures:</p> <ul style="list-style-type: none"> • Cognitive function. • Motor function. • PRD.
Starting date	<p>Study Start Date: 1 February 2019.</p> <p>Estimated Study Completion Date: not available.</p>
Contact information	Kazuhiro Hongyo. Osaka University. Geriatrics and General medicine.
Notes	Information from UMIN-CTR.

Abbreviations: AHI: Apnea-Hypopnea Index; BMI: Body Mass Index; CHF: Congestive Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; CPAP: Continuous Positive Airway Pressure; ENT: ear, nose and throat; ESS: Epworth Sleepiness Scale; IOPI: Iowa Oral Performance Instrument; ODI: oxygen desaturation index; OSA: Obstructive Sleep Apnea; PAP: positive airway pressure; PSQI: Pittsburgh Sleep Quality Index; PRD: Periodic Repolarization Dynamics; PVT: psychomotor vigilance test; RCT: Randomised Clinical Trial; SaO₂: oxygen desaturation; SD: Standard Deviation; SMD: Standardised Mean Difference; SF-36: 36-item Short Form health survey; VAS: visual analogue scale; WHOQOL-BREF: World Health Organization Quality of Life




DATA AND ANALYSES

Comparison 1. Myofunctional therapy versus sham therapy

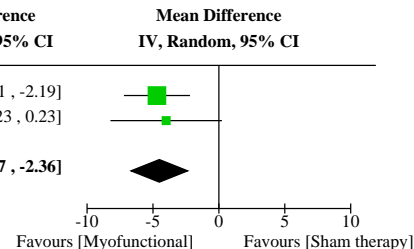
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months	2	82	Mean Difference (IV, Random, 95% CI)	-4.52 [-6.67, -2.36]
1.2 Sleep quality (PSQI): endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3 AHI: endpoint score. Follow-up: 3 months	2	82	Mean Difference (IV, Fixed, 95% CI)	-13.20 [-18.48, -7.93]
1.4 Snoring frequency (number of classified snores > 60 dBA per hour of sleep): change from baseline. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.5 Snoring frequency (subjective visual analogue scale): endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.6 Snoring intensity: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected


Analysis 1.1. Comparison 1: Myofunctional therapy versus sham therapy, Outcome 1: Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months

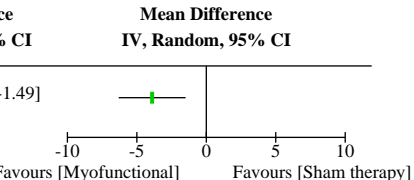
Study or Subgroup	Myofunctional therapy			Sham therapy			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Diaferia 2017	7.5	3.7	27	12.2	5.2	24	74.0%	-4.70 [-7.21, -2.19]	
Guimaraes 2009	8	6	16	12	6	15	26.0%	-4.00 [-8.23, 0.23]	
Total (95% CI)			43			39	100.0%	-4.52 [-6.67, -2.36]	

Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%
 Test for overall effect: Z = 4.11 (P < 0.0001)
 Test for subgroup differences: Not applicable

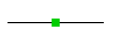
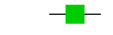



Analysis 1.2. Comparison 1: Myofunctional therapy versus sham therapy, Outcome 2: Sleep quality (PSQI): endpoint score. Follow-up: 3 months

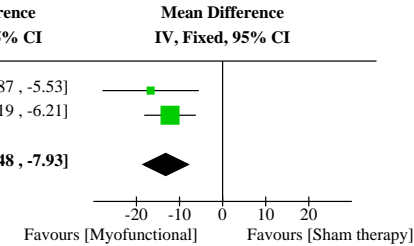
Study or Subgroup	Favours [Myofunctional]			Sham therapy			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Guimaraes 2009	6.9	2.5	16	10.8	4.1	15		-3.90 [-6.31, -1.49]	



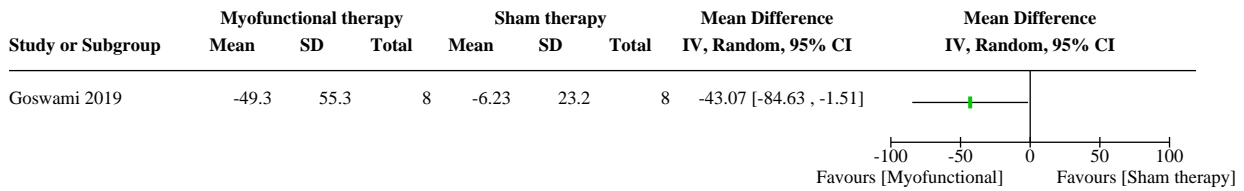
Analysis 1.3. Comparison 1: Myofunctional therapy versus sham therapy, Outcome 3: AHI: endpoint score. Follow-up: 3 months

Study or Subgroup	Favours [Myofunctional]			Sham therapy			Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Diaferia 2017	13.9	18.5	27	30.6	21.8	24	22.3%	-16.70 [-27.87, -5.53]	
Guimaraes 2009	13.7	8.5	16	25.9	8.5	15	77.7%	-12.20 [-18.19, -6.21]	
Total (95% CI)			43			39	100.0%	-13.20 [-18.48, -7.93]	

