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Appendices

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Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea–hypopnoea syndrome: a systematic review and economic analysis

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Appendix 1

Literature search strategies

Searches for systematic reviews and guidelines

Cochrane Database of Systematic Reviews (Cochrane Library 2006, issue 3) (www.thecochranelibrary.com)

Searched 17 October 2006. The 53 records retrieved were scanned to remove references to infants and children and 11 records were downloaded.

1. MeSH descriwptor Sleep Apnea Syndromes explode all trees
2. apnea or apnoea
3. hypopnea or hypopnoea
4. hypoapnea or hypoapnoea
5. "sahs" or "shs" or "osas" or "osa"
6. (#1 OR #2 OR #3 OR #4 OR #5)
7. MeSH descriptor Positive-Pressure Respiration explode all trees
8. cpap or apap or ncpap or autocpap or auto-cpap
9. positive near3 airway near3 pressure
10. (#7 OR #8 OR #9)
11. (#6 AND #10)

Database of Abstracts of Reviews of Effects (CRD administration database)

Searched 17 October 2006. Sixty-six records were retrieved.

1. s apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea
2. s sahs or shs or osas or osa
3. s s1 or s2
4. s cpap or apap or ncpap or autocpap
5. s positive(3w)airway(3w)pressure
6. s s4 or s5
7. s s3 and s6

Health Technology Assessment Database (CRD administration database)

Searched 17 October 2006. Eight records were retrieved.

1. s apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea
2. s sahs or shs or osas or osa
3. s s1 or s2
4. s cpap or apap or ncpap or autocpap
5. s positive(3w)airway(3w)pressure
6. s s4 or s5
7. s s3 and s6

National Research Register (2006, issue 3)(www.update-software.com/National/)

Searched 17 October 2006. Seventy-seven records were retrieved.

1. SLEEP APNEA SYNDROMES explode all trees (MeSH)
2. (apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea)
3. (sahs or shs or osas or osa)
4. (#1 or #2 or #3)
5. POSITIVE-PRESSURE RESPIRATION explode all trees (MeSH)
6. (cpap or apap or ncpap or autocpap)
7. (positive near airway near pressure)
8. (#5 or #6 or #7)
9. (#4 and #8)

Scottish Intercollegiate Guidelines Network (www.sign.ac.uk)

Searched 17 October 2006.The websitwe was scanned and one record was retrieved.

National Guideline Clearinghouse (www.guideline.gov/)

Searched 17 October 2006. The following search terms were used. The results were scanned and seven records were retrieved.

1. apnea
2. apnoea
3. hypopnea
4. hypopnoea
5. hypoapnea
6. hypoapnoea
7. sahs
8. shs
9. osas
10. osa

Health Services/Technology Assessment Text (HSTAT) (www.ncbi.nlm.nih.gov/books/bv.fcgi?rid = hstat)

Searched 17 October 2006. The following search terms were used. The results were scanned and one record was retrieved.

1. apnea
2. apnoea
3. hypopnea
4. hypopnoea
5. hypoapnea
6. hypoapnoea

Turning Research into Practice Database (Trip) (www.tripdatabase.com/)
Searched 17 October 2006. The following search terms were used. The results were scanned and two records were retrieved.

1. cpap or apap or ncpap or autocpap
2. apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea

Health Evidence Bulletins Wales (http://hebw.cf.ac.uk/index.html)
Searched 17 October 2006. The website was scanned and no records were retrieved.

Clinical Evidence (www.clinicalevidence.com)
Searched 17 October 2006. Chapters were scanned online and eight records were retrieved.

National Library for Health Guidelines Finder (www.library.nhs.uk/guidelinesfinder/)
Searched 20 October 2006. One record was retrieved.

1. apnea or apnoea
2. hypopnoea or hypopnea
3. hypoapnea or hypoapnoea

Searches for trials

MEDLINE (1966 to November week 3 2006) (OVID)
Searched 29 November 2006. 2346 records were retrieved.

1. exp sleep apnea syndromes/
2. (apnea or apnoea).ti,ab.
3. (hypopnea or hypopnoea).ti,ab.
4. (hypoapnea or hypoapnoea).ti,ab.
5. sleep disordered breathing.ti,ab.
6. (sleep adj2 respirat$disorder$).ti,ab.
7. sahs.ti,ab.
8. shs.ti,ab.
9. osa.ti,ab.
10. osas.ti,ab.
11. osahs.ti,ab.
12. or/1–11
13. exp positive-pressure respiration/
14. (positive adj3 airway adj3 pressure).ti,ab.
15. (cpap or ncpap or apap or bipap).ti,ab.
16. (c pap or bi pap or nc pap).ti,ab.
17. autocpap.ti,ab.
18. or/13–16
19. 12 and 18

MEDLINE In-Process & Other Non-Indexed Citations (28 November 2006) (OVID)
Searched 29 November 2006. 113 records were retrieved.

1. (apnea or apnoea).ti,ab.
2. (hypopnea or hypopnoea).ti,ab.
3. (hypoapnea or hypoapnoea).ti,ab.
4. sleep disordered breathing.ti,ab.
5. (sleep adj2 respirat$disorder$).ti,ab.
6. sahs.ti,ab.
7. shs.ti,ab.
8. osa.ti,ab.
9. osas.ti,ab.
10. osahs.ti,ab.
11. or/1–10
12. (positive adj3 airway adj3 pressure).ti,ab.
13. (cpap or ncpap or apap or bipap).ti,ab.
14. (c pap or bi pap or nc pap).ti,ab.
15. autocpap.ti,ab.
16. or/12–15
17. 11 and 16

EMBASE (1980 to 2006 week 47) (OVID)
Searched 29 November 2006. 2744 records were retrieved.

1. Sleep Apnea Syndrome/
2. (apnea or apnoea).ti,ab.
3. (hypopnoea or hypopnea).ti,ab.
4. (hypoapnea or hypoapnoea).ti,ab.
5. Sleep Disordered Breathing/
6. sleep disordered breathing.ti,ab.
7. (sleep adj2 respirat$disorder$).ti,ab.
8. sahs.ti,ab.
9. shs.ti,ab.
10. osa.ti,ab.
11. osas.ti,ab.
12. osahs.ti,ab.
13. or/1–12
14. positive end expiratory pressure/
15. (positive adj3 airway adj3 pressure).ti,ab.
16. (cpap or ncpap or apap or bipap).ti,ab.
17. (c pap or bi pap or nc pap).ti,ab.
18. autocpap.ti,ab.
19. or/14–18
20. 13 and 19

Cochrane Central Register of Controlled Trials (Cochrane Library 2006, issue 4) (www.thecochranelibrary.com)
Searched 29 November 2006. 461 records were retrieved.

1. MeSH descriptor Sleep Apnea Syndromes explode all trees
2. apnea or apnoea
3. hypopnea or hypopnoea
4. hypoapnea or hypoapnoea
5. "sleep disordered breathing"
6. sleep near2 respirat* disorder*
7. sahs or shs or osa or osas or osahs
8. (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)
9. MeSH descriptor Positive-Pressure Respiration explode all trees
10. positive near3 airway near3 pressure
11. cpap or ncpap or apap or bipap
12. c-pap or bi-pap or nc-pap
13. autocpap
14. (#9 OR #10 OR #11 OR #12 OR #13)
15. (#8 AND #14)

CINAHL (1982 to November week 3 2006) (OVID)
Searched 29 November 2006. 419 records were retrieved.

1. exp Sleep Apnea Syndromes/
2. (apnea or apnoea).ti,ab.
3. (hypopnea or hypopnoea).ti,ab.
4. (hypoapnea or hypoapnoea).ti,ab.
5. sleep disordered breathing.ti,ab.
6. (sleep adj2 respirat$disorder$).ti,ab.
7. sahs.ti,ab.
8. shs.ti,ab.
9. osa.ti,ab.
10. osas.ti,ab.
11. osahs.ti,ab.
12. or/1–11
13. exp Positive Pressure Ventilation/
14. (positive adj3 airway adj3 pressure).ti,ab.
15. (cpap or ncpap or apap or bipap).ti,ab.
16. (c pap or bi pap or nc pap).ti,ab.
17. autocpap.ti,ab.
18. or/13–17
19. 12 and 18

Science Citation Index (1900 to 25 November 2006) (Web of Knowledge)
Searched 29 November 2006. 2745 records were retrieved.

1. TS = (apnea or apnoea)
2. TS = (hypopnea or hypopnoea)
3. TS = (hypoapnea or hypoapnoea)
4. TS = "sleep disordered breathing"
5. TS = (sahs or shs or osa or osas or osahs)
6. #1 or #2 or #3 or #4 or #5
7. TS = (positive same airway same pressure)
8. TS = (cpap or ncpap or apap or bipap)
9. TS = ("c pap" or "nc pap" or "bi pap")
10. TS = autocpap
11. #7 or #8 or #9 or #10
12. #6 and #11

ISI Proceedings Science & Technology (1990 to 25 November 2006) (Web of Knowledge)
Searched 29 November 2006. 407 records were retrieved.

1. TS = (apnea or apnoea)
2. TS = (hypopnea or hypopnoea)
3. TS = (hypoapnea or hypoapnoea)
4. TS = "sleep disordered breathing"
5. TS = (sahs or shs or osa or osas or osahs)
6. #1 or #2 or #3 or #4 or #5
7. TS = (positive same airway same pressure)
8. TS = (cpap or ncpap or apap or bipap)
9. TS = ("c pap" or "nc pap" or "bi pap")
10. TS = autocpap
11. #7 or #8 or #9 or #10
12. #6 and #11

Zetoc Conferences (1993 to 29 November 2006) (http://zetoc.mimas.ac.uk/)
Searched 29 November 2006. 113 records were retrieved.

1. conference: autocpap
2. conference: bi pap
3. conference: c pap
4. conference: nc pap
5. conference: bipap
6. conference: apap
7. conference: ncpap
8. conference: cpap
9. conference: positive airway pressure

The records retrieved from this search in Zetoc were loaded into an endnote library and duplicates were removed. The following search was then carried out within that endnote library:

1. apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea
2. sleep or sahs or shs or osa or osas or osahs

SIGLE (1980 to March 2005) (SilverPlatter)
Searched 29 November 2006. Three records were retrieved.

1. (apnea or apnoea) in ti,ab
2. (hypopnea or hypopnoea) in ti,ab
3. (hypoapnea or hypoapnoea) in ti,ab
4. sleep disordered breathing in ti,ab
5. (sleep near2 respirat* disorder*) in ti,ab
6. (sahs or shs or osa or osas or osahs) in ti,ab
7. #1 or #2 or #3 or #4 or #5 or #6
8. (positive near3 airway near3 pressure) in ti,ab
9. (cpap or ncpap or apap or bipap) in ti,ab
10. (c pap or bi pap or nc pap) in ti,ab
11. autocpap in ti,ab
12. #8 or #9 or #10 or #11
13. #7 and #12

Index to Theses (1716 to 16 October 2006) (www.theses.com/)
Searched 29 November 2006.
Fourteen records were retrieved.

1. (apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea or sleep) and (cpap or ncpap or apap or bipap or c pap or bi pap or nc pap or autocpap)
2. (apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea or sleep)and (positive airway pressure)
3. (sahs or shs or osa or osas or osahs) and (cpap or ncpap or apap or bipap or c pap or bi pap or nc pap or autocpap)
4. (sahs or shs or osa or osas or osahs) and (positive airway pressure)

NHS Economic Evaluation Database (NHS EED) (CRD internal administration system)
Searched 1 December 2006. Twenty-four records were retrieved.

1. s apnea or apnoea
2. s hypopnea or hypopnoea
3. s hypoapnea or hypoapnoea
4. s sleep(w)disordered(w)breathing
5. s sleep(2w)respirat$(w)disorder$
6. s sahs or shs or osa or osas or osahs
7. s s1 or s2 or s3 or s4 or s5 or s6
8. s positive(3w)airway(3w)pressure
9. s cpap or ncpap or apap or bipap
10. s c(w)pap or bi(w)pap or nc(w)pap
11. s autocpap
12. s s8 or s9 or s10 or s11
13. s s7 and s12

Health Economic Evaluations Database (HEED) (1995 to November 2006) (CD-ROM)
Searched 1 December 2006. Seventeen records were retrieved.

1. ax = apnea or apnoea or hypopnea or hypopnoea or hypoapnea or hypoapnoea
2. ax = sleep and disorder*
3. ax = sahs or shs or osa or osas or osahs
4. cs = 1 or 2 or 3
5. ax = positive and airway and pressure
6. ax = cpap or ncpap or apap or bipap or pap or autocpap
7. cs = 5 or 6
8. cs = 4 and 7

EconLit (1969 to October 2006) (SilverPlatter)
Searched 1 December 2006. No records were retrieved.

1. (apnea or apnoea) in ti,ab
2. (hypopnea or hypopnoea) in ti,ab
3. (hypoapnea or hypoapnoea) in ti,ab
4. sleep disordered breathing in ti,ab
5. (sleep near2 respirat* disorder*) in ti,ab
6. (sahs or shs or osa or osas or osahs) in ti,ab
7. #1 or #2 or #3 or #4 or #5 or #6
8. (positive near3 airway near3 pressure) in ti,ab
9. (cpap or ncpap or apap or bipap) in ti,ab
10. (c pap or bi pap or nc pap) in ti,ab
11. autocpap in ti,ab
12. #8 or #9 or #10 or #11
13. #7 and #12

EconPapers (http://econpapers.repec.org/)
Searched 1 December 2006. The search results were scanned and no records were retrieved.

1. apnea
2. apnoea
3. hypopnea
4. hypopnoea
5. hypoapnea
6. hypoapnoea
7. sleep and disorder*

Cost-effectiveness searches

The following databases were searched for economic evaluations of sleep apnoea.

NHS Economic Evaluation Database (NHS EED) (CRD internal administration system)
Searched 13 January 2007. Forty-two records were retrieved.

1. S sleep(w)apn$
2. S apn$
3. S hypoapn$
4. S sleep(w)disordered(w)breathing
5. S sleep(2w)respirat$(2w)disorder$
6. S sahs or shs or osa or osas or soahs
7. S s1 or s2 or s3 or s4 or s5 or s6

Health Technology Assessment Database (CRD administration database)
Searched 13 January 2007. Eight records were retrieved.

1. S sleep(w)apn$
2. S apn$
3. S hypoapn$
4. S sleep(w)disordered(w)breathing
5. S sleep(2w)respirat$(2w)disorder$
6. S sahs or shs or osa or osas or soahs
7. S s1 or s2 or s3 or s4 or s5 or s6
8. S econ$or cost$
9. S s7 and s8

Health Economic Evaluations Database (HEED) (1995 to January 2007) (CD-ROM)
Searched 13 January 2007. Seventy records were retrieved.

1. Apn* or hypoapn*
2. 'Sleep disordered' within 3
3. sahs or shs or osa or osas or soahs

IDEAS (http:\\ideas.repec.org)
Searched 13 January 2007. No records were retrieved.

1. Apnoea or apnea or hypoapnoea or hypoapnea

MEDLINE (1950 to 10 January 2007) (OVID)
Searched 13 January 2007. 494 records were retrieved.

1. exp sleep apnea syndromes/(12843)
2. (apnea or apnoea).ti,ab. (17402)
3. (hypopnea or hypopnoea or hypoapnea or hypoapnoea).ti,ab. (2515)
4. sleep disordered breathing.ti,ab. (1603)
5. (sleep adj2 respirat$disorder$).ti,ab. (154)
6. (sahs or shs or osa or osas or osahs).ti,ab. (4375)
7. or/1–6 (21688)
8. economics/(24617)
9. exp "costs and cost analysis"/(125794)
10. economic value of life/(4779)
11. economics, medical/(6672)
12. economics,nursing/(3725)
13. (econom$or cost or costs or costly or costing or prices or pricing or pharmacoeconomic$).ti,ab. (239906)
14. (expenditure$not energy).ti,ab. (10278)
15. (value adj3 money).ti,ab. (472)
16. budget$.ti,ab. (10745)
17. or/8–16 (337377)
18. 7 and 17 (521)
19. (letter or editorial or historical-article).pt. (1006834)18 not 19 (504)
20. animals/not (humans/and animals/) (3010245)
21. 20 not 21 (494)

EMBASE (1980 to 2007 week 1) (OVID)
Searched 13 January 2007. 569 records were retrieved.

1. sleep apnea syndrome/(11977)
2. (apnea or apnoea).ti,ab. (15034)
3. (hypopnoea or hypopnea or hypoapnea or hypoapnoea).ti,ab. (2219)
4. sleep disordered breathing/(484)
5. sleep disordered breathing.ti,ab. (1555)
6. (sleep adj2 respirat$disorder$).ti,ab. (100)
7. (sahs or shs or osa or osas or osahs).ti,ab. (3866)
8. or/1–7 (19042)
9. health economics/(8941)
10. exp economic evaluation/(84200)
11. exp health care cost/(85556)
12. exp pharmacoeconomics/(44276)
13. (econom$or cost or costs or costly or costing or prices or pricing or pharmacoeconomic$).ti,ab. (189706)
14. (expenditure$not energy).ti,ab. (8248)
15. (value adj3 money).ti,ab. (376)
16. budget$.ti,ab. (7647)
17. or/9–16 (280800)
18. 8 and 17 (655)
19. (letter or editorial or note).pt. (712099)
20. 18 not 19 (586)
21. (energy or oxygen) adj3 (cost or expenditure$)).ti,ab. (10286)
22. (metabolic adj3 cost$).ti,ab. (502)
23. exp animal/or exp animal experiment/ (1206737)
24. (rat or rats or mouse or mice or hamster$ or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh. (1857239)
25. or/21–24 (2100839)
26. 20 not 25 (569)

Searches to inform the model

All searches were conducted in Ovid MEDLINE.

Traffic accidents and cardiovascular events

The following strategy was used to identify literature linking traffic accidents and cardiovascular events (particularly stroke and coronary heart disease) to sleep apnoea.