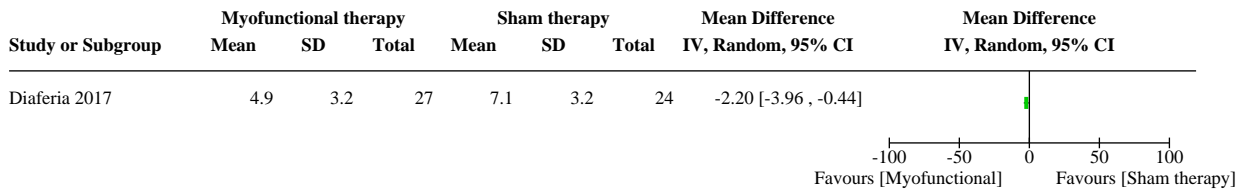
Heterogeneity: Chi² = 0.48, df = 1 (P = 0.49); I² = 0%
 Test for overall effect: Z = 4.90 (P < 0.00001)
 Test for subgroup differences: Not applicable



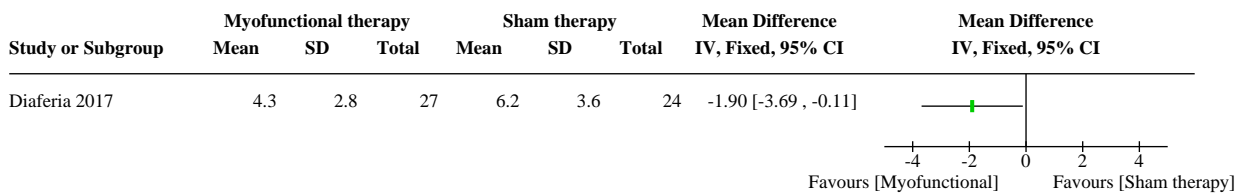
Analysis 1.4. Comparison 1: Myofunctional therapy versus sham therapy, Outcome 4: Snoring frequency (number of classified snores > 60 dBA per hour of sleep): change from baseline. Follow-up: 3 months



Analysis 1.5. Comparison 1: Myofunctional therapy versus sham therapy, Outcome 5: Snoring frequency (subjective visual analogue scale): endpoint score. Follow-up: 3 months



Analysis 1.6. Comparison 1: Myofunctional therapy versus sham therapy, Outcome 6: Snoring intensity: endpoint score. Follow-up: 3 months

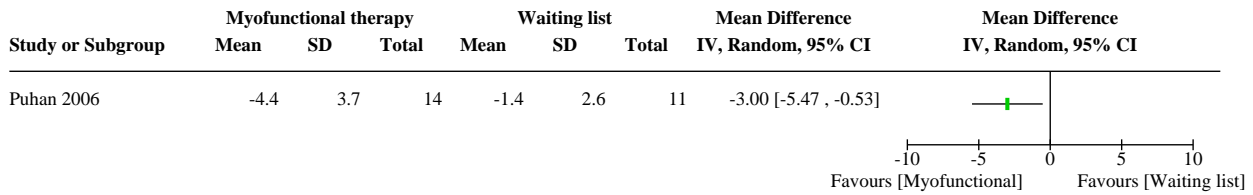


Comparison 2. Myofunctional therapy versus waiting list

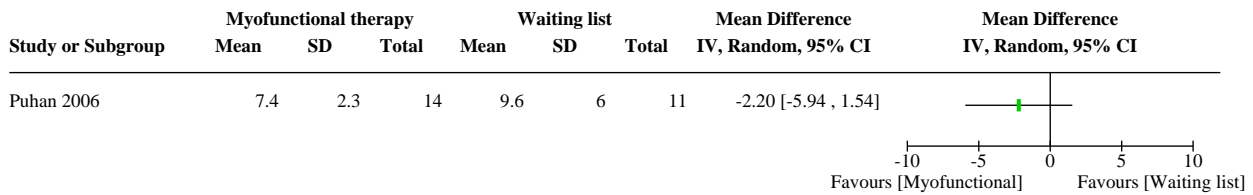
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Daytime sleepiness (ESS): change from baseline. Follow-up: 4 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.2 Daytime sleepiness (ESS): endpoint score. Follow-up: 4 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.3 Sleep quality (PSQI): change from baseline. Follow-up: 4 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.4 Sleep quality (PSQI): endpoint score. Follow-up: 4 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2.5 AHI: change from baseline. Follow-up: 4 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.6 AHI: endpoint score. Follow-up: 4 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

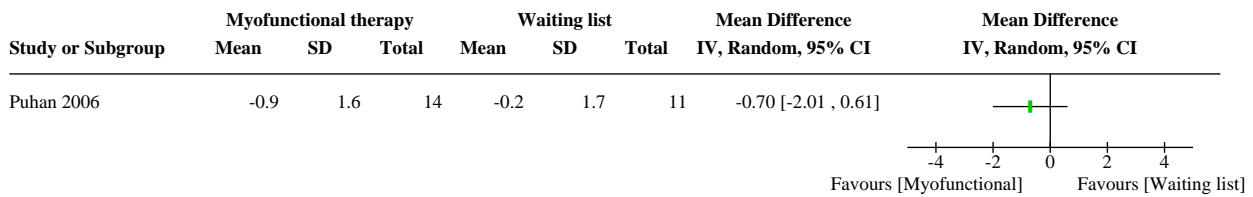
Analysis 2.1. Comparison 2: Myofunctional therapy versus waiting list, Outcome 1: Daytime sleepiness (ESS): change from baseline. Follow-up: 4 months



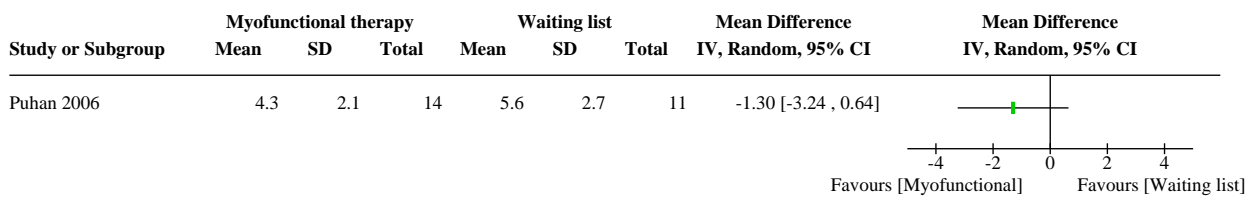
Analysis 2.2. Comparison 2: Myofunctional therapy versus waiting list, Outcome 2: Daytime sleepiness (ESS): endpoint score. Follow-up: 4 months



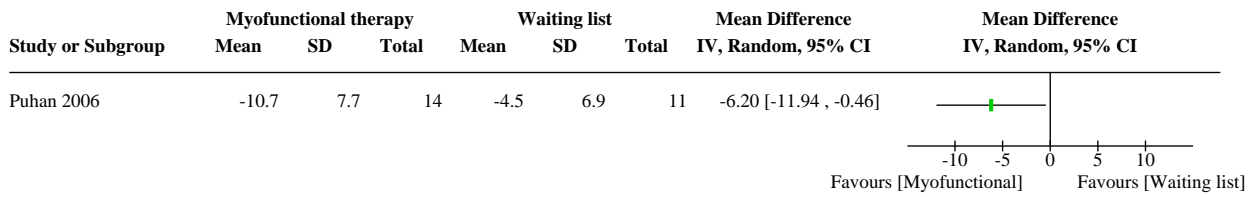
Analysis 2.3. Comparison 2: Myofunctional therapy versus waiting list, Outcome 3: Sleep quality (PSQI): change from baseline. Follow-up: 4 months



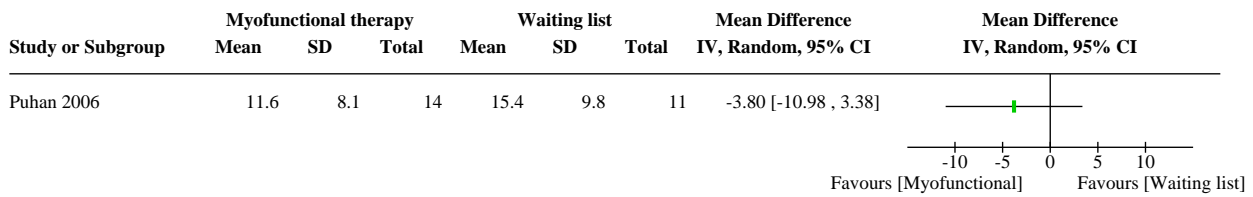
Analysis 2.4. Comparison 2: Myofunctional therapy versus waiting list, Outcome 4: Sleep quality (PSQI): endpoint score. Follow-up: 4 months



Analysis 2.5. Comparison 2: Myofunctional therapy versus waiting list, Outcome 5: AHI: change from baseline. Follow-up: 4 months



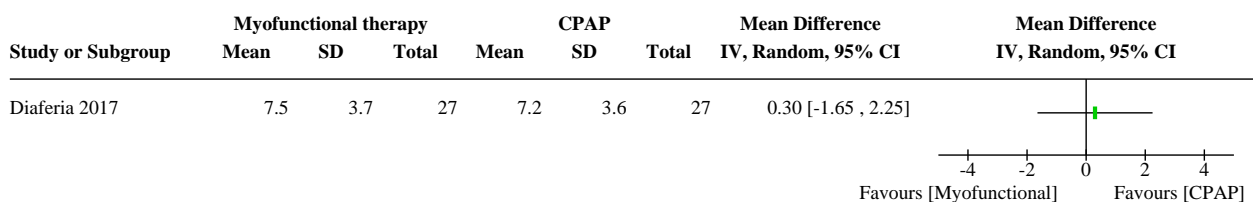
Analysis 2.6. Comparison 2: Myofunctional therapy versus waiting list, Outcome 6: AHI: endpoint score. Follow-up: 4 months