MEDLINE (In-Process & Other Non-Indexed Citations and MEDLINE 1950 to Present)

Searched 15 January 2007. The results of set 13 were scanned for epidemiological records and sets of selected records were downloaded.

1. Accidents, Traffic/
2. road accidents.ti,ab.
3. traffic accidents.ti,ab.
4. (stroke or strokes).ti,ab.
5. (chd or cardiovascular disease).ti,ab.
6. exp heart diseases/or exp vascular diseases/
7. exp Cerebrovascular Accident/
8. or/1–7
9. exp sleep apnea syndromes/
10. 18 and 9
11. ep.fs.
12. 10 and 11
13. limit 12 to yr = "1990 – 2007"

Quality of life studies

The following strategy was used to identify quality of life studies/utilities studies in MEDLINE.

MEDLINE (In-Process & Other Non-Indexed Citations and MEDLINE 1950 to Present)

Searched 8 July 2007. 491 records were downloaded (set 43) and assessed for relevance.

1. exp sleep apnea syndromes/
2. (apnea or apnoea).ti,ab.
3. (hypopnea or hypopnoea).ti,ab.
4. (hypoapnea or hypoapnoea).ti,ab.
5. sleep disordered breathing.ti,ab.
6. (sleep adj2 respirat$disorder$).ti,ab.
7. (sahs or shs or osa or osas or osahs).ti,ab.
8. or/1–7
9. quality of life/
10. (quality adj2 life).ti,ab.
11. utility.ti,ab.
12. utilities.ti,ab.
13. standard gamble.ti,ab.
14. tto.ti,ab.
15. (time tradeoff or time trade off).ti,ab.
16. (eq or euroqol).ti,ab.
17. osa 18.ti,ab.
18. sf 36.ti,ab.
19. sgrq.ti,ab.
20. respiratory questionnaire.ti,ab.
21. practical sleep scale.ti,ab.
22. sleep scale.ti,ab.
23. scopa.ti,ab.
24. objective daytime sleepiness.ti,ab.
25. oxford sleep resistance.ti,ab.
26. osler test.ti,ab.
27. stai.ti,ab.
28. emotional control scale.ti,ab.
29. cecs.ti,ab.
30. life orientation test.ti,ab.
31. satisfaction with life scale.ti,ab.
32. swls.ti,ab.
33. calgary sleep apnea quality.ti,ab.
34. (functional outcomes adj2 sleep).ti,ab.
35. osa patient oriented severity.ti,ab.
36. osa18.ti,ab.
37. cohen$pediatric osa.ti,ab.
38. (comment or letter or editorial).pt.
39. or/9–37
40. 8 and 39
41. 40 not 38
42. limit 41 to yr = "2000 – 2007"
43. limit 42 to english language (491)

Rates of road accidents

Searches for recent studies on rates of road accidents were undertaken using the strategy described by Ayas and colleagues in their meta-analysis of all studies that examined RTA rates in patients with OSAHS before and after CPAP.[122] Ayas *et al*. reported their search as follows: 'A comprehensive search of MEDLINE (1966 to March 2005) using Ovid was conducted using the following exploded MESH terms: *sleep apnea syndromes* AND *positive pressure respiration* OR *continuous positive airway pressure* AND *automobile driving* OR *accident*.'

This search was rerun in Ovid MEDLINE (1950 to March week 1 2007) and included searches of in process citations. The search results were limited to those added to MEDLINE after February 2005 to ensure that no records were missed. The correct medical subject heading (MeSH) term ACCIDENTS was used rather than the term ACCIDENT noted by Ayas *et al*., on the assumption that this was a transcription error in their paper.

Eight new records were identified.

1. exp sleep apnea syndromes/
2. exp positive pressure respiration/
3. exp continuous positive airway pressure/
4. 1 and (2 or 3)
5. exp automobile driving/
6. exp accidents/
7. 5 or 6

8. 4 and 7
9. 200503$.ep.
10. (200504$or 200505$or 200506$or 200507$or 200508$or 200509$or 20051$).ep.
11. (2006$or 2007$).ep.
12. (200503$or 200504$or 200505$or 200506$or 200507$or 200508$or 200509$or 20051$).ed.
13. (2006$or 2007$).ed.
14. or/9–13
15. 8 and 14 (8)

Search for data on life expectancy for individuals who have suffered a stroke

Ovid MEDLINE (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1950 to Present>) was searched on 27 April 2007 for a known paper on post-stroke life expectancy by Dennis and Burn.[164] Once identified, the 'Find similar' option was selected and also the citing papers option to identify similar records. After assessing those references for relevance, a series of searches was undertaken and the results in sets 5, 11, 12, 15, 17, 22 and 24 were assessed to identify further relevant studies.

1. dennis $.au. and stroke.ti. (130)
2. burn $.au. (1073)
3. 1 and 2 (6)
4. find similar to Long-term survival after first-ever stroke: the Oxfordshire Community Stroke Project. (76)
5. from 5 keep 2–3, 5–6 (4)
6. *cerebrovascular disorders/(27223)
7. *survival rate/(335)
8. 7 and 8 (0)
9. stroke$1.ti. (30599)
10. 8 and 10 (2)
11. (7 or 10) and survival rate/(634)
12. from 12 keep 4,8,14,17,33,44,81,109,132–134,148,159 (13)
13. *cerebrovascular accident/(16575)
14. 8 and 14 (2)
15. 14 and survival rate/(386)
16. 16 not 13 (375)
17. cerebrovascular accident/(22109)
18. survival rate/(77068)
19. survival analysis/(59922)
20. exp great britain/(220221)
21. 18 and (19 or 20) and 21 (48)
22. stroke register.ti,ab. (162)
23. 23 and 21 (33)

Google was searched (27 April 2007) using the following search terms:

1. life expectancy stroke
2. stroke life expectancy
3. life tables stroke.

Appendix 2
Excluded studies

Study	Reasons(s) for exclusion				
	Appropriate intervention[a]	**Relevant comparator[b]**	**Appropriate study design[c]**	**Appropriate participants[d]**	**Appropriate outcome measures[e]**
Abe *et al.*, 2005[178]	No	No	No	Yes	No
Adlakha and Gross, 2006[179]	No	No	No	Yes	No
Ahmed *et al.*, 2005[180]	Yes	No	No	Yes	Yes
Akashiba *et al.*, 1993[181]	No	No	No	Yes	Yes
Almirall *et al.*, 2005[182]	Yes	No	No	Yes	Yes
ANDEM, 1992[175]	No	No	No	No	No
Anonymous, 2003[183]	No	No	No	No	No
Antic *et al.*, 2006[184]	Yes	No	No	Yes	Yes
Ayas *et al.*, 2006[185]	No	No	No	No	No
Babar and Quan, 2003[186]	No	No	No	No	No
Badia *et al.*, 1997[187]	Yes	Yes	Unclear	Yes	Yes
Bakshi *et al.*, 2005[188]	No	No	No	Yes	No
Barry, 1999[189]	No	No	No	No	No
Becker *et al.*, 1989[190]	No	No	No	Yes	No
Becker *et al.*, 1995[191]	No	No	No	Yes	No
Beecroft *et al.*, 2003[192]	Yes	No	No	Yes	Yes
Berka *et al.*, 2006[193]	No	No	No	Yes	Yes
Bloch and Basile, 2006[194]	No	No	No	No	No
Bradley *et al.*, 1990[195]	No	No	No	No	No
Braghiroli *et al.*, 1998[196]	No	No	No	No	No
Buechner *et al.*, 2001[197]	No	No	No	Yes	Yes
Buttner and Ruhle, 2004[198]	Yes	No	No	Yes	Yes
Castronovo *et al.*, 2003[199]	Yes	No	No	Yes	Yes
Chakravorty *et al.*, 1998[200]	Yes	No	No	Yes	Yes
Chasens *et al.*, 2003[201]	Yes	No	No	Yes	Yes
Chazan *et al.*, 2004[202]	Yes	No	No	Yes	No
Chrysostomakis *et al.*, 2004[203]	No	No	No	Yes	No
Ciftci *et al.*, 2005[204]	Yes	No	No	No	Yes
Clark *et al.*, 1996[149]	Yes	Yes	No	Yes	Yes
Deegan and McNicholas, 1995[205]	No	No	No	No	No
Dhillon *et al.*, 2003[206]	Yes	No	No	Yes	Yes

continued

Study	Reasons(s) for exclusion				
	Appropriate intervention[a]	Relevant comparator[b]	Appropriate study design[c]	Appropriate participants[d]	Appropriate outcome measures[e]
Donadio *et al*., 2006[207]	Yes	Yes	No	Yes	Yes
Dorkova and Tkacova, 2006[208]	No	No	No	Yes	Yes
Douglas and Engleman, 1998[209]	No	No	No	No	No
Douglas, 2004[210]	No	No	No	No	No
Drummond *et al*., 2005[211]	Yes	Yes	Yes	No	Yes
Engleman *et al*., 1993[212]	Yes	Yes	No	Yes	Yes
Engleman, 2002[213]	No	No	No	No	No
Fairbairn *et al*., 2006[214]	Yes	Yes	No	Yes	Yes
Ficker *et al*., 1997[215]	No	No	Yes	Yes	Yes
Ficker *et al*., 2002[216]	Yes	No	Yes	Yes	Yes
Fitzpatrick *et al*., 2005[217]	No	Yes	Yes	No	No
Flemons *et al*., 1998[218]	Yes	Yes	Yes	Yes	Yes
Fletcher, 2000[219]	No	No	No	No	No
Gagnadoux, 2006[220]	No	No	No	No	No
Golish, 2000[221]	No	No	No	No	No
Goncalves *et al*., 2005[222]	Yes	No	No	Yes	Yes
Gotsopoulos 2002[223]	No	No	Yes	Yes	Yes
Grimm *et al*., 2000[224]	Yes	No	No	No	Yes
Hahn *et al*., 2003[225]	No	No	No	Yes	Yes
Hermida *et al*., 2003[226]	Yes	Yes	No	Yes	Yes
Hermida *et al*., 2003[227]	Yes	Yes	No	Yes	Yes
Hermida *et al*., 2004[228]	Yes	Yes	No	Yes	Yes
Hernandez *et al*., 1999[229]	Yes	Yes	Yes	Yes	No
Hetzel *et al*., 1994[230]	Yes	No	No	Yes	Yes
Hira, *et al*., 1998[231]	Yes	Yes	No	Yes	Yes
Hirshkowitz and Sharafkhaneh, 2005[232]	No	No	No	No	No
Hla *et al*., 2002[233]	Yes	No	No	No	Yes
Hoster *et al*., 1995[234]	No	No	Yes	Yes	No
Huang *et al*., 2001[235]	No	No	Unclear	No	Yes
Iellamo and Montana, 2006[236]	No	No	No	No	No
Itzhaki *et al*., 2006[237]	Yes	No	No	Yes	Yes
Jenkinson *et al*., 2001[144]	Yes	Yes	Yes	No	Yes
Juhasz *et al*., 1997[238]	No	No	Yes	Yes	No
Kajaste *et al*., 2004[239]	Yes	Yes	Yes	Yes	Yes
Kaleth *et al*., 2003[240]	Yes	No	No	Yes	No
Kaleth *et al*., 2005[241]	Yes	No	Yes	Yes	No
Karacan and Karatas, 1995[242]	No	No	No	Yes	Yes
Kiely *et al*., 1999[243]	Yes	No	No	Yes	Yes
Konermann *et al*., 1995[244]	Yes	No	No	Yes	Yes
Krieger *et al*., 1986[245]	No	No	No	No	Yes

Study	Reasons(s) for exclusion				
	Appropriate intervention[a]	**Relevant comparator[b]**	**Appropriate study design[c]**	**Appropriate participants[d]**	**Appropriate outcome measures[e]**
Lafond *et al.*, 2005[246]	Yes	No	No	Yes	Yes
Lafond *et al.*, 2007[247]	No	No	Yes	Yes	Yes
Lewis *et al.*, 2002[248]	Yes	No	No	Yes	Yes
Li *et al.*, 2004[249]	Yes	Unclear	Yes	No	Yes
Litvin *et al.*, 2006[250]	No	No	No	Yes	No
Logan *et al.*, 2003[251]	Yes	No	No	Yes	Yes
Mador *et al.*, 2005[252]	Yes	No	Yes	Yes	Yes
Malow, 2005[253]	Yes	Yes	Yes	Yes	No
Marrone *et al.*, 1990[254]	No	No	No	Yes	No
Marshall and Coughlin, 2004[255]	Yes	No	No	Yes	Yes
Mayer *et al.*, 1993[256]	No	No	Yes	Yes	Yes
McArdle *et al.*, 2001[257]	Yes	Yes	Yes	Yes	No
McEvoy and Thornton, 1984[258]	Yes	No	No	Yes	Yes
McFadyen *et al.*, 2001[259]	Yes	Yes	No	Yes	Yes
McNab *et al.*, 2006[260]	No	No	No	Yes	Yes
Morrish *et al.*, 2004[261]	No	No	No	Yes	No
Mulgrew *et al.*, 2007[262]	Yes	No	Yes	Yes	Yes
Nagasaka *et al.*, 1997[263]	No	Yes	No	Yes	No
Newsom-Davis *et al.*, 2001[264]	No	No	No	No	Yes
Nooman *et al.*, 1998[265]	No	No	No	Yes	Yes
Pepin *et al.*, 2006[266]	Yes	Yes	Unclear	Yes	No
Phillips *et al.*, 1990[267]	Yes	No	Unclear	Yes	Yes
Poluektov and Eligulashvili, 1994[268]	No	No	No	No	No
Resta *et al.*, 1997[176]	No	No	No	Yes	No
Risk and Winzner, 2004[269]	No	No	No	Yes	Yes
Rosenthal *et al.*, 2003[270]	Yes	No	No	Yes	Yes
Rosenthal *et al.*, 2006[271]	No	No	No	Yes	Yes
Sakakibara, 2005[272]	No	No	No	No	No
Sanders and Strollo, 1998[273]	No	No	No	No	No
Sanders, 2001[274]	No	No	No	No	No
Sanner *et al.*, 2000[275]	Yes	Yes	No	Yes	Yes
Sanner *et al.*, 2003[276]	Yes	No	No	Yes	Yes
Schutte-Rodin *et al.*, 2006[277]	No	No	No	No	No
Seiler *et al.*, 1998[278]	Yes	No	Yes	Yes	Yes
Shadan *et al.*, 2006[279]	Yes	No	No	Yes	No
Shashikumar *et al.*, 2002[177]	No	Yes	No	Yes	Yes
Shimizu *et al.*, 2003[280]	Yes	No	No	Yes	No
Skomro *et al.*, 2003[281]	Yes	No	No	No	Yes
Smith *et al.*, 2005[282]	Yes	No	No	Yes	Yes

continued

Study	Reasons(s) for exclusion				
	Appropriate intervention[a]	Relevant comparator[b]	Appropriate study design[c]	Appropriate participants[d]	Appropriate outcome measures[e]
Stammnitz *et al*., 1993[283]	No	No	No	Yes	Yes
Stoohs *et al*., 1993[284]	Yes	No	No	Yes	No
Suhner *et al*., 2003[285]	Yes	No	No	Yes	Yes
Veale *et al*., 2003[286]	Yes	No	No	Yes	Yes
Verbraecken *et al*., 2002[287]	Yes	Unclear	No	No	No
Voronin *et al*., 2002[288]	No	Yes	No	No	Yes
Weaver, 2004[289]	Yes	Yes	Yes	Yes	No
Weisfogel *et al*., 2003[290]	Yes	No	No	No	Yes
Weissenberg *et al*., 1994[291]	No	No	No	Yes	Yes
Westbrook, 1990[292]	No	No	No	No	No
Westbrook *et al*., 2004[293]	Yes	No	No	Yes	Yes
Wiest *et al*., 1998[294]	No	No	No	No	No
Woodson *et al*., 2003[295]	Yes	No	Yes	Yes	Yes
Woodson *et al*., 2003[296]	Yes	No	Yes	Yes	Yes
Worsnop *et al*., 1994[297]	Yes	Yes	Yes	No	Yes
Yen *et al*., 1997[298]	Yes	No	No	Yes	No
Zimmerman *et al*., 2005[299]	Yes	No	No	Yes	Yes

a Does the study look at CPAP/APAP devices, and does the intervention last ≥ 1 week?
b Does the study have relevant comparators (placebo/sham treatment/no treatment or oral devices)?
c Is the study a randomised controlled trial (RCT)?
d Does the study include participants with obstructive sleep apnoea–hypopnoea syndrome (OSAHS), ≥ 16 years old, who do not specifically relate to a population with brain disease, heart failure or chronic airways disease?
e Does the study look at subjective daytime sleepiness, objective daytime sleepiness, subjective health status, blood pressure, apnoea–hypopnoea index (AHI), oxygen desaturation > 4%, driver simulation tests or other psychometric assessments?

Appendix 3

Quality assessment

Source	Was the method used to assign participants to treatment groups or the sequence of treatments really random?	Was treatment allocation concealed?	Were the groups similar at baseline in terms of ESS and AHI?	If not, were adjustments made for differences in baseline characteristics of the treatment groups?	Did the analysis include an intention-to-treat analysis?	Were appropriate methods used to account for missing data in the intention-to-treat analysis?	What proportion of participants was lost to follow-up for the primary outcomes?	Was the study described as blind or double-blind?
Arias *et al*., 2005[56]	?	?	?	X	X	NA	7.4%	✓
Arias *et al*., 2006[63]	✓	?	?	NA	X	NA	8.7%	✓
Ballester *et al*., 1999[96]	?	?	✓	NA	?	NA	NR	X
Barbé *et al*., 2001[83]	✓	?	✓	NA	X (1 not included)	NA	1.8%	✓
Barnes *et al*., 2002[89]	✓	X	?	NA	✓	✓	23%	X
Barnes *et al*., 2004[82]	✓	X	?	NA	X (14 not included)	NA	33.3%	X
Becker *et al*., 2003[109]	?	✓	✓	NA	X (28 not included)	NA	46.6%	X
Campos-Rodriguez *et al*., 2006[65]	?	X	✓	NA	X (4 not included)	NA	5.6%	✓
Chakravorty *et al*., 2002[97]	?	?	?[e]	NA	X (18 not included)	NA	25.4%	X
Cibele *et al*., 2006[72]	?	?	?	NA	?	NA	?	✓
Coughlin *et al*., 2007[62]	✓	✓	?	NA	X (1 not included)	NA	2.3%	✓
Cross *et al*., 2005[88]	?	?	?	NA	?	NA	NR	✓
Dimsdale *et al*., 2000[58]	✓	X[b]	✓ (RDI)	NA	X	NA	?	✓
Drager *et al*., 2006[69]	?	?	?	?	?	?	?	✓
Engleman *et al*., 2002[103]	?	?	?	NA	X (3 not included)	NA	5.8%	✓
Engleman *et al*., 1999[78]	?	?	?	NA	X (3 not included and 2 additional for PASAT)	NA	8.1%	X
Engleman *et al*., 1998[93]	?	?	?	NA	X (1 not included)	NA	4.3%[c]	✓
Engleman *et al*., 1997[92]	?	?	?	NA	X (2 not included)	NA	11.1%	X
Engleman *et al*., 1996[91]	?	?	?	NA	X (3 not included)	NA	18.8%	X
Engleman *et al*., 1994[90]	?	?	?	NA	X (3 not included)	NA	8.6%	X

Who was blinded?	Studies using sham CPAP as comparator	Was the study parallel design? (sham CPAP)	Were the participants CPAP naïve? (sham CPAP)	Crossover trials	Was an appropriate analysis using paired data performed? (crossover)	Was there a treatment by period interaction? (crossover)
Participants	✓	X	✓	✓	✓	X
Participants	✓	X	✓	✓	X	?
NA	NA	✓	?	X	NA	NA
Participants, psychologist administering tests	✓	✓	?	X	NA	NA
Staff administering psychometric tests	NA	X	?	✓	✓	X
Staff administering psychometric tests	NA	X	?	✓	✓	✓ (ESS)
NA	✓	✓	?	X	NA	NA
Participants, outcome assessor and nurse following CPAP monitors	✓	✓	✓	X	NA	NA
NA	NA	✓	?	X	NA	NA
?	NA	X	?	✓	?	?
Participants and investigators	✓	X	✓	✓	✓	X
Participants and outcome assessors	✓	X	?	✓	?	?
Participants and investigators (not involved with CPAP titration)	✓	✓	✓	X	NA	NA
Outcome assessors	NA	✓	?	X	NA	NA
Staff scoring sleep data	NA	X	?	✓	✓	?
NA	NA	X	?	✓	✓	X
NA	NA	X	?	✓	✓	✓ (ESS)[d]
NA	NA	X	?	✓	✓	✓ (MSLT)
NA	NA	X	?	✓	✓	?
NA	NA	X	?	✓	✓	✓ (PASAT 2)[d]

continued

Source	Was the method used to assign participants to treatment groups or the sequence of treatments really random?	Was treatment allocation concealed?	Were the groups similar at baseline in terms of ESS and AHI?	If not, were adjustments made for differences in baseline characteristics of the treatment groups?	Did the analysis include an intention-to-treat analysis?	Were appropriate methods used to account for missing data in the intention-to-treat analysis?	What proportion of participants was lost to follow-up for the primary outcomes?	Was the study described as blind or double-blind?
Faccenda *et al*., 2001[94]	✓	?	?	NA	X (3 not included)	NA	4.2%	X
Ferguson *et al*., 1996[81]	?	?	✓ (AHI)	NA	X (2 not included)	NA	7.4%	X
Ferguson *et al*., 1997[80]	?	?	✓	NA	X (4 not included)	NA	16.7%	X
Fleetham *et al*., 2002[101]	?	?	✓	NA	?	?	?	X
Henke *et al*., 2001[85]	?	?	✓	NA	X (10 not included)	NA	22.2%[e]	✓
Hoekema *et al*., 2006[102]	✓	?	✓	NA	✓	?	None reported	NA
Hui *et al*., 2006[64]	✓	?	✓	NA	X (10 not included)	NA	17.9%	✓
Jenkinson *et al*., 1999[77]	✓	✓	✓	NA	?	NA	5.6%	✓
Jokic *et al*., 1999[108]	?	?	?	NA	X (1 not included)	NA	0%	✓
Lam *et al*., 2007[70]	✓	?	✓	NA	X (10 not included)	NA	9.9%	X
L'Estrange *et al*., 1999[104]	?	?	NA	?	?	NA	40%	X
Lim, 2005[110]	?	?	✓	NA	?	NA	?	X
Lojander *et al*., 1996[99]	?	?	✓	NA	X (5 not included, 4 not analysed as per protocol)	NA	33.3%	X
McArdle and Douglas, 2001[95]	✓	✓	?	NA	?	NA	4.3%	X
Marshall *et al*., 2005[79]	✓	X	?	NA	X (2 not included)	NA	6.4%	✓
Monasterio *et al*., 2001[100]	✓	?	✓	NA	X (17 not included)	NA	12%	✓
Montserrat *et al*., 2001[86]	✓	?	✓ (AHI)	NA	X (2 not included)	NA	4.3%	✓

Who was blinded?	Studies using sham CPAP as comparator	Was the study parallel design? (sham CPAP)	Were the participants CPAP naïve? (sham CPAP)	Crossover trials	Was an appropriate analysis using paired data performed? (crossover)	Was there a treatment by period interaction? (crossover)
NA	NA	X	?	✓	✓	
NA	NA	X	?	✓	✓	X
NA	NA	X	?	✓	✓	X
NA	NA	✓	?	NA	NA	NA
Participants and staff in contact with them	✓	Partial crossover	?	X	NA	NA
NA	NA	✓	NA	X	NA	NA
Participants and outcome assessors	✓	✓	✓	X	NA	NA
Patients and staff scoring and administering	✓	✓	✓	X	NA	NA
Staff scoring sleep data and administering psychometric tests	NA	X	?	✓	Yes	?
NA	NA	✓	?	X	NA	NA
NA	NA	X	?	✓	?	?
NA	NA	✓	?	X	NA	NA
NA	NA	✓	?	X	NA	NA
NA	NA	X	?	✓	✓	X
Participants, investigator collecting daytime data	✓	X	✓	✓	✓	X
Staff who did data entry and analysis	NA	✓	?	X	NA	NA
Patients and interviewers	✓	Partial crossover	?	X	NA	NA

continued

Source	Was the method used to assign participants to treatment groups or the sequence of treatments really random?	Was treatment allocation concealed?	Were the groups similar at baseline in terms of ESS and AHI?	If not, were adjustments made for differences in baseline characteristics of the treatment groups?	Did the analysis include an intention-to-treat analysis?	Were appropriate methods used to account for missing data in the intention-to-treat analysis?	What proportion of participants was lost to follow-up for the primary outcomes?	Was the study described as blind or double-blind?
Norman *et al.*, 2006[73]	✓	X[b]	✓ CPAP had higher baseline SBP than control	✓	X	NA	?	✓
Olson *et al.*, 2002[107]	?	?	?	?	?	?	?	X
Pepperell *et al.*, 2002[87]	?	✓	✓	NA	✓	✓	11.9%	✓
Randerath *et al.*, 2002[105]	?	?	✓ (AHI)	NA	?	NA	NR	X
Redline *et al.*, 1998[59]	✓	?	✓ (ESS)	NA	X (14 not included)	NA	12.6%	NA
Robinson *et al.*, 2006[68]	?	X[b]	?	?	?	NA	8.6%	✓
Skinner *et al.*, 2004[60]	?	?	?	NA	X (1 not included)	NA	7.1%	X
Skinner *et al.*, 2004[61]	?	Un-clear	Unclear	NA	✓	NA	0%	X
Spicuzza *et al.*, 2006[66]	?	?	✓ (AHI not assessed)	NA	?	?	NR	?
Tan *et al.*, 2002[106]	?	?	?	NA	✓ (3 not included)	?	12.5%	X
West *et al.*, 2006[67]	✓	?	✓	NA	X (1 participant received a defective machine delivering minimal pressure; data were included in sham CPAP group)	NA	4.8%	✓

✓, yes, meets criteria; X, no, does not meet criteria; ?, unclear whether meets criteria; AHI, apnoea–hypopnoea index; ESS, Epworth Sleepiness Scale; MSLT, Multiple Sleep Latency Test; NA, not applicable; NR, not reported; PASAT, Paced Auditory Serial Addition Task; RDI, respiratory disturbance index; SBP, systolic blood pressure.

a AHI seemed higher in CPAP group although both fell into the severe category. ESS was similar.

b Although pre-sealed, opaque envelopes were used, they were not sequentially numbered.

c The one patient who dropped out was replaced by the next available recruit.

d An unpaired comparison of first treatment assessment period was conducted based on the evidence of carryover for this variable.

e Six dropped out and four completed the study but were dropped from the analysis as polysomnography was conducted at the incorrect time.

Who was blinded?	Studies using sham CPAP as comparator	Was the study parallel design? (sham CPAP)	Were the participants CPAP naïve? (sham CPAP)	Crossover trials	Was an appropriate analysis using paired data performed? (crossover)	Was there a treatment by period interaction? (crossover)
Participants and investigators (not involved with CPAP titration)	✓	✓	✓	X	NA	NA
NA	X	Partial crossover	✓	✓	?	?
Patients and investigators	✓	✓	?	X	NA	NA
NA	NA	X	?	✓	X	?
NA	NA	✓	?	X	NA	NA
Participants and outcome assessors	✓	X	?	✓	✓	X
NA	NA	X	✓	✓	✓	?
NA	NA	X	✓	✓	✓	X
Participants and clinical staff in contact with them	✓	✓	✓	X	NA	NA
NA	✓	X	?	✓	✓	X
Participants and investigators	✓	✓	✓	X	NA	NA

Appendix 4

Clinical effectiveness

TABLE 41 *Subgroup analysis for the Epworth Sleepiness Scale (CPAP versus placebo/usual care)*

	Number of trials	Random effects [MD (95% CI)]	Fixed effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Baseline ESS				
Mild (0–9)	2		–1.1 (–1.8 to –0.3)	0%
Moderate (10–15)	16	–2.3 (–3.0 to –1.6)	–2.1 (–2.6 to –1.7)	51%
Severe (16–24)	5	–5.0 (–6.5 to –3.5)	–5.0 (–6.1 to –4.0)	46%
Baseline AHI				
Mild (AHI 5–14)	3	–1.5 (–3.4 to 0.4)		36%
Moderate (AHI 15–30)	7	–2.0 (–3.0 to –1.1)		65%
Severe (AHI > 30)	13	–3.4 (–4.6 to –2.3)		71%
Study design				
Crossover	7	–2.0 (–4.5 to –1.7)		36%
Parallel	13	–3.5 (–4.8 to –2.3)		73%
Change data	3 (two parallel and one crossover)	–1.5 (–2.6 to –0.4)		
Comparator				
Sham CPAP	12	–3.0 (–4.2 to –1.9)		36%
Oral placebo	6	–2.1 (–3.5 to –0.8)		63%
Conservative/usual care	5	–2.7 (–4.1 to –1.3)		56%

AHI, apnoea–hypopnoea index; ESS, Epworth Sleepiness Scale.

TABLE 42 *Removal of individual studies from the Epworth Sleepiness Scale meta-analysis (CPAP versus placebo/usual care)*

Baseline symptom severity	Overall treatment effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Mild (ESS 0–9)		
Barbé *et al.*, 2001[83]	0.0 (–2.3, 2.3)	
Robinson *et al.*, 2006[68]	–1.2 (–2.0, –0.4)	
Moderate (ESS 10–15)		
Ballester *et al.*, 1999[96]	–2.1 (–2.8, –1.5)	41%
Barnes *et al.*, 2002[89]	–2.4 (–3.2, –1.7)	52%
Barnes *et al.*, 2004[82]	–2.5 (–3.2, –1.8)	46%
Becker *et al.*, 2003[109]	–2.3 (–3.0, –1.6)	52%
Campos-Rodriguez *et al.*, 2006[65]	–2.5 (–3.2, –1.7)	50%
Coughlin *et al.*, 2007[62]	–2.3 (–3.0, –1.5)	51%
Engleman *et al.*, 1997[92]	–2.4 (–3.1, –1.7)	52%
Engleman *et al.*, 1998[93]	–2.2 (–2.8, –1.5)	42%
Engleman *et al.*, 1999[78]	–2.3 (–3.0, –1.6)	53%
Faccenda *et al.*, 2001[94]	–2.3 (–3.1, –1.6)	54%
Hui *et al.*, 2006[64]	–2.4 (–3.1, –1.7)	53%
Lam *et al.*, 2007[70]	–2.3 (–3.0, –1.6)	54%
Marshall *et al.*, 2005[79]	–2.3 (–3.1, –1.6)	54%
Monasterio *et al.*, 2001[100]	–2.4 (–3.1, –1.6)	54%
Redline *et al.*, 1998[59]	–2.5 (–3.2, –1.7)	50%
West *et al.*, 2006[67]	–2.3 (–3.0, –1.5)	52%
Severe (ESS 14–24)		
Chakravorty *et al.*, 2002[97]	–5.4 (–7.0, –3.7)	46%
Henke *et al.*, 2001[85]	–5.1 (–6.9, –3.4)	58%
Jenkinson *et al.*, 1999[77]	–5.0 (–7.2, –2.8)	59%
Montserrat *et al.*, 2001[86]	–4.4 (–5.5, –3.2)	0%
Pepperell *et al.*, 2002[87]	–5.1 (–7.2, –3.0)	58%

ESS, Epworth Sleepiness Scale.

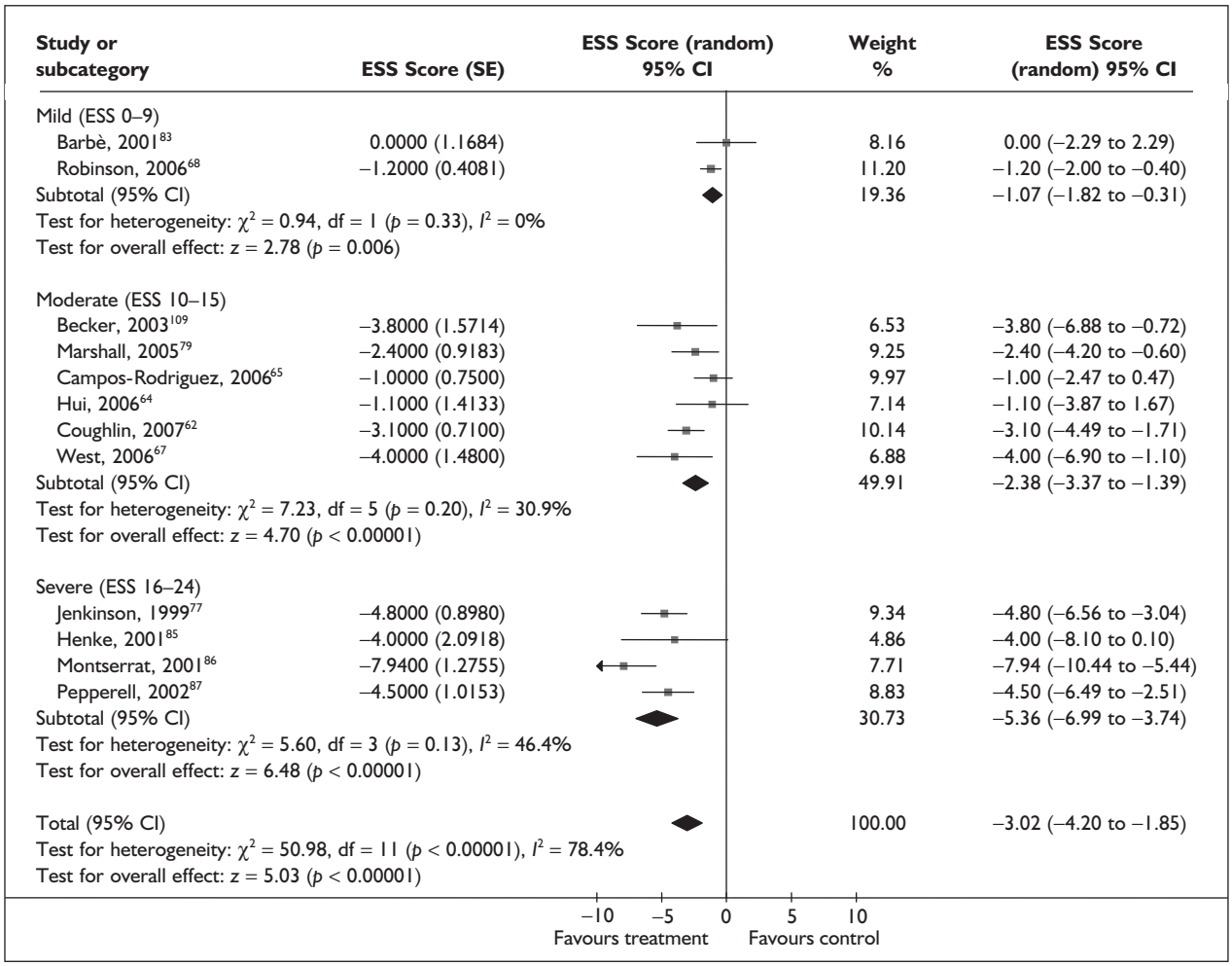

FIGURE 22 *Epworth Sleepiness Scale (CPAP versus sham CPAP) stratified by severity of sleepiness at baseline (ESS).*

TABLE 43 *Subgroup analysis for the Epworth Sleepiness Scale (CPAP versus dental devices)*

	Number of trials	Random effects (MD (95% CI)]	Fixed effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Baseline ESS				
Mild (0–9)	0			
Moderate (10–15)	6	–0.9 (–2.1 to 0.4)	–0.5 (–1.3 to 0.2)	0%
Severe (16–24)	0			
Baseline AHI				
Mild (AHI 5–14)	0			
Moderate (AHI 15–30)	4	–0.2 (–1.1 to 0.7)		0%
Severe (AHI > 30)	2	–1.8 (–6.0 to 2.3)		88%
Study design				
Crossover	4	–1.0 (–1.1 to 0.7)		72%
Parallel	2	–0.6 (–2.7 to 1.5)		41%

AHI, apnoea–hypopnoea index; ESS, Epworth Sleepiness Scale.