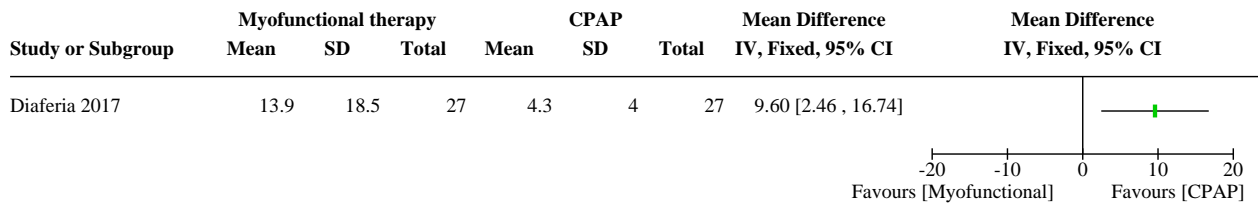
Comparison 3. Myofunctional therapy versus CPAP

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.2 AHI: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.3 Snoring frequency: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.4 Snoring intensity: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

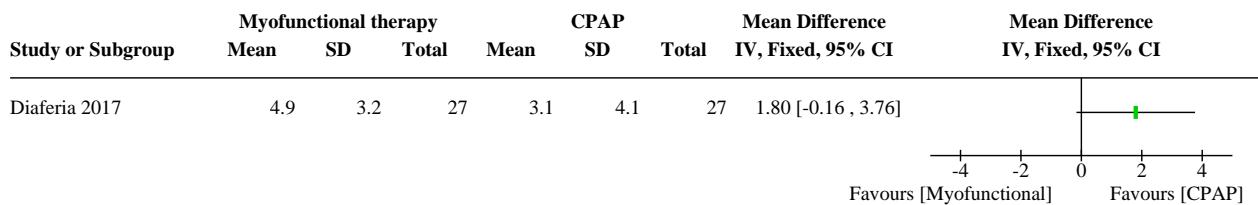
Analysis 3.1. Comparison 3: Myofunctional therapy versus CPAP, Outcome 1: Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months



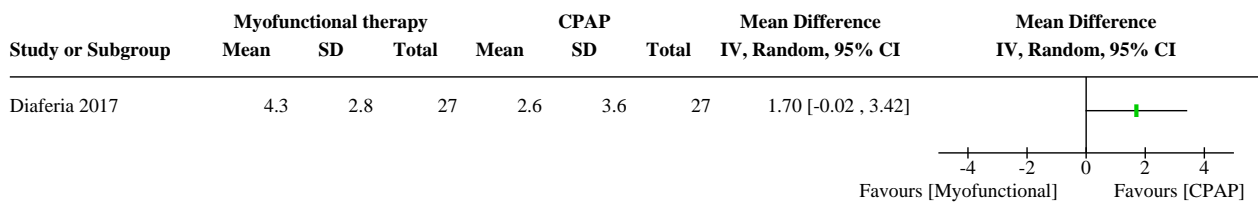
Analysis 3.2. Comparison 3: Myofunctional therapy versus CPAP, Outcome 2: AHI: endpoint score. Follow-up: 3 months



Analysis 3.3. Comparison 3: Myofunctional therapy versus CPAP, Outcome 3: Snoring frequency: endpoint score. Follow-up: 3 months



Analysis 3.4. Comparison 3: Myofunctional therapy versus CPAP, Outcome 4: Snoring intensity: endpoint score. Follow-up: 3 months



Comparison 4. Myofunctional therapy versus CPAP + Myofunctional therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.2 AHI: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.3 Snoring frequency: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.4 Snoring intensity: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 4.1. Comparison 4: Myofunctional therapy versus CPAP + Myofunctional therapy, Outcome 1: Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months

Study or Subgroup	Myofunctional			CPAP + Myofunctional therapy			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Diaferia 2017	7.5	3.7	27	7.3	5.7	22	0.20 [-2.56, 2.96]	

Analysis 4.2. Comparison 4: Myofunctional therapy versus CPAP + Myofunctional therapy, Outcome 2: AHI: endpoint score. Follow-up: 3 months

Study or Subgroup	Myofunctional			CPAP + Myofunctional therapy			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Diaferia 2017	13.9	18.5	27	3.4	2.7	22	10.50 [3.43, 17.57]	

Analysis 4.3. Comparison 4: Myofunctional therapy versus CPAP + Myofunctional therapy, Outcome 3: Snoring frequency: endpoint score. Follow-up: 3 months

Study or Subgroup	Myofunctional			CPAP + Myofunctional therapy			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Diaferia 2017	4.9	3.2	27	3.9	4.2	22	1.00 [-1.13, 3.13]	

Analysis 4.4. Comparison 4: Myofunctional therapy versus CPAP + Myofunctional therapy, Outcome 4: Snoring intensity: endpoint score. Follow-up: 3 months

Study or Subgroup	Myofunctional			CPAP + Myofunctional therapy			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Diaferia 2017	4.3	2.8	27	3.1	3.2	22	1.20 [-0.50, 2.90]	