TABLE 44 *Removal of individual studies from the Epworth Sleepiness Scale meta-analysis (CPAP versus dental devices)*

Baseline symptom severity	Overall treatment effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Moderate (ESS 10–15)		
Barnes *et al.*, 2004[82]	–1.2 (–2.8 to 0.5)	64%
Engleman *et al.*, 2002[103]	–0.1 (–0.9 to 0.6)	0%
Ferguson *et al.*, 1997[80]	–1.2 (–2.7 to 0.4)	65%
Fleetham *et al.*, 2002[101]	–1.1 (–2.7 to 0.4)	66%
Lam *et al.*, 2007[70]	–0.7 (–2.1 to 0.7)	65%
Tan *et al.*, 2007[106]	–0.9 (–2.3 to 0.6)	68%

ESS, Epworth Sleepiness Scale.

TABLE 45 *Subgroup analysis for the Maintenance of Wakefulness Test (CPAP versus placebo/usual care)*

	Number of trials	Random effects [MD (95% CI)]	Fixed effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Baseline ESS				
Mild (0–9)	0			
Moderate 10–15)	4	2.3 (0.4–4.3)	2.3 (0.4–4.3)	0%
Severe (16–24)	1	6.5 (2.6–10.4)	6.5 (2.6–10.4)	
Overall effect		3.3 (1.3, 5.3)	3.2 (1.4–5.0)	11.3%
Baseline AHI				
Mild (AHI 5–14)	1	1.8 (–2.8 to 6.4)		
Moderate (AHI 15–30)	3	4.1 (1.0–7.3)		50%
Severe (AHI > 30)	1	1.9 (–6.2 to 10.0)		
Study design				
Crossover	3	2.4 (0.3–4.4)		0%
Parallel	2	5.6 (2.1–9.2)		0%

AHI, apnoea–hypopnoea index; ESS, Epworth Sleepiness Scale.

TABLE 46 *Removal of individual studies from the Maintenance of Wakefulness Test meta-analysis (CPAP versus placebo/usual care)*

Study	Overall treatment effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Barnes *et al.*, 2004[82]	4.4 (1.9–6.9)	0%
Engleman *et al.*, 1999[78]	3.8 (1.2–6.3)	27%
Jenkinson *et al.*, 1999[77]	2.3 (0.4–4.3)	0%
Marshall *et al.*, 2005[79]	3.1 (0.8–5.5)	25%
West *et al.*, 2006[67]	3.5 (1.1–5.9)	32%

TABLE 47 *Subgroup analysis for the Multiple Sleep Latency Test (CPAP versus placebo/usual care)*

	Number of trials	Random effects [MD (95% CI)]	Fixed effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Baseline ESS				
Mild (0–9)	1	2.0 (–0.8 to 4.8)		
Moderate 10–15)	4	0.2 (–1.8 to 2.2)		69%
Severe (16–24)	1	–6.1 (–27.3 to 15.1)		
Not reported	1	1.1 (–0.8 to 3.0)		
Overall effect		0.6 (–0.7 to 1.9)	0.8 (–0.1 to 1.6)	46%
Baseline AHI				
Mild (AHI 5–14)	2	–0.7 (–2.9 to 1.4)		0%
Moderate (AHI 15–30)	2	0.0 (–2.1 to 2.1)		60%
Severe (AHI > 30)	3	2.3 (0.9–3.7)		0%
Study design				
Crossover	4	1.0 (–0.6 to 2.5)		45%
Parallel	3	0.2 (–2.4 to 2.7)		43%

AHI, apnoea–hypopnoea index; ESS, Epworth Sleepiness Scale.

TABLE 48 *Removal of individual studies from the Multiple Sleep Latency Test meta-analysis (CPAP versus placebo/usual care)*

Study	Overall treatment effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Barbé *et al.*, 2001[83]	0.4 (–1.1 to 1.9)	52%
Barnes *et al.*, 2002[89]	0.9 (–0.4 to 2.3)	45%
Chakravorty *et al.*, 2002[97]	0.7 (–0.7 to 2.0)	54%
Engleman *et al.*, 1994[90]	0.5 (–1.2 to 2.2)	55%
Engleman *et al.*, 1997[92]	0.7 (–0.8 to 2.1)	55%
Engleman *et al.*, 1998[98]	0.0 (–1.0 to 1.2)	9%
Monasterio *et al.*, 2001[100]	1.2 (0.0–2.4)	19%

TABLE 49 *Subgroup analysis for daytime mean arterial pressure (CPAP versus placebo/usual care)*

	Number of trials	Random effects [MD (95% CI)]	Fixed effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Baseline ESS				
Mild (0–9)	1	1.1 (–2.9 to 5.1)		
Moderate 10–15)	3	–3.4 (–7.9 to 1.2)		58%
Severe (16–24)	1	–4.2 (–6.4 to –2.0)		
Not reported	1	–1.0 (–2.7 to 0.7)		
Overall effect		–2.1 (–4.3 to 0.0)	–2.00 (–3.16 to –0.83)	59%
Baseline AHI				
Mild (AHI 5–14)				
Moderate (AHI 15–30)	1	1.1 (–2.9 to 5.1)		
Severe (AHI > 30)	5	–2.7 (–4.9 to –0.4)		59%
Study design				
Crossover (end point)	1	–1.0 (–2.7 to 0.7)		
Parallel (end point)	0			
Crossover (change)	1	1.1 (–2.9 to 5.1)		
Parallel (change)	4	–3.5 (–6.2 to –0.7)		48%

AHI, apnoea–hypopnoea index; ESS, Epworth Sleepiness Scale.

TABLE 50 *Removal of individual studies for daytime mean arterial pressure (CPAP versus placebo/usual care)*

Study	Overall treatment effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Becker *et al.*, 2003[109]	–1.7 (–3.5 to 0.1)	48%
Campos-Rodriguez *et al.*, 2006[65]	–2.4 (–4.9 to 0.1)	66%
Engleman *et al.*, 1996[91]	–2.6 (–5.4 to 0.3)	60%
Hui *et al.*, 2006[64]	–2.2 (–4.7 to 0.4)	67%
Pepperell *et al.*, 2002[87]	–1.4 (–3.6 to 0.8)	42%
Robinson *et al.*, 2006[68]	–2.7 (–4.9 to –0.4)	59%

TABLE 51 *Subgroup analysis for daytime systolic blood pressure (CPAP versus placebo/usual care)*

	Number of trials	Random effects [MD (95% CI)]	Fixed effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Baseline AHI				
Mild (AHI 5–14)	1	–2.9 (–13.5 to 7.7)		
Moderate (AHI 15–30)	0			
Severe (AHI > 30)	6	–1.0 (–3.3 to 1.4)		0%
Overall effect	7	–1.1 (–3.4 to 1.2)	–1.1 (–3.4 to 1.2)	0%
Study design				
Crossover (end point)	2	–0.4 (–3.5 to 2.7)		0%
Parallel (end point)	2	1.2 (–4.0 to 6.4)		0%
Crossover (change)	1	–2.9 (–13.5 to 7.7)		
Parallel (change)	2	–5.2 (–12.4 to 2.1)		

AHI, apnoea–hypopnoea index.

TABLE 52 *Subgroup analysis for daytime diastolic blood pressure (CPAP versus placebo/usual care)*

	Number of trials	Random effects [MD (95% CI)]	Fixed effect [MD (95% CI)]	Statistical heterogeneity (I^2)
Baseline AHI				
Mild (AHI 5–14)	1	–2.6 (–12.8 to 7.6)		
Moderate (AHI 15–30)	0			
Severe (AHI > 30)	6	–1.2 (–3.1 to 0.7)		40%
Overall effect	7	–1.2 (–2.9 to 0.5)	–0.06 (–2.37 to 0.25)	29%
Study design				
Crossover (end point)	2	–0.9 (–2.9 to 1.0)		31%
Parallel (end point)	2	0.5 (–2.7 to 3.7)		0%
Crossover (change)	1	–2.6 (–12.8 to 7.6)		
Parallel (change)	2	–5.7 (–14.8 to 3.4)		76%

AHI, apnoea–hypopnoea index.

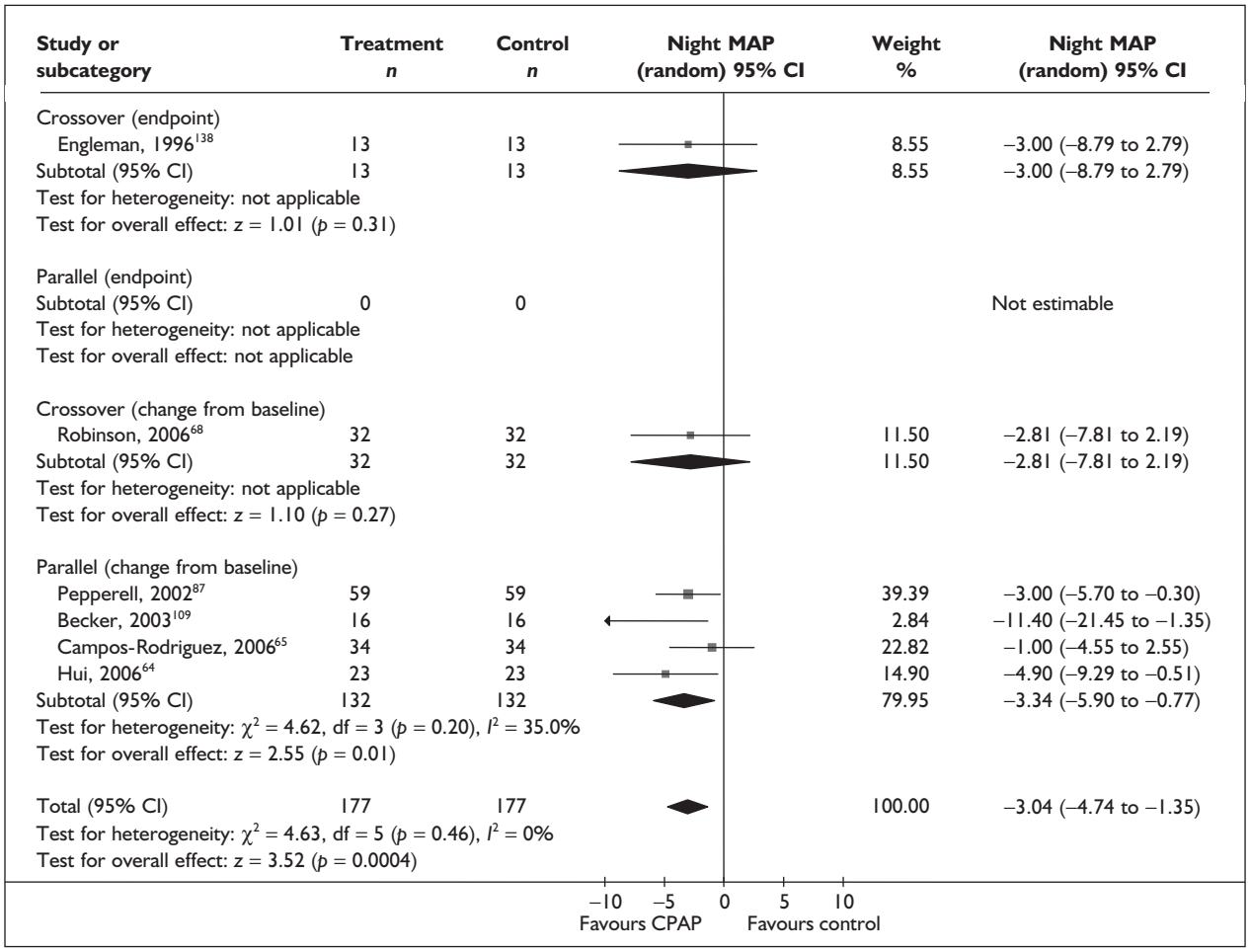

FIGURE 23 *Night-time mean blood pressure (CPAP versus placebo/usual care).*

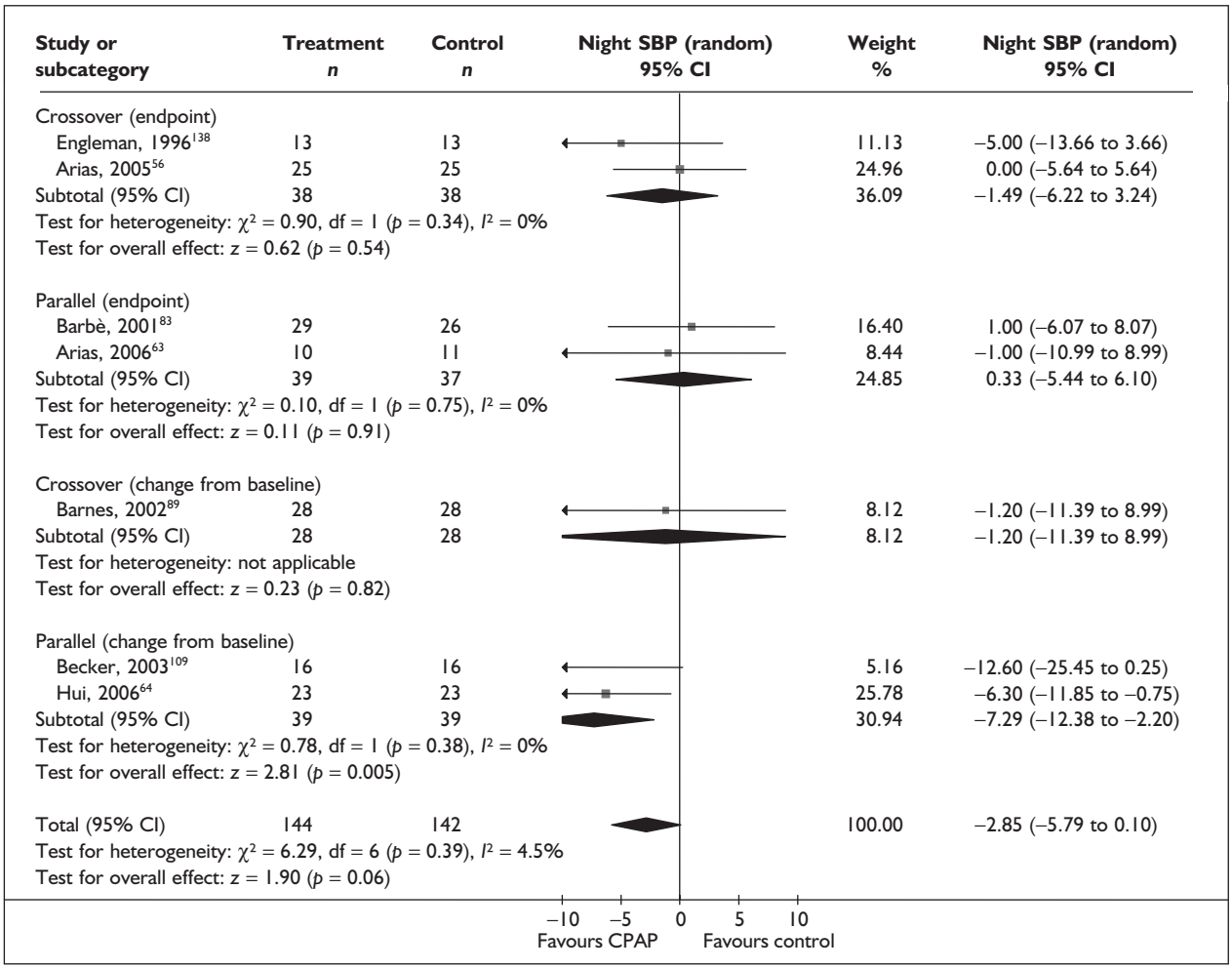

FIGURE 24 *Night-time systolic blood pressure (CPAP versus placebo/usual care).*

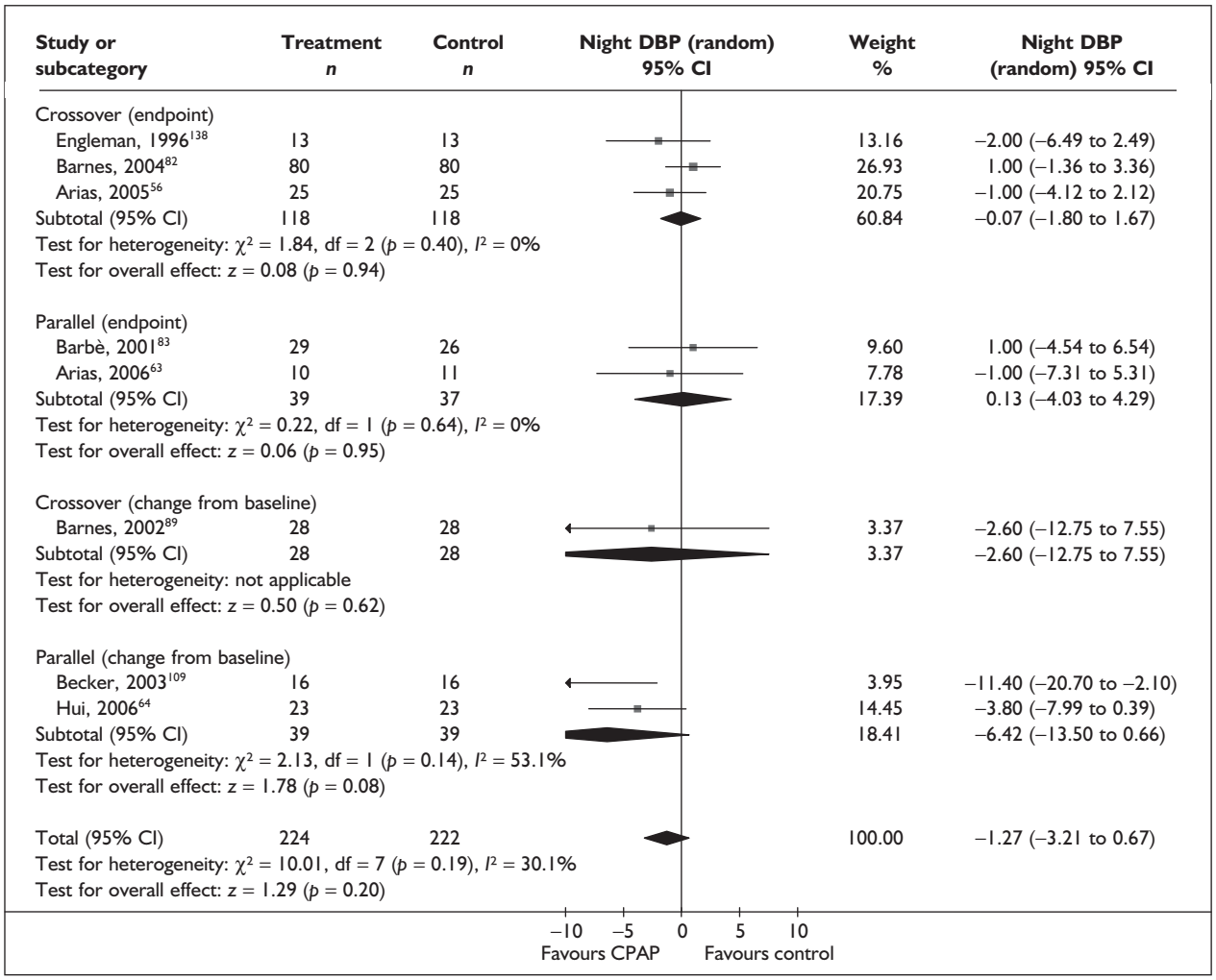

FIGURE 25 *Night-time diastolic blood pressure (CPAP versus placebo/usual care).*