Comparison 5. Myofunctional therapy versus respiratory exercises + nasal dilator strip

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.2 Sleep quality (PSQI): endpoint score. Follow-up: 3 months	2	97	Mean Difference (IV, Random, 95% CI)	-1.94 [-3.17, -0.72]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.3 AHI: endpoint score. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 5.1. Comparison 5: Myofunctional therapy versus respiratory exercises + nasal dilator strip, Outcome 1: Daytime sleepiness (ESS): endpoint score. Follow-up: 3 months

Study or Subgroup	Myofunctional therapy			Respir exerc +Nasal strip			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Kayamori 2015	8.9	4.4	30	8.7	5.8	28	0.20 [-2.46, 2.86]	

Analysis 5.2. Comparison 5: Myofunctional therapy versus respiratory exercises + nasal dilator strip, Outcome 2: Sleep quality (PSQI): endpoint score. Follow-up: 3 months

Study or Subgroup	Myofunctional therapy			Respir exerc +Nasal strip			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
Ieto 2015	4	2.6	19	6.4	3.9	20	34.9%	-2.40 [-4.47, -0.33]	
Kayamori 2015	4.3	2.5	30	6	3.3	28	65.1%	-1.70 [-3.21, -0.19]	
Total (95% CI)			49			48	100.0%	-1.94 [-3.17, -0.72]	

Heterogeneity: Tau² = 0.00; Chi² = 0.29, df = 1 (P = 0.59); I² = 0%
Test for overall effect: Z = 3.12 (P = 0.002)
Test for subgroup differences: Not applicable

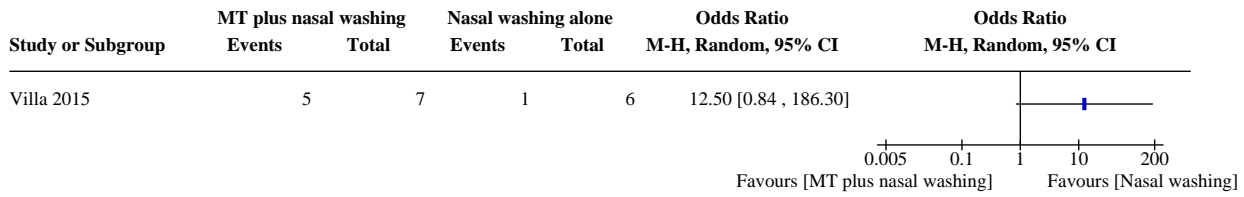
Analysis 5.3. Comparison 5: Myofunctional therapy versus respiratory exercises + nasal dilator strip, Outcome 3: AHI: endpoint score. Follow-up: 3 months

Study or Subgroup	Myofunctional therapy			Respir exerc +Nasal strip			Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Kayamori 2015	15	10.3	30	18.8	10.1	28	-3.80 [-9.05, 1.45]	

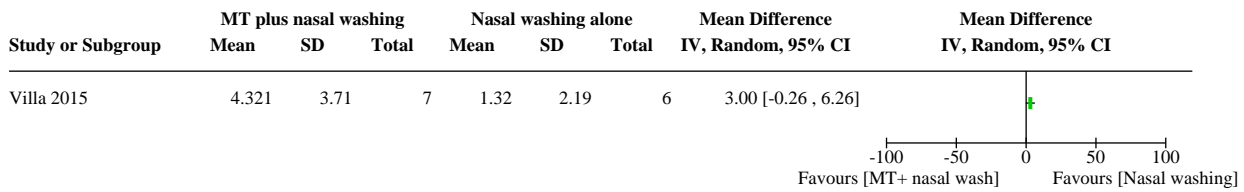
Comparison 6. Myofunctional therapy plus nasal washing versus nasal washing alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 AHI decrease to below 5	1		Odds Ratio (M-H, Random, 95% CI)	Totals not selected
6.2 AHI score change	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.3 AHI score after treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

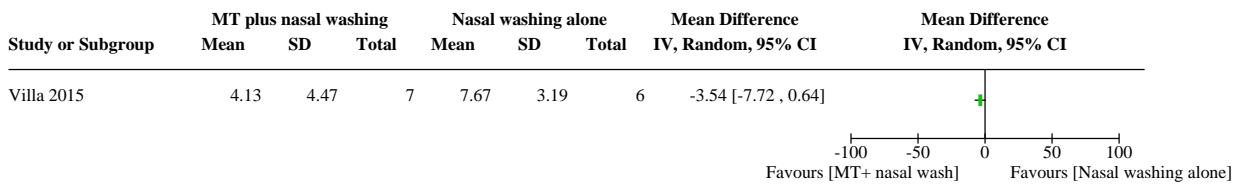
Analysis 6.1. Comparison 6: Myofunctional therapy plus nasal washing versus nasal washing alone, Outcome 1: AHI decrease to below 5



Analysis 6.2. Comparison 6: Myofunctional therapy plus nasal washing versus nasal washing alone, Outcome 2: AHI score change