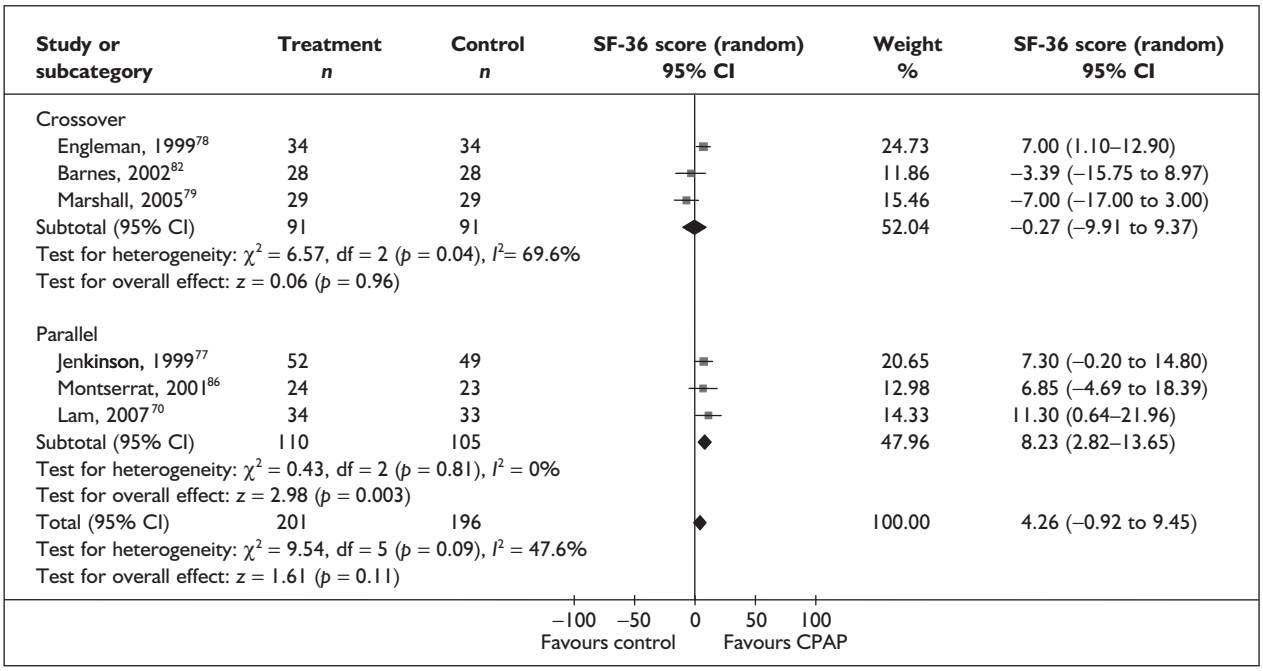

FIGURE 26a *SF-36 subscales (CPAP versus placebo/usual care): bodily pain.*

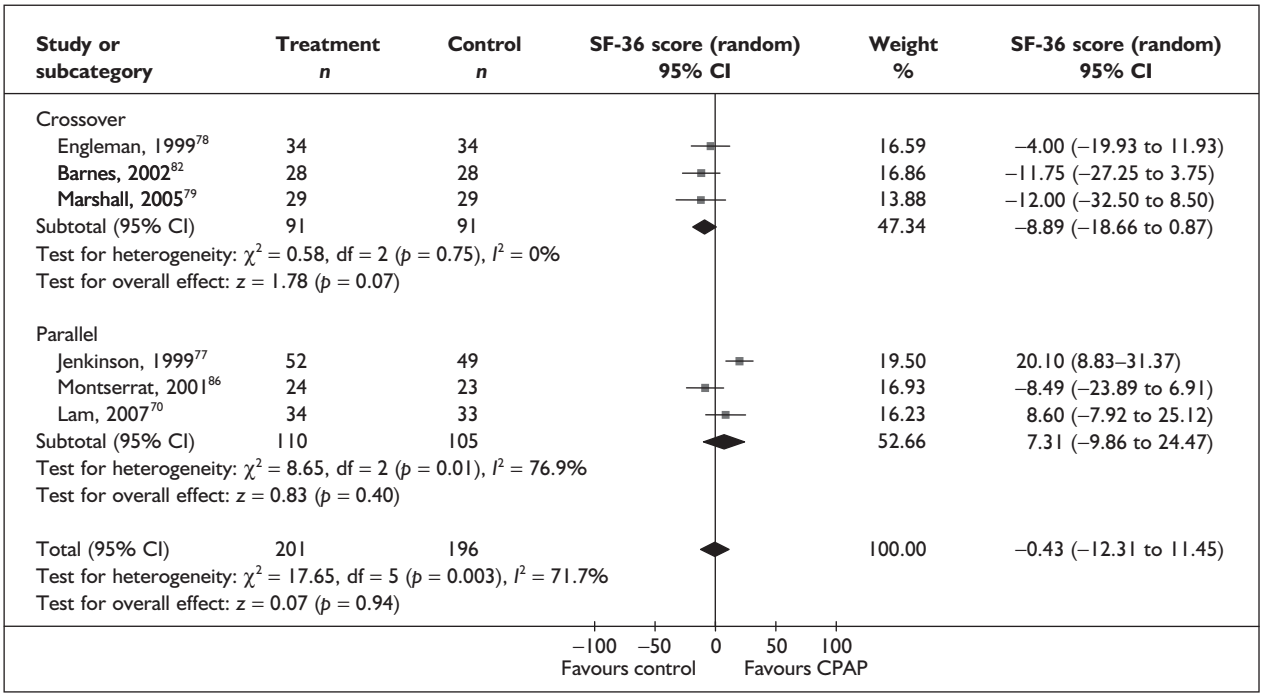

FIGURE 26b *SF-36 subscales (CPAP versus placebo/usual care): emotional role.*

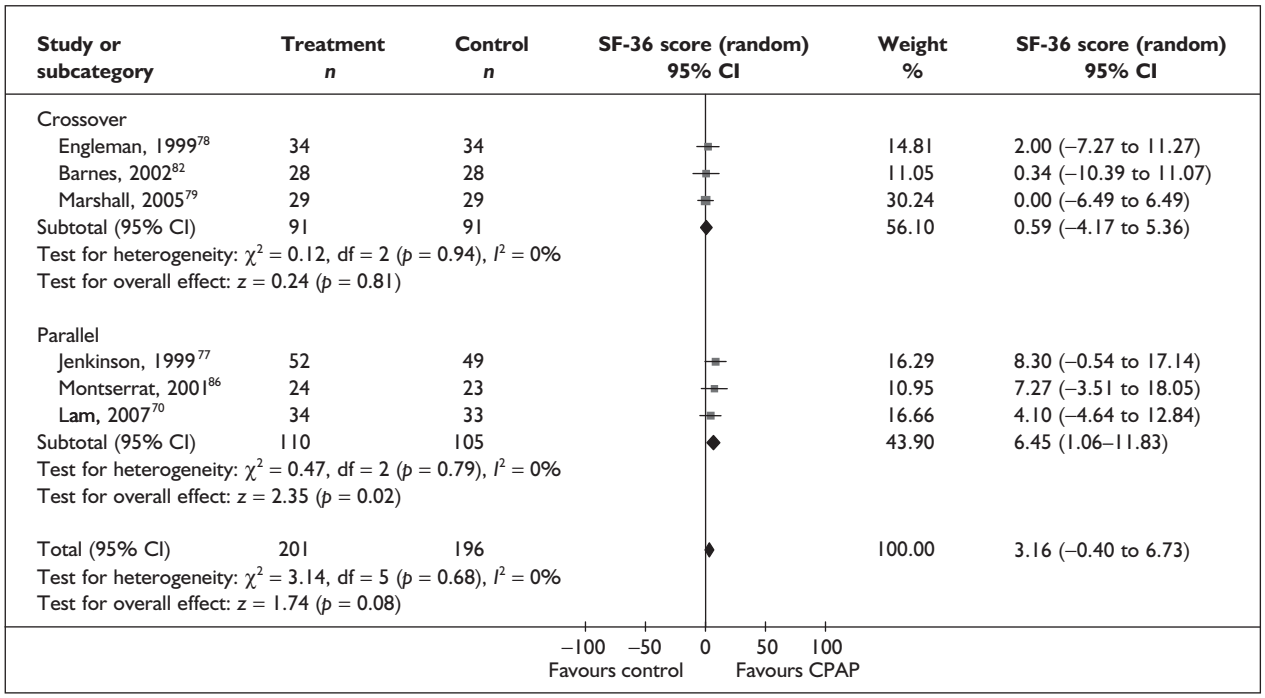

FIGURE 26c *SF-36 subscales (CPAP versus placebo/usual care): general health.*

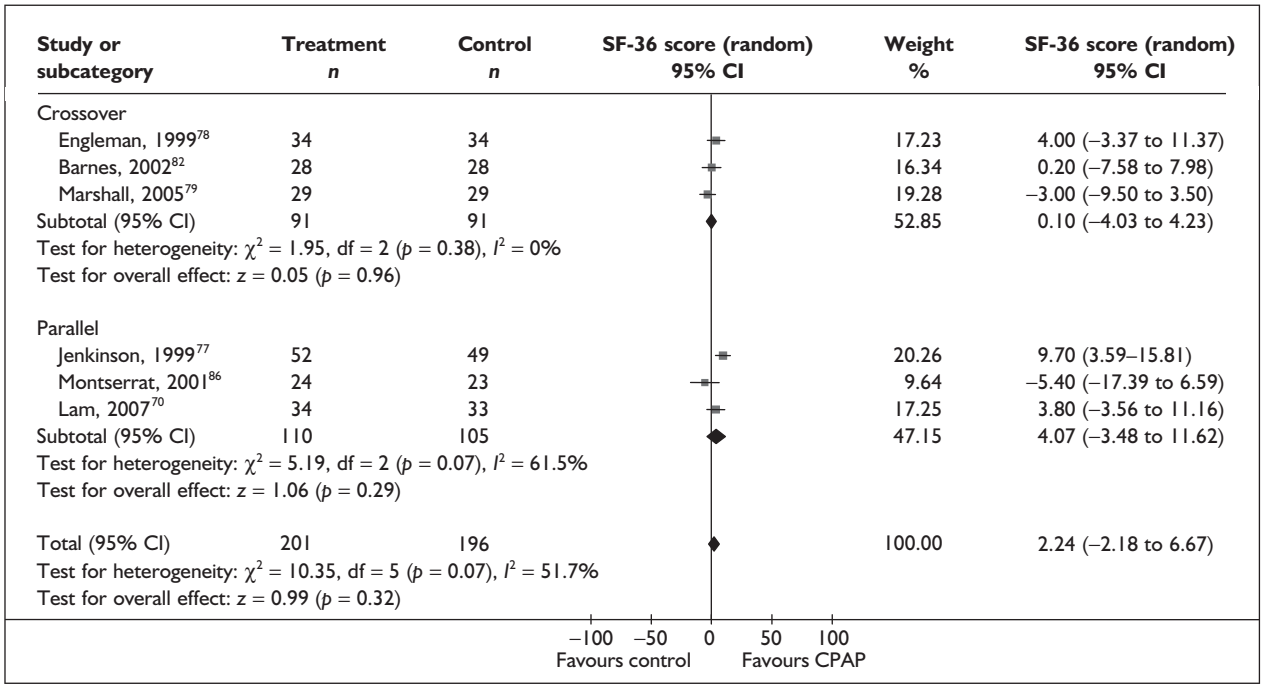

FIGURE 26d *SF-36 subscales (CPAP versus placebo/usual care): mental health.*

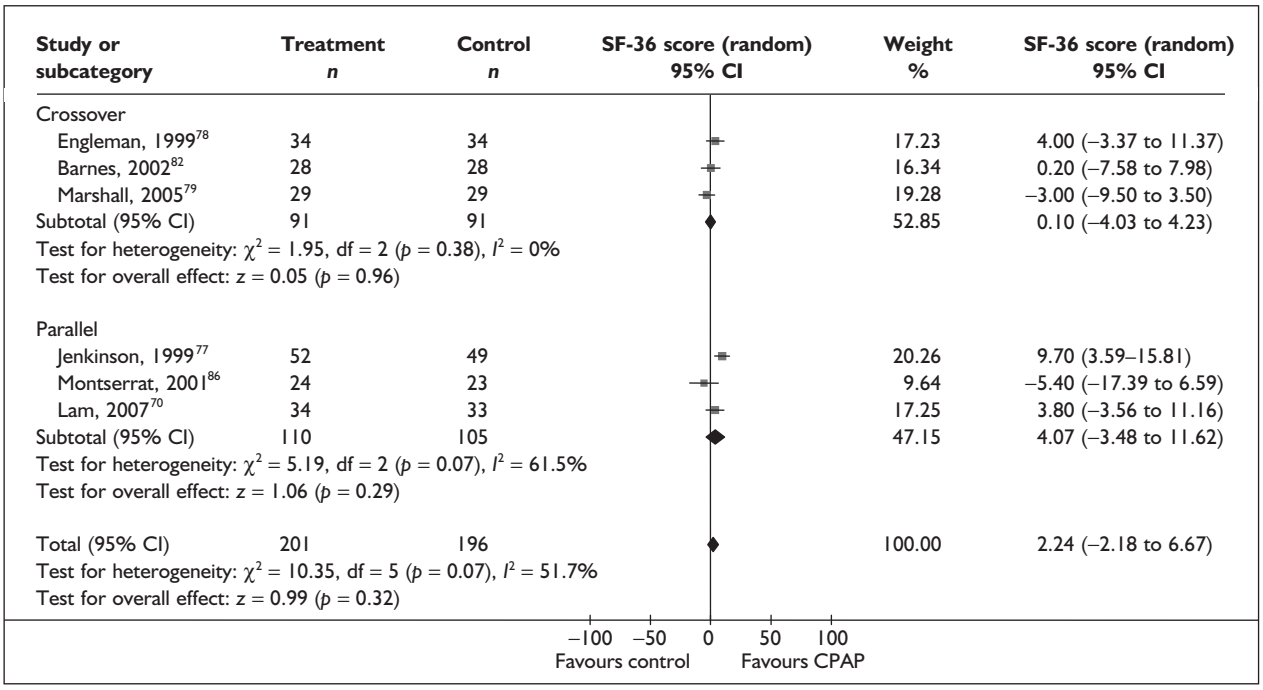

FIGURE 26e *SF-36 subscales (CPAP versus placebo/usual care): physical function.*

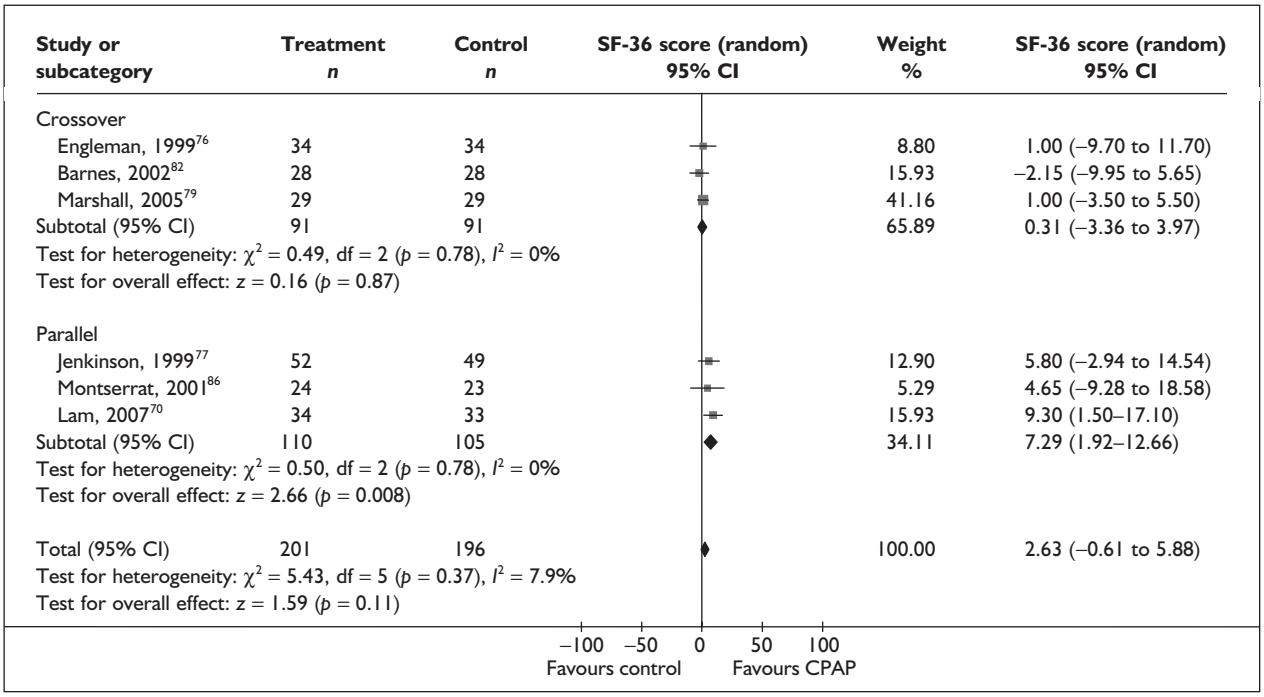

FIGURE 26f *SF-36 subscales (CPAP versus placebo/usual care): physical role.*

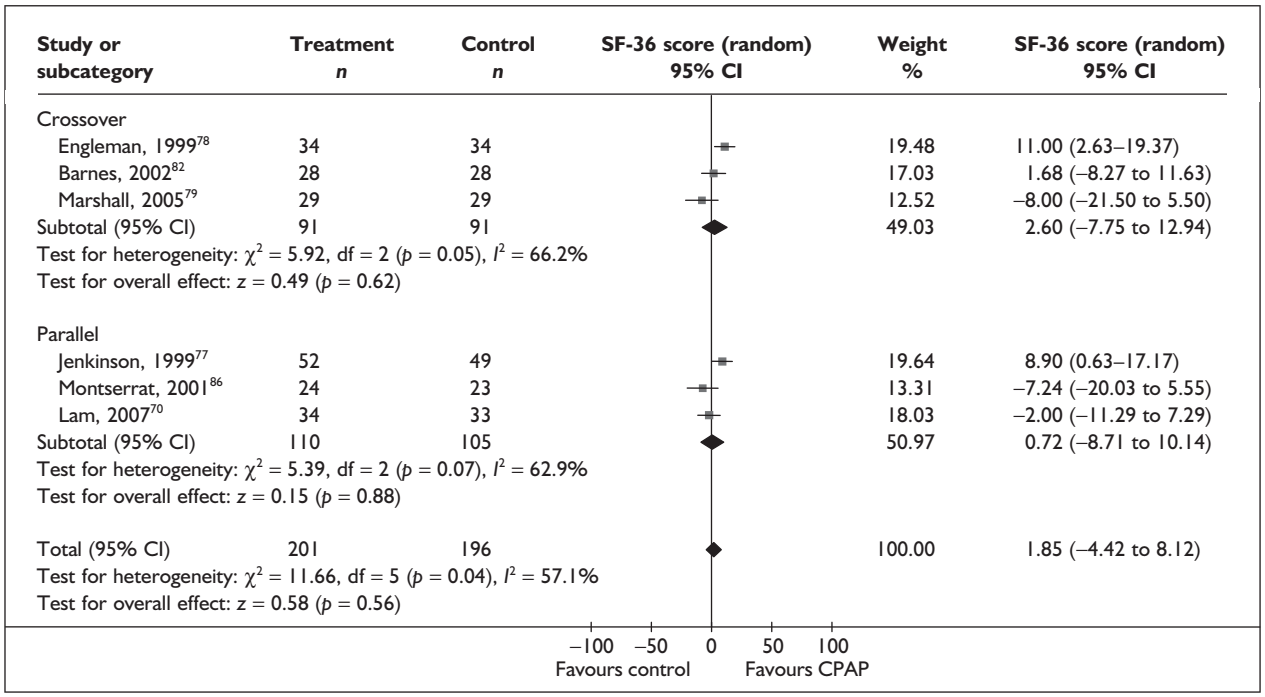

FIGURE 26g *SF-36 subscales (CPAP versus placebo/usual care): social function.*

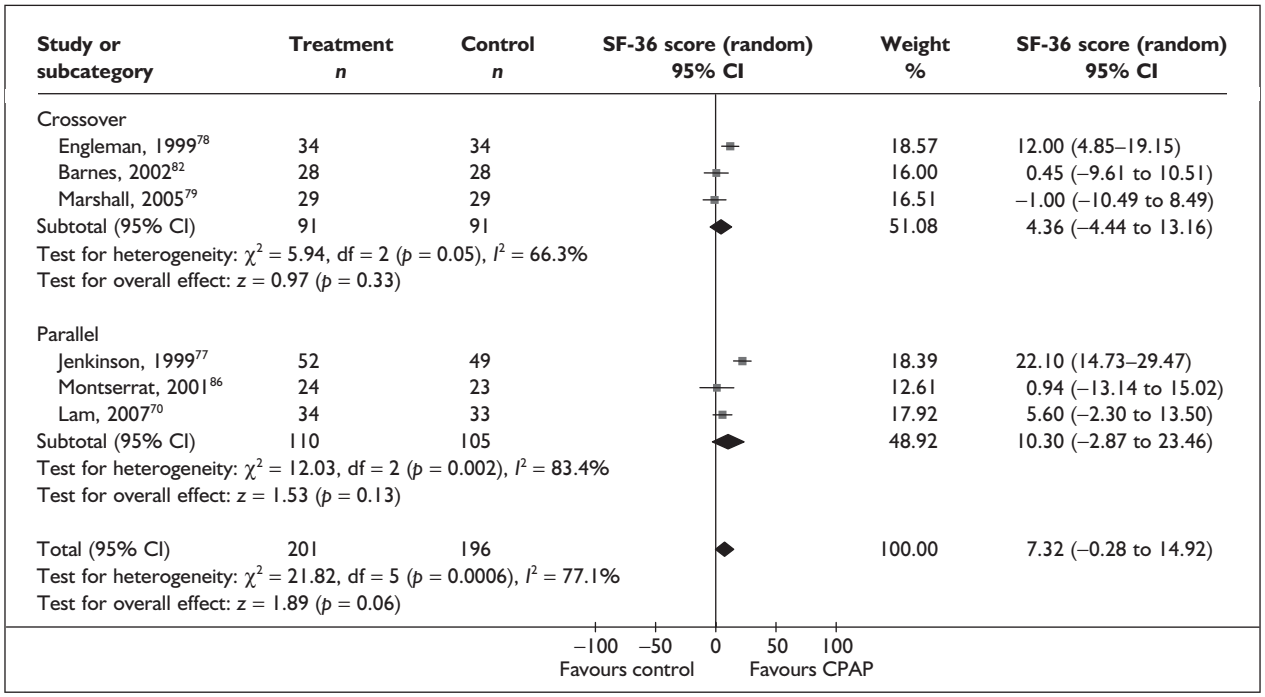

FIGURE 26h *SF-36 subscales (CPAP versus placebo/usual care): vitality.*

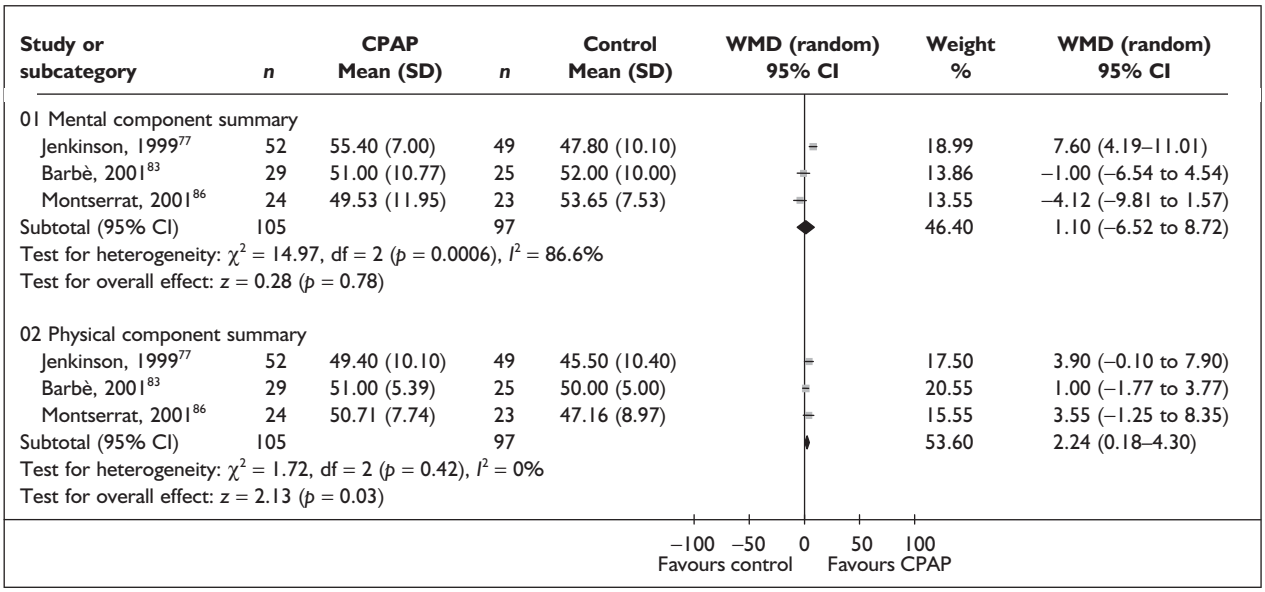

FIGURE 26j *SF-36 subscales (CPAP versus placebo/usual care): SF-36 component score.*

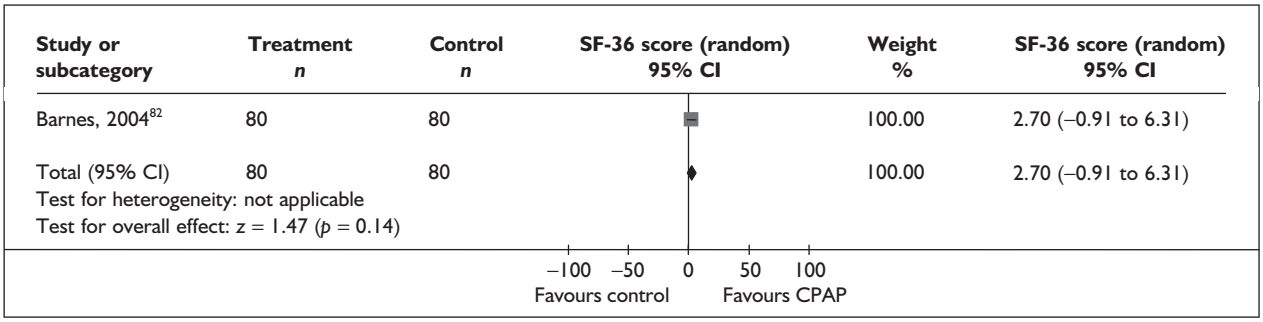

FIGURE 26k *SF-36 subscales (CPAP versus placebo/usual care): SF-36 total score.*

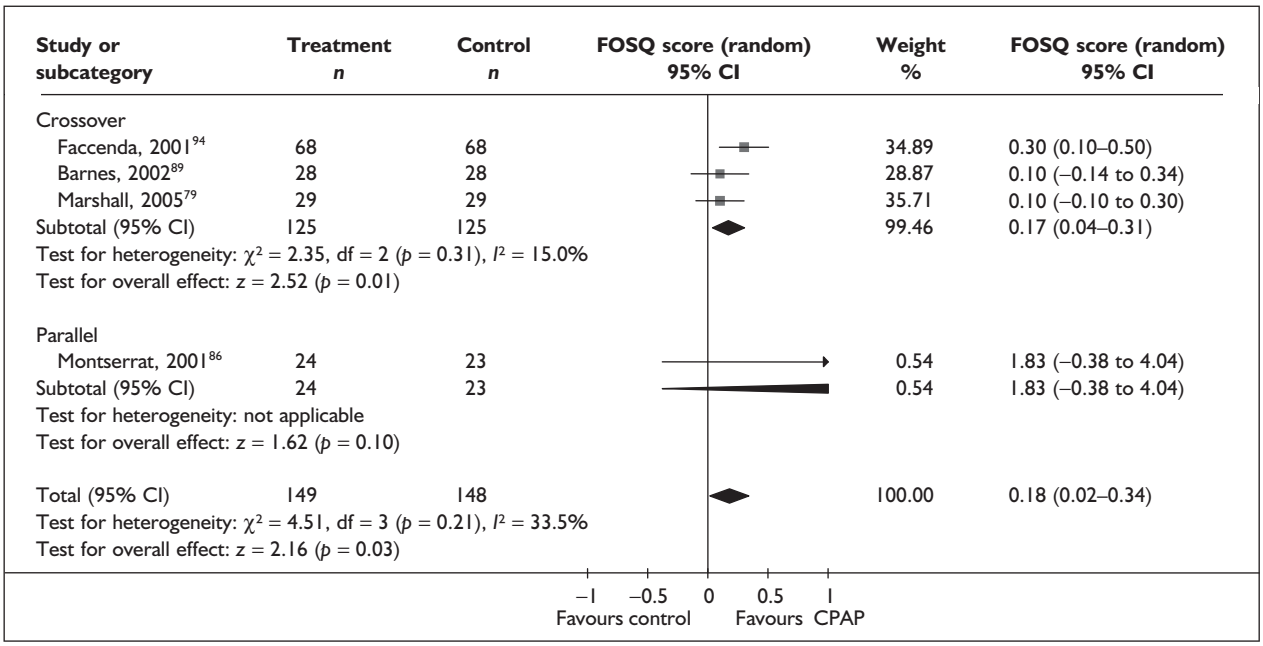

FIGURE 27a *Functional Outcomes of Sleep Questionnaire subscales (CPAP versus control):FOSQ activity level.*

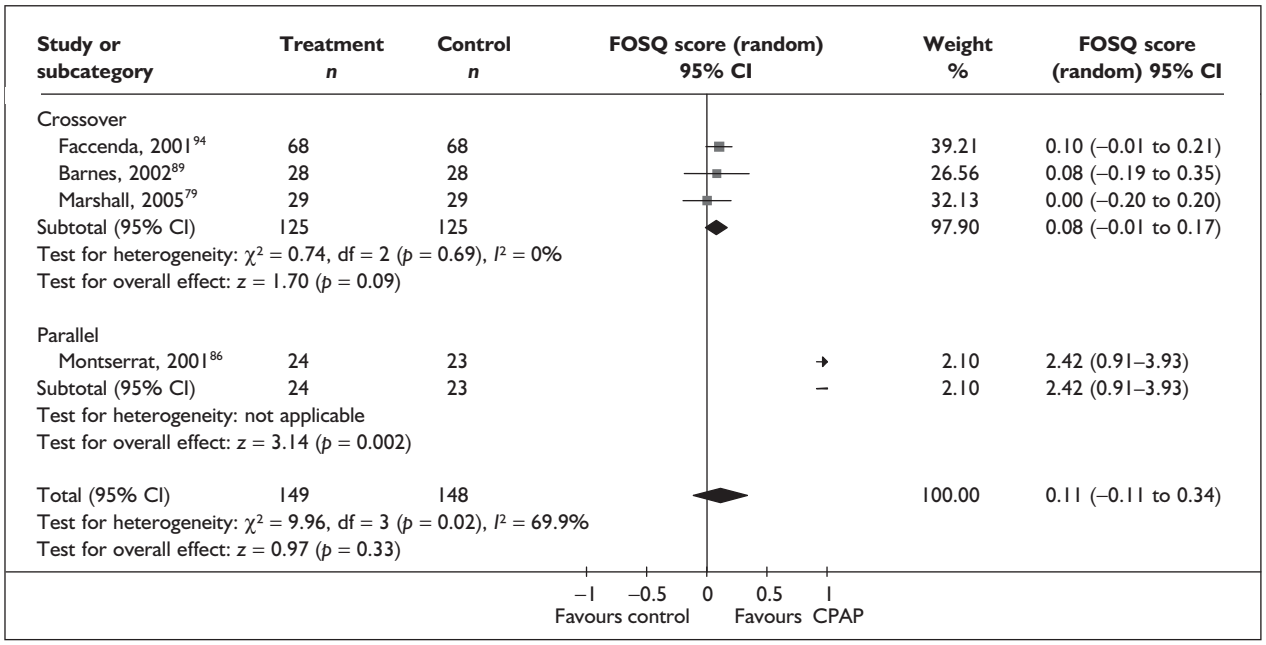

FIGURE 27b *Functional Outcomes of Sleep Questionnaire subscales (CPAP versus control): FOSQ general productivity.*