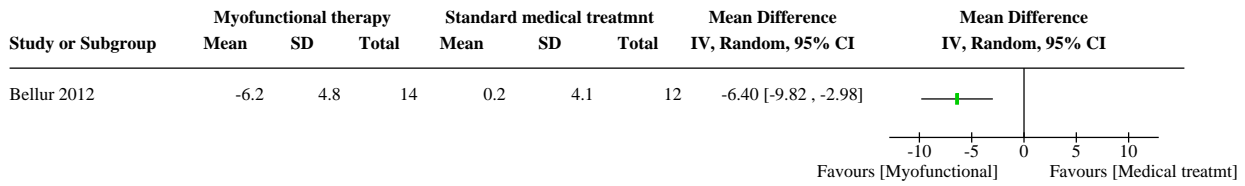
Analysis 6.3. Comparison 6: Myofunctional therapy plus nasal washing versus nasal washing alone, Outcome 3: AHI score after treatment



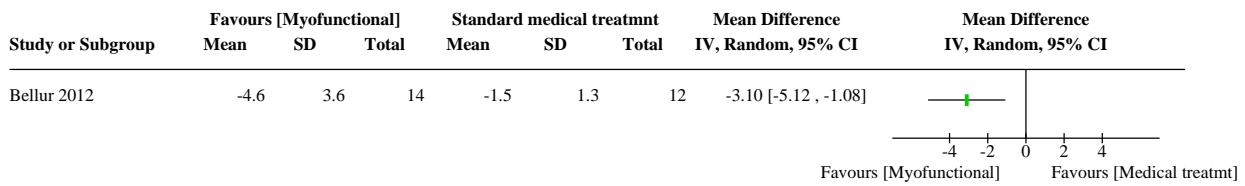
Comparison 7. Myofunctional therapy versus Standard medical treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Daytime sleepiness (ESS): change from baseline. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.2 Sleep quality (PSQI): change from baseline. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.3 Snoring frequency: change from baseline. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7.4 Snoring intensity: change from baseline. Follow-up: 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

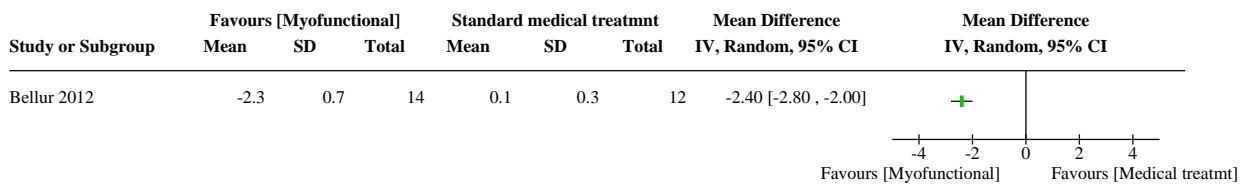
Analysis 7.1. Comparison 7: Myofunctional therapy versus Standard medical treatment, Outcome 1: Daytime sleepiness (ESS): change from baseline. Follow-up: 3 months



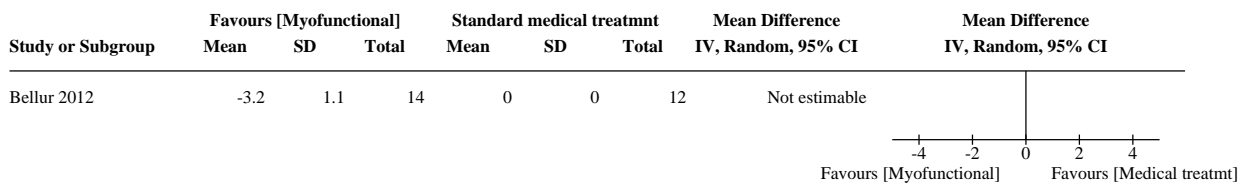
Analysis 7.2. Comparison 7: Myofunctional therapy versus Standard medical treatment, Outcome 2: Sleep quality (PSQI): change from baseline. Follow-up: 3 months



Analysis 7.3. Comparison 7: Myofunctional therapy versus Standard medical treatment, Outcome 3: Snoring frequency: change from baseline. Follow-up: 3 months



Analysis 7.4. Comparison 7: Myofunctional therapy versus Standard medical treatment, Outcome 4: Snoring intensity: change from baseline. Follow-up: 3 months



ADDITIONAL TABLES

Table 1. Summary of characteristics of included studies

Study	Comparators	Duration of intervention (months)	Participants (N) (% men)	Age Mean	ESSMean	PSQI Mean	AHIMean	BMI Mean
Bellur 2012	Standard medical treatment	3	26	50.7	8.9	7.4	40.9	31.8
Erturk 2013	Standard medical treatment Inspiratory muscle training	3	41	NA	NA	NA	NA	NA
Puhan 2006	Waiting list	4	25 (84%)	48.6	11.5	5.5	21.2	25.8
Kayamori 2015	Respiratory exercises plus nasal dilator strip	3	60 (59%)	45.9	10.1	6.6	18.4	28.8
Guimaraes 2009	Sham therapy	3	39 (68%)	49.6	14	10.5	22.4	30.3
Diaferia 2017	Sham therapy CPAP CPAP plus Myofunctional Therapy	3	140 (100%)	45.5	12.6	NA	30.9	27.6
Leto 2015	Respiratory exercises plus nasal dilator strip	3	39 (56%)	46.5	9.2	6.4	15.3	28.2
Goswami 2019	Sham therapy	3	16 (63%)	51	7.5	NA	8.7	27.5
Villa 2015	Nasal washing alone	2	13 (88%)	4.8	NA	NA	16.8	NA