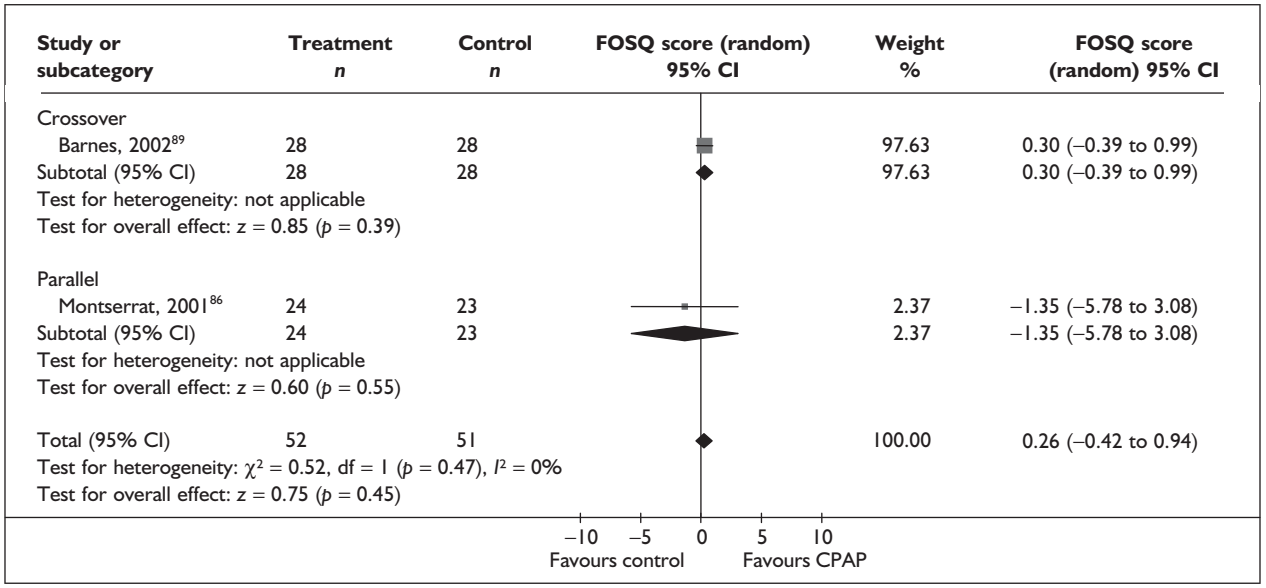

FIGURE 27c *Functional Outcomes of Sleep Questionnaire subscales (CPAP versus control): FOSQ intimacy and sexual activity.*

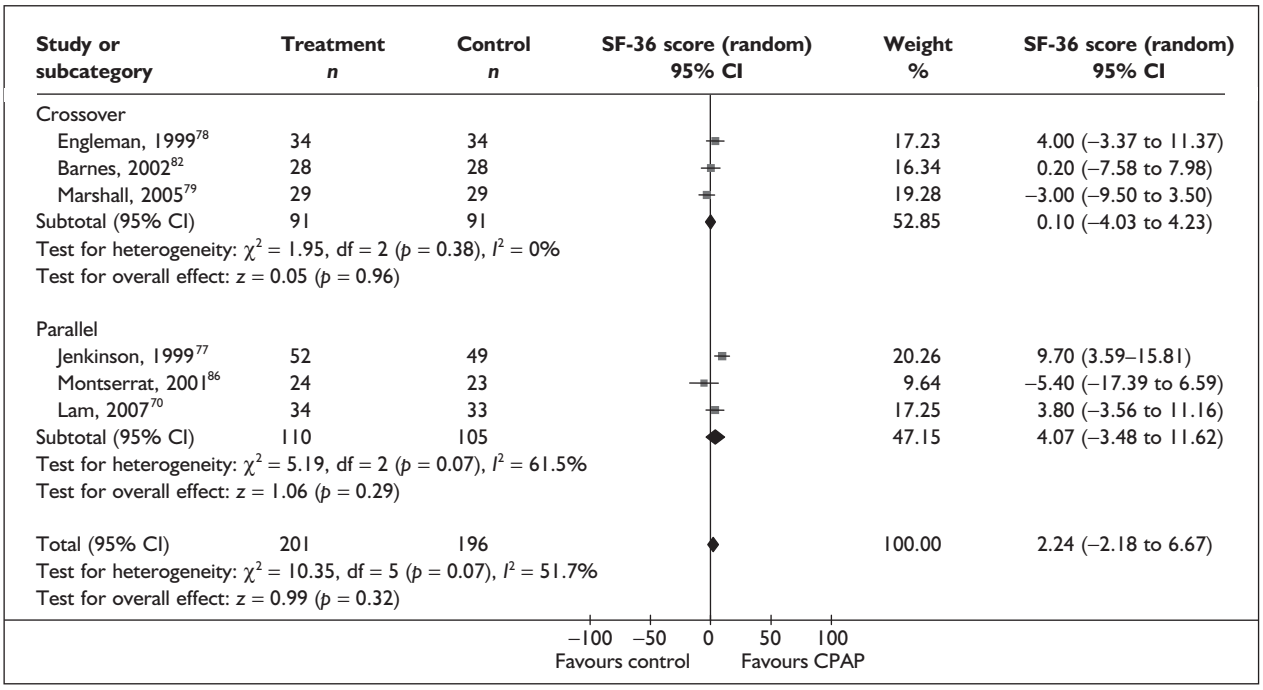

FIGURE 27d *Functional Outcomes of Sleep Questionnaire subscales (CPAP versus control): FOSQ social outcome.*

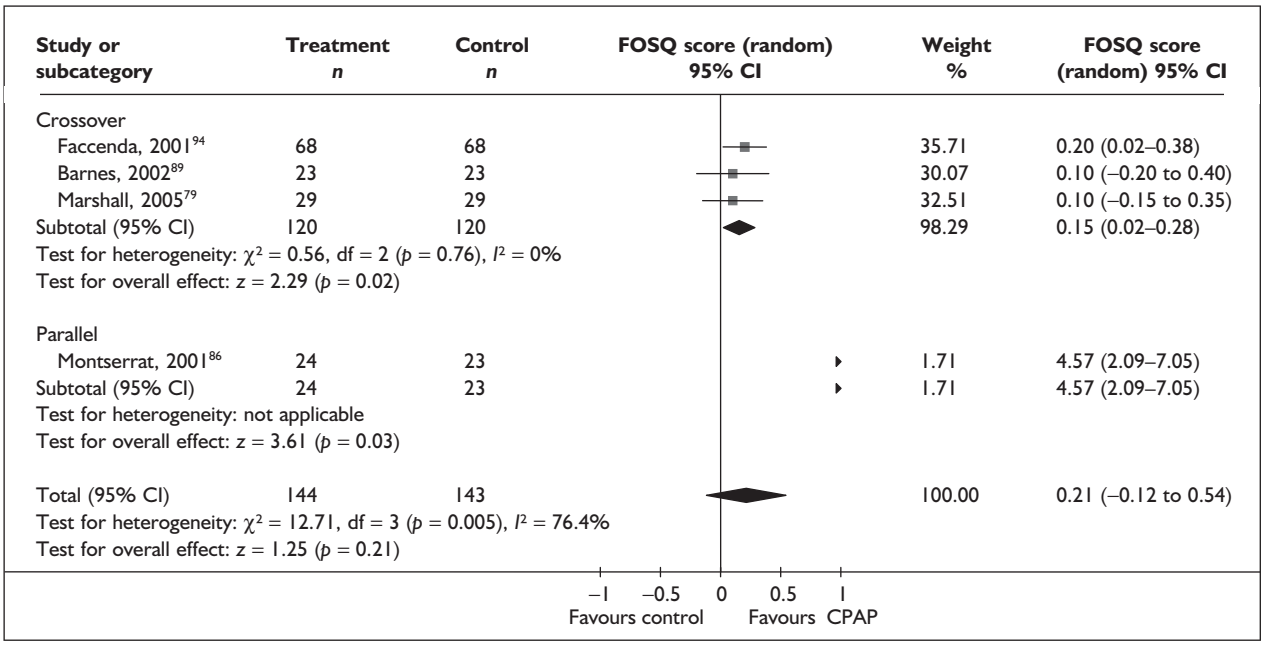

FIGURE 27e *Functional Outcomes of Sleep Questionnaire subscales (CPAP versus control): FOSQ vigilance.*

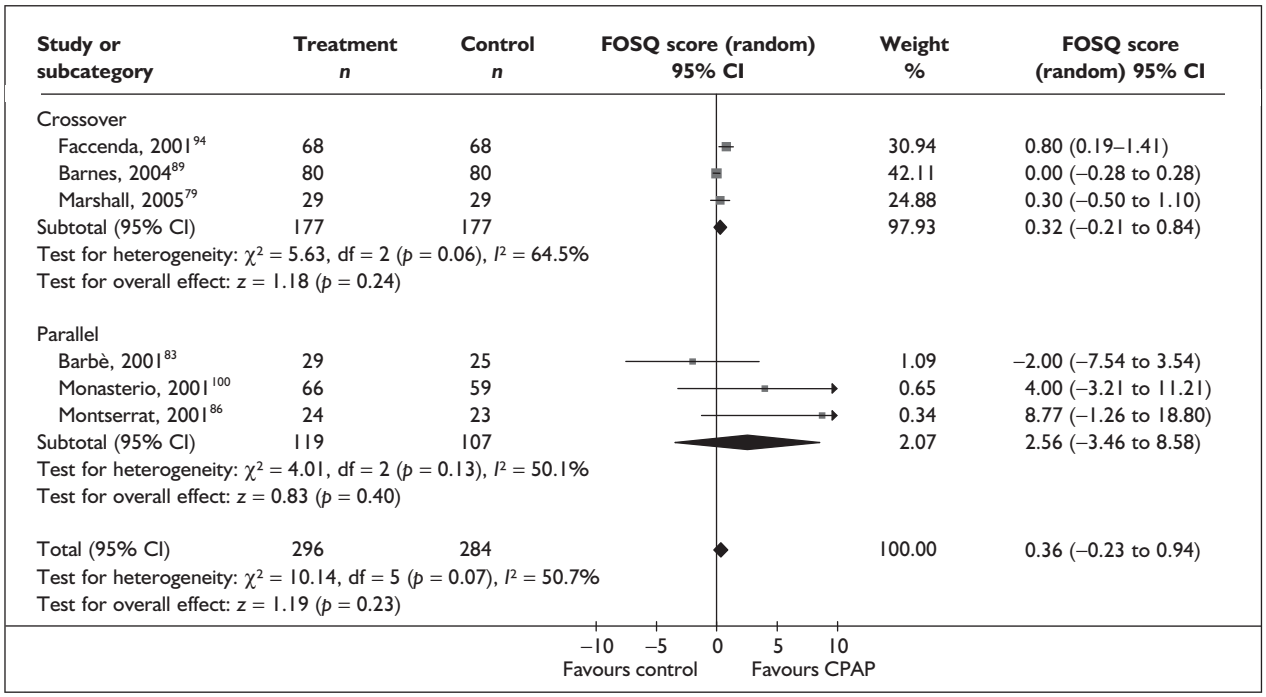

FIGURE 27f *Functional Outcomes of Sleep Questionnaire subscales (CPAP versus control): FOSQ total score.*

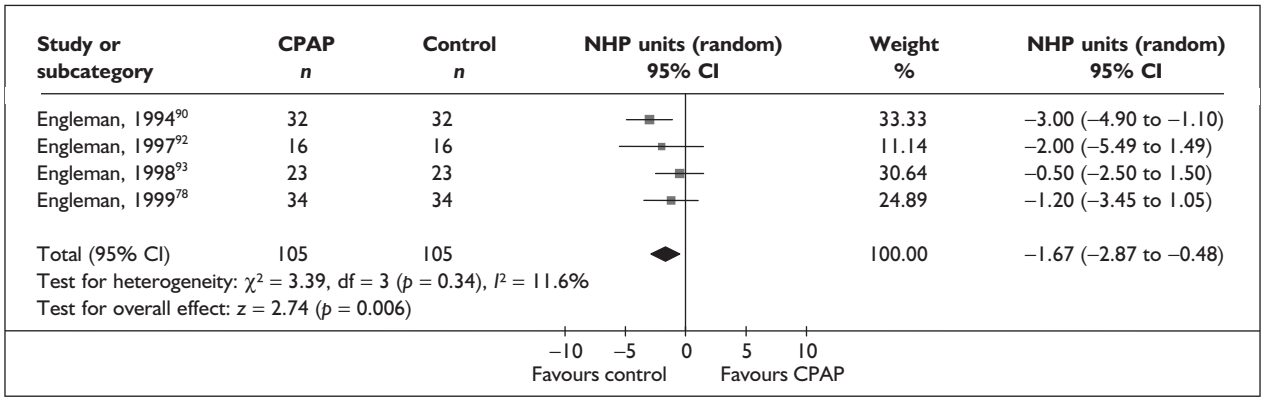

FIGURE 28 *Nottingham Health Profile (Part 2) (CPAP versus placebo/usual care).*

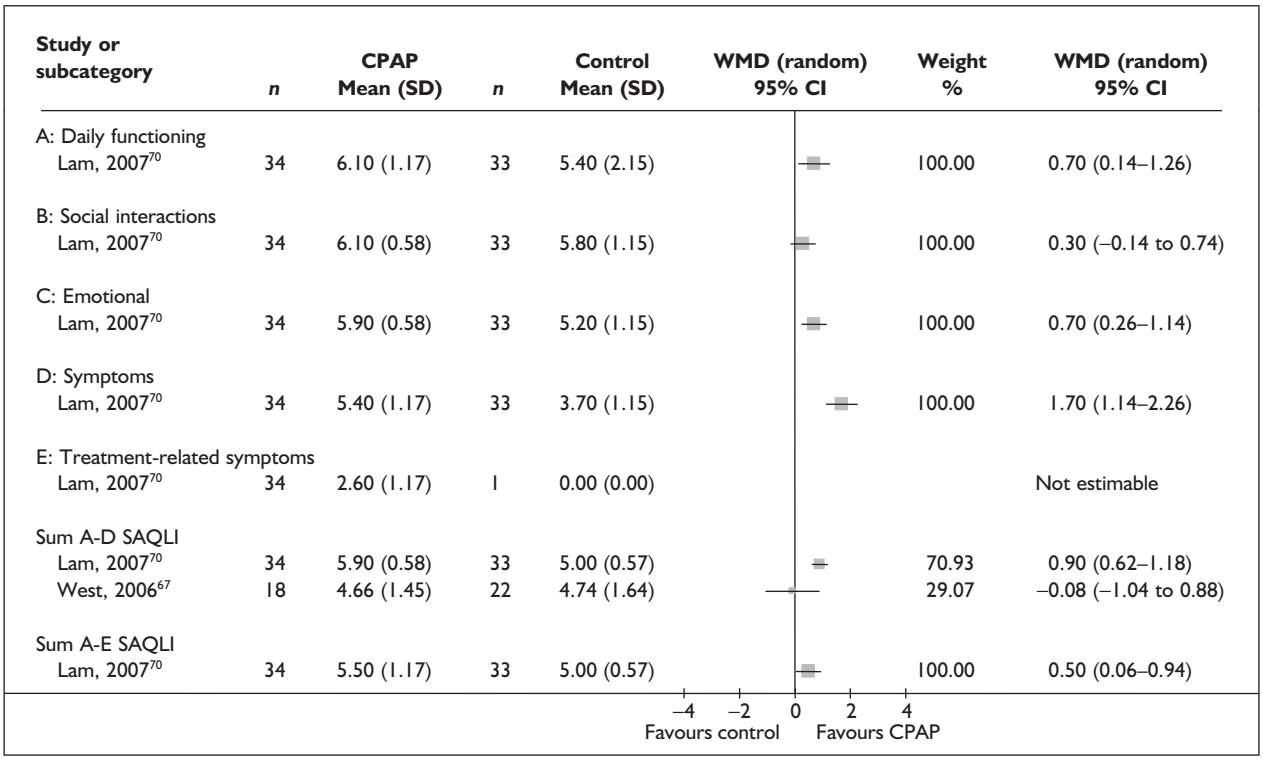

FIGURE 29 *Sleep apnoea quality of life index (CPAP versus placebo/usual care).*

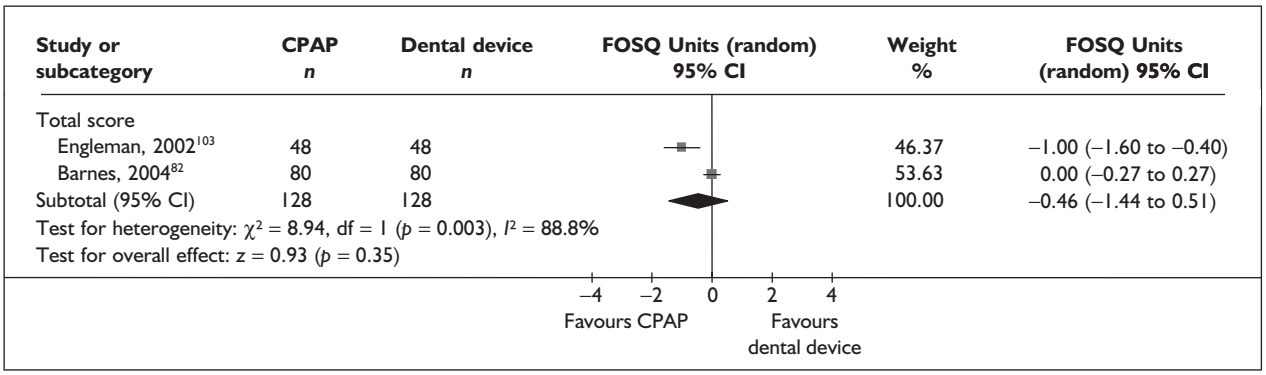

FIGURE 30 *Functional Outcomes of Sleep Questionnaire (CPAP versus dental devices).*