Abbreviations: AHI: Apnoea Hypopnoea Index; BMI: body mass index; CPAP: Continuous Positive Airway Pressure; ESS: Epworth Sleepiness Scale; MT: Myofunctional therapy; NA: Not available; PSQI: Pittsburgh Sleep Quality Index. Means calculated for baseline values.

APPENDICES

Appendix 1. Database search strategies

Cochrane Airways Trials Register via CRS

#	search terms
1	MESH DESCRIPTOR Sleep Apnea Syndromes EXPLODE ALL AND INSEGMENT
2	((sleep* or nocturnal) NEAR2 (apnoea* or apnoea*)):ti,ab,kw AND INSEGMENT
3	(sleep* NEAR2 disordered NEAR2 breathing):ti,ab,kw AND INSEGMENT
4	((sleep* or nocturnal) NEAR2 (hypopnea* or hypopnoea* or hypo-apnoea* or hypo-apnea* or apneic-hypopneic or apnoeic-hypopnoeic)):ti,ab,kw AND INSEGMENT
5	(OSA or SAHS):ti,ab,kw AND INSEGMENT
6	OSAHS:ti,ab,kw AND INSEGMENT
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6
8	MESH DESCRIPTOR Myofunctional Therapy AND INSEGMENT
9	(myofunction* or myolog* or myotherap*):ti,ab,kw AND INSEGMENT
10	MESH DESCRIPTOR Oropharynx EXPLODE ALL AND INSEGMENT
11	MESH DESCRIPTOR Tongue AND INSEGMENT
12	MESH DESCRIPTOR Palate, Soft AND INSEGMENT
13	(oropharyngeal* or oropharynx or orofacial* or tongue* or soft palate or palatial or oral):ti,ab,kw AND INSEGMENT
14	#10 OR #11 OR #12 OR #13
15	MESH DESCRIPTOR Exercise Therapy EXPLODE ALL AND INSEGMENT
16	(exercise* or therap*):ti,ab,kw AND INSEGMENT
17	#15 OR #16
18	#17 AND #14
19	#8 OR #9 OR #18
20	#19 AND #7
21	INREGISTER
22	#20 AND #21

CENTRAL via CRS web

#	search terms
1	MESH DESCRIPTOR Sleep Apnea Syndromes EXPLODE ALL AND CENTRAL:TARGET
2	((sleep* or nocturnal) NEAR2 (apnoea* or apnoea*)):ti,ab,kw AND CENTRAL:TARGET
3	(sleep* NEAR2 disordered NEAR2 breathing):ti,ab,kw AND CENTRAL:TARGET
4	((sleep* or nocturnal) NEAR2 (hypopnea* or hypopnoea* or hypo-apnoea* or hypo-apnea* or apneic-hypopneic or apnoeic-hypopnoeic)):ti,ab,kw AND CENTRAL:TARGET
5	(OSA or SAHS):ti,ab,kw AND CENTRAL:TARGET
6	OSAHS:ti,ab,kw AND CENTRAL:TARGET
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6 AND CENTRAL:TARGET
8	MESH DESCRIPTOR Myofunctional Therapy AND CENTRAL:TARGET
9	(myofunction* or myolog* or myotherap*):ti,ab,kw AND CENTRAL:TARGET
10	MESH DESCRIPTOR Oropharynx EXPLODE ALL AND CENTRAL:TARGET
11	MESH DESCRIPTOR Tongue AND CENTRAL:TARGET
12	MESH DESCRIPTOR Palate, Soft AND CENTRAL:TARGET
13	(oropharyngeal* or oropharynx or orofacial* or tongue* or soft palate or palatial or oral):ti,ab,kw AND CENTRAL:TARGET
14	#10 OR #11 OR #12 OR #13 AND CENTRAL:TARGET
15	MESH DESCRIPTOR Exercise Therapy EXPLODE ALL AND CENTRAL:TARGET
16	(exercise* or therap*):ti,ab,kw AND CENTRAL:TARGET
17	#15 OR #16 AND CENTRAL:TARGET
18	#17 AND #14 AND CENTRAL:TARGET
19	#8 OR #9 OR #18 AND CENTRAL:TARGET
20	#19 AND #7 AND CENTRAL:TARGET

MEDLINE (Ovid) ALL

#	Searches
1	exp Sleep Apnea Syndromes/

(Continued)

2	((sleep\$ or nocturnal) adj2 (apnoea\$ or apnoea\$)).tw.
3	(sleep\$ adj2 disordered adj2 breathing).tw.
4	((sleep\$ or nocturnal) adj2 (hypopnea\$ or hypopnoea\$ or hypo-apnoea\$ or hypo-apnea\$ or apneic-hypopneic or apnoeic-hypopnoeic)).tw.
5	(OSA or SAHS).ti,ab.
6	OSAHS.ti,ab.
7	or/1-6
8	Myofunctional Therapy/
9	(myofunction\$ or myolog\$ or myotherap\$).tw.
10	exp Oropharynx/
11	Tongue/
12	Palate, Soft/
13	(oropharyngeal\$ or oropharynx or orofacial\$ or tongue\$ or soft palate or palatial or oral).tw.
14	or/10-13
15	exp Exercise Therapy/
16	(exercise\$ or therap\$).tw.
17	15 or 16
18	14 and 17
19	8 or 9 or 18
20	7 and 19
21	(controlled clinical trial or randomised controlled trial).pt.
22	(randomised or randomised).ab,ti.
23	placebo.ab,ti.
24	dt.fs.
25	randomly.ab,ti.
26	trial.ab,ti.
27	groups.ab,ti.
28	or/21-27
29	Animals/

(Continued)

30	Humans/
31	29 not (29 and 30)
32	28 not 31
33	20 and 32

Embase (Ovid)

#	Searches
1	exp sleep disordered breathing/
2	((sleep\$ or nocturnal) adj2 (apnoea\$ or apnoea\$)).tw.
3	(sleep\$ adj2 disordered adj2 breathing).tw.
4	((sleep\$ or nocturnal) adj2 (hypopnea\$ or hypopnoea\$ or hypo-apnoea\$ or hypo-apnea\$ or apneic-hypopneic or apnoeic-hypopnoeic)).tw.
5	(OSA or SAHS).ti,ab.
6	OSAHS.ti,ab.
7	or/1-6
8	muscle training/
9	(myofunction\$ or myolog\$ or myotherap\$).tw.
10	exp oropharynx/
11	exp tongue/
12	soft palate/
13	(oropharyngeal\$ or oropharynx or orofacial\$ or tongue\$ or soft palate or palatial or oral).tw.
14	or/10-13
15	exp exercise/
16	(exercise\$ or therap\$).tw.
17	15 or 16
18	14 and 17
19	8 or 9 or 18
20	7 and 19

(Continued)

21	Randomized Controlled Trial/
22	randomization/
23	controlled clinical trial/
24	Double Blind Procedure/
25	Single Blind Procedure/
26	Crossover Procedure/
27	(clinica\$ adj3 trial\$).tw.
28	((singl\$ or doubl\$ or trebl\$ or tripl\$) adj3 (mask\$ or blind\$ or method\$)).tw.
29	exp Placebo/
30	placebo\$.ti,ab.
31	random\$.ti,ab.
32	((control\$ or prospectiv\$) adj3 (trial\$ or method\$ or stud\$)).tw.
33	(crossover\$ or cross-over\$).ti,ab.
34	or/21-33
35	exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
36	human/ or normal human/ or human cell/
37	35 and 36
38	35 not 37
39	34 not 38
40	20 and 39

ClinicalTrials.gov

Search field	Search terms
Study type	Interventional
Condition	sleep apnoea
Intervention	Myofunctional OR myotherapy OR ((oropharyngeal OR oropharynx OR orofacial OR tongue OR soft palate OR palatial OR oral) AND (exercise))

WHO ICTRP

Search field	Search terms
Condition	sleep apnoea
Intervention	Myofunctional OR myotherapy OR ((oropharyngeal OR oropharynx OR orofacial OR tongue OR soft palate OR palatial OR oral) AND (exercise))

HISTORY

Protocol first published: Issue 10, 2019

Review first published: Issue 11, 2020

CONTRIBUTIONS OF AUTHORS

J-R Rueda wrote the final draft of the protocol and the draft of the full review. He co-ordinated contributions from the co-authors. He is the guarantor of the final review.

I Mugueta-Aguinaga, J Vilaró and M Rueda-Etxebarria drafted the clinical sections of the Background. They selected the studies for the full review, extracted data and conducted the 'Risk of bias' assessment.

Contributions of editorial team

Chris Cates (Co-ordinating Editor) edited the review.

Milo Puhan (Contact Editor) edited the review and advised on content.

Emma Dennett (Managing Editor) co-ordinated the editorial process, advised on content and edited the review.

Emma Jackson (Assistant Managing Editor) organised peer review and edited the references and other sections of the review.

Elizabeth Stovold (Information Specialist) designed the search strategy and arranged for peer review of the search strategy.

Emma Banchoff (statistician): checked the data in the review.

DECLARATIONS OF INTEREST

J-R Rueda: none known.

I Mugueta-Aguinaga: none known.

J Vilaró: received fees from Smiths Medical for giving presentations at scientific conferences.

M Rueda-Etxebarria: none known.

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- A, Other

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Cochrane's screen4me was used for the review.