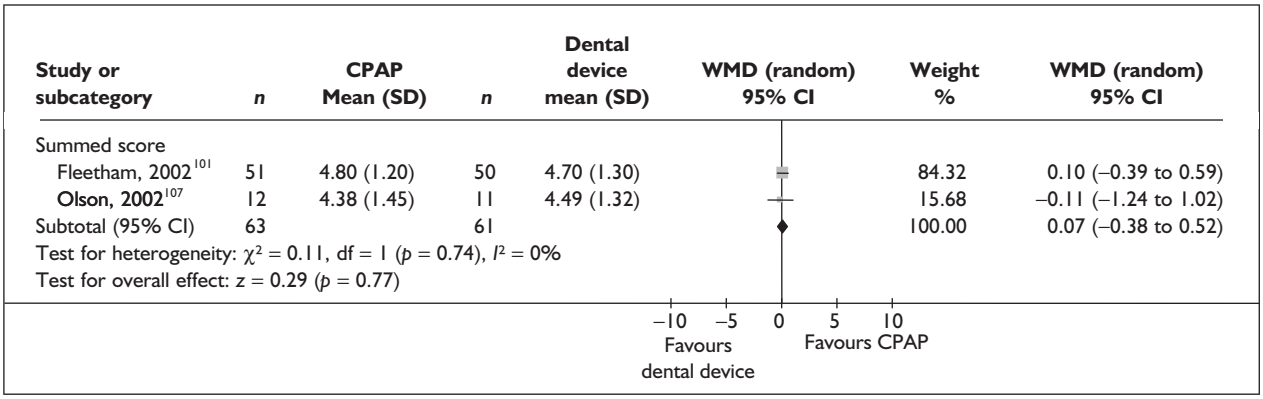

FIGURE 31 *Sleep apnoea quality of life index – summed score (CPAP versus dental devices).*

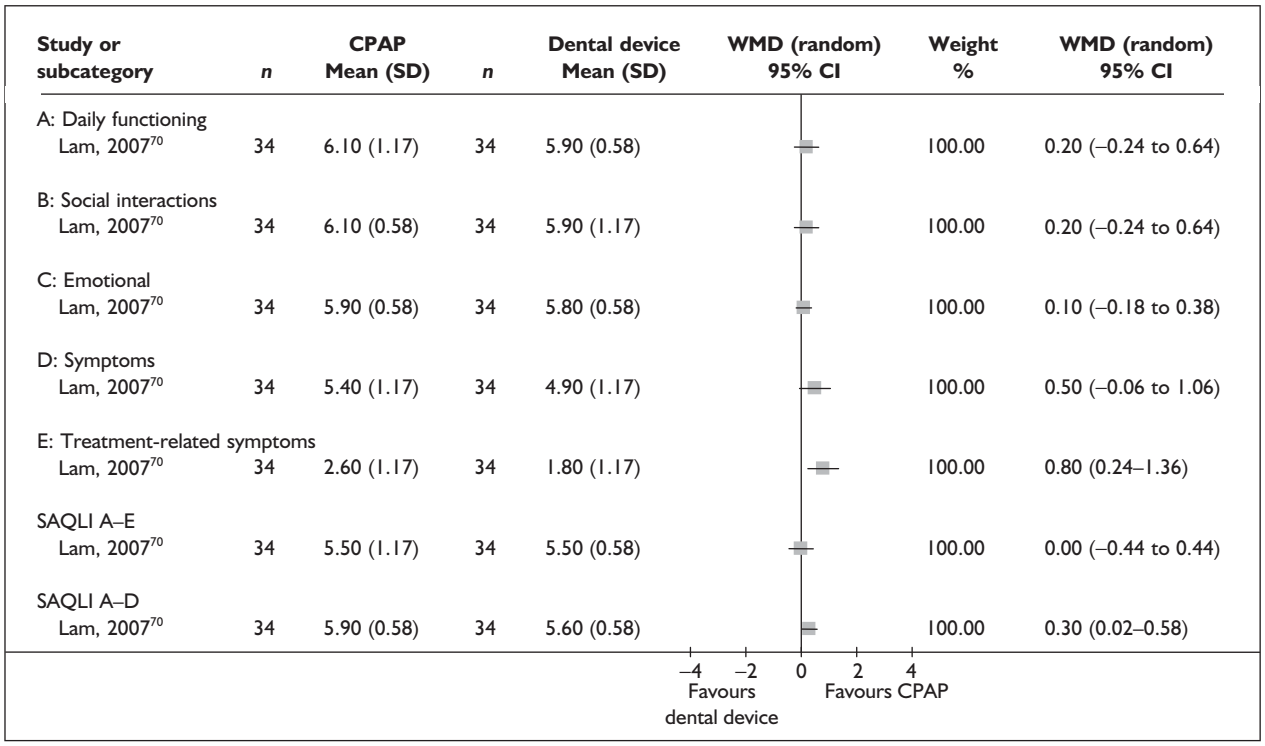

FIGURE 32 *Sleep apnoea quality of life index – subscales and summed scores A–D and A–E (CPAP versus dental devices).*

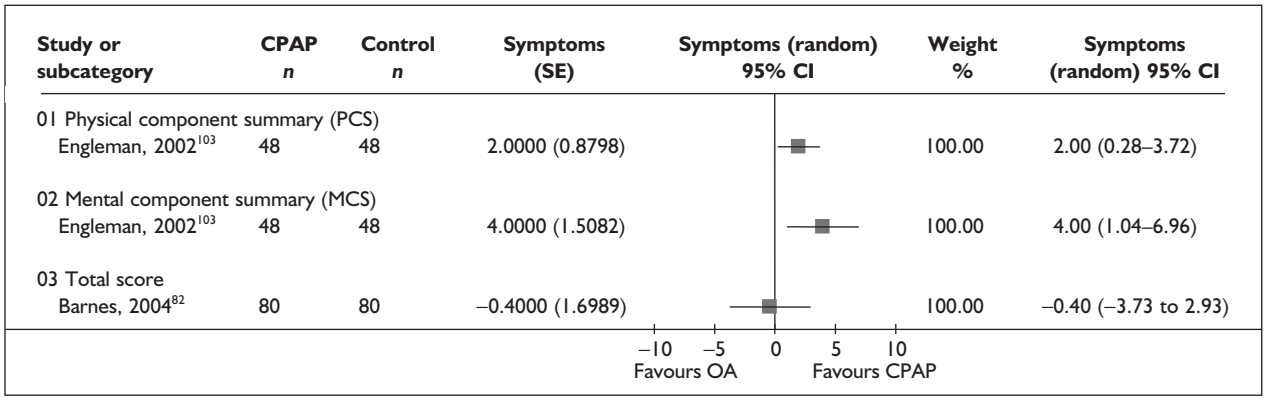

FIGURE 33 *SF-36 summary and total scores (CPAP versus dental devices).*

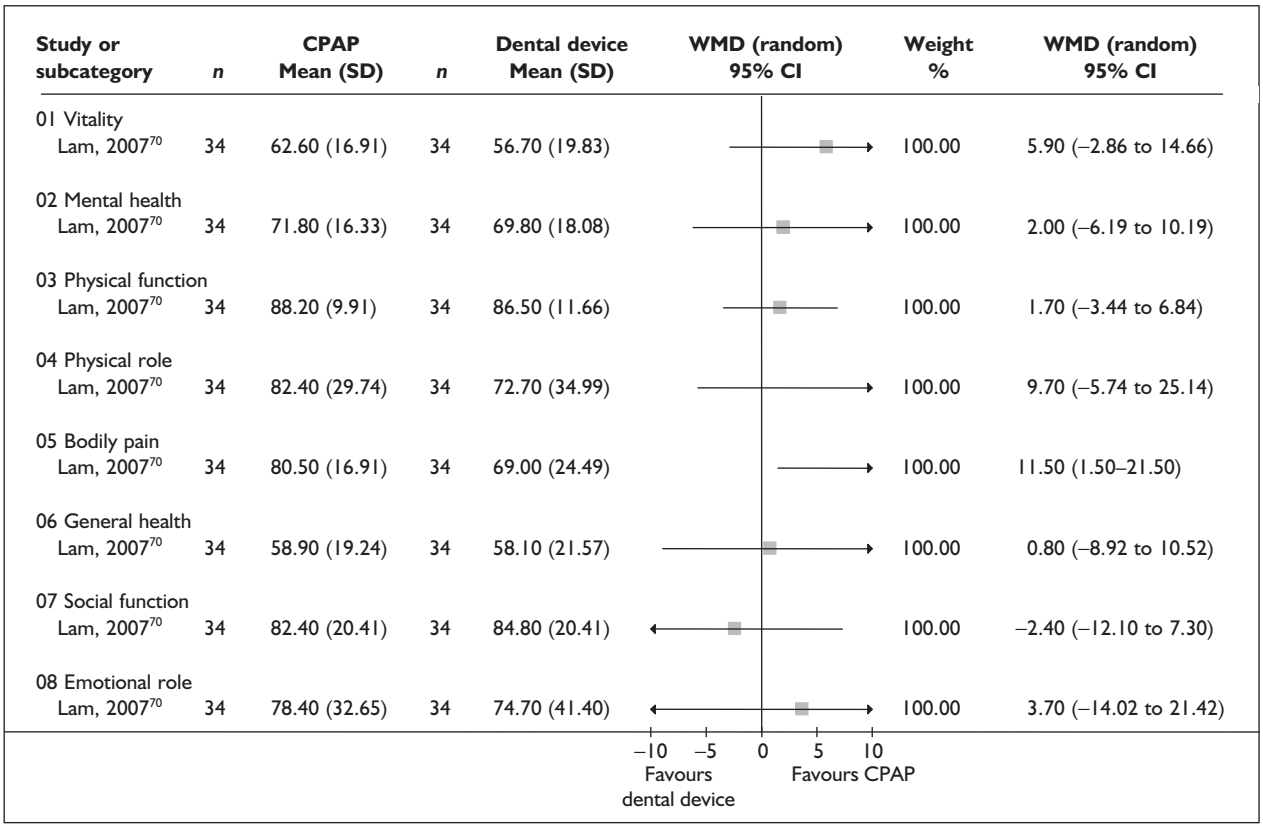

FIGURE 34 *SF-36 subscales (CPAP versus dental devices).*

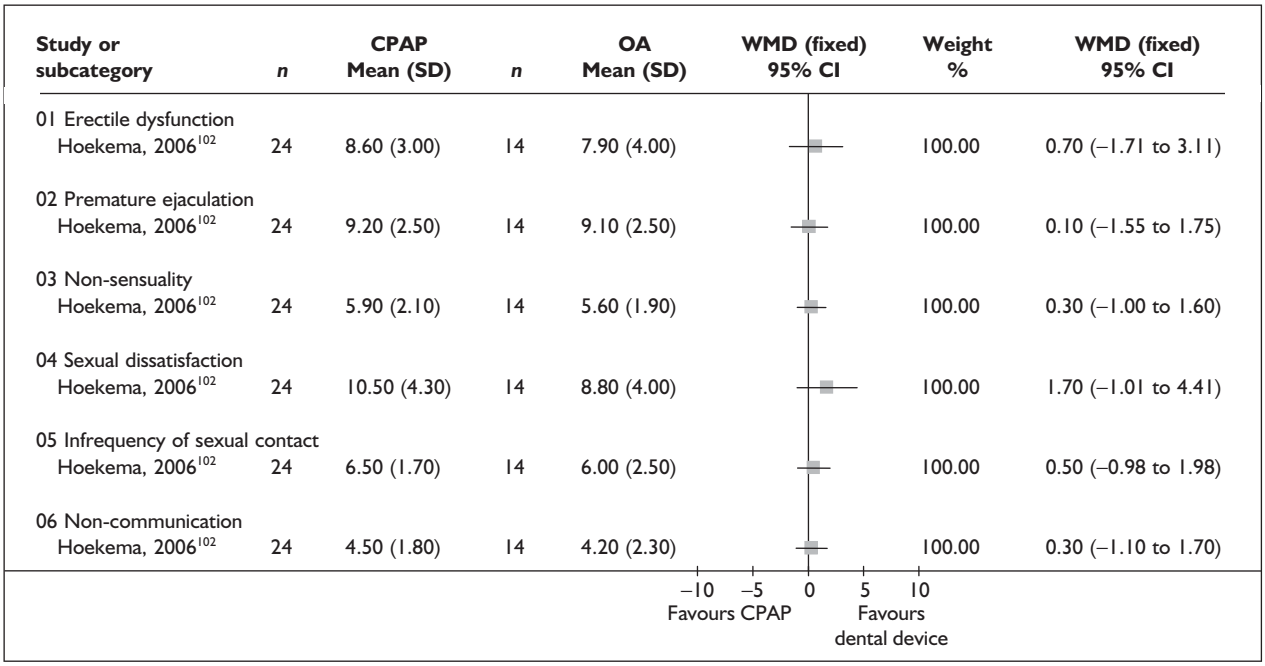

FIGURE 35 *Golombok Rust Inventory of Sexual Satisfaction (CPAP versus dental devices).*

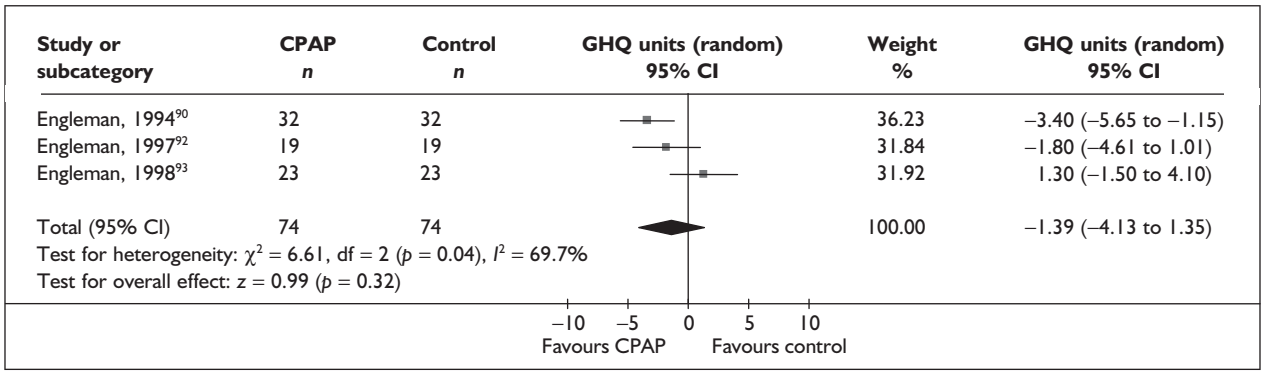

FIGURE 36 *General Health Questionnaire-28 (CPAP versus placebo).*

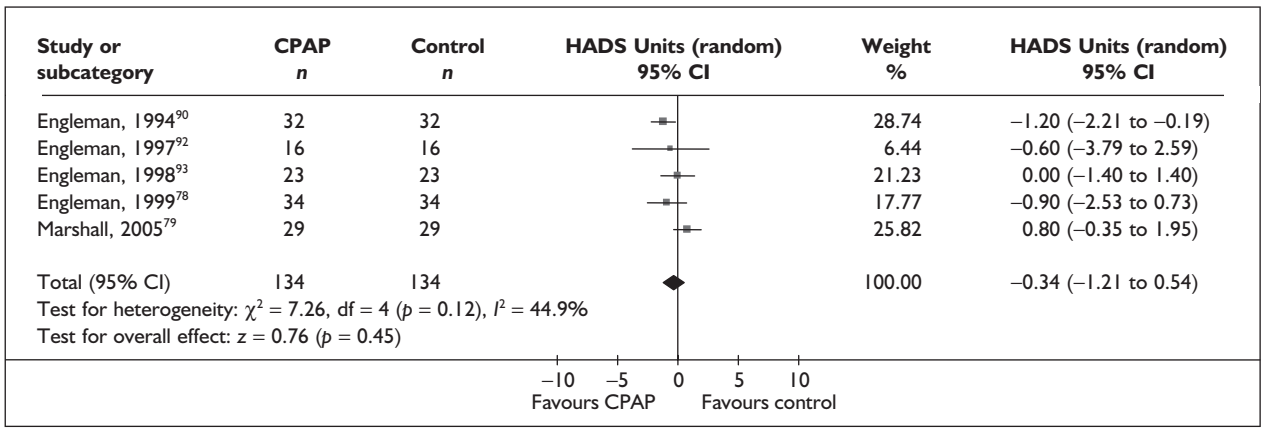

FIGURE 37 *Hospital Anxiety and Depression Scale – anxiety (CPAP versus placebo).*

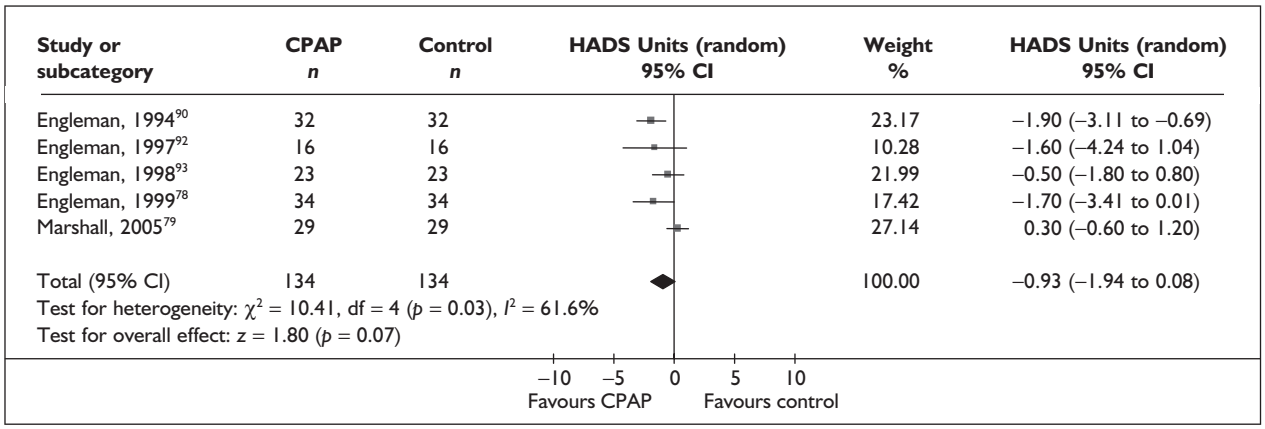

FIGURE 38 *Hospital Anxiety and Depression Scale – depression (CPAP versus placebo).*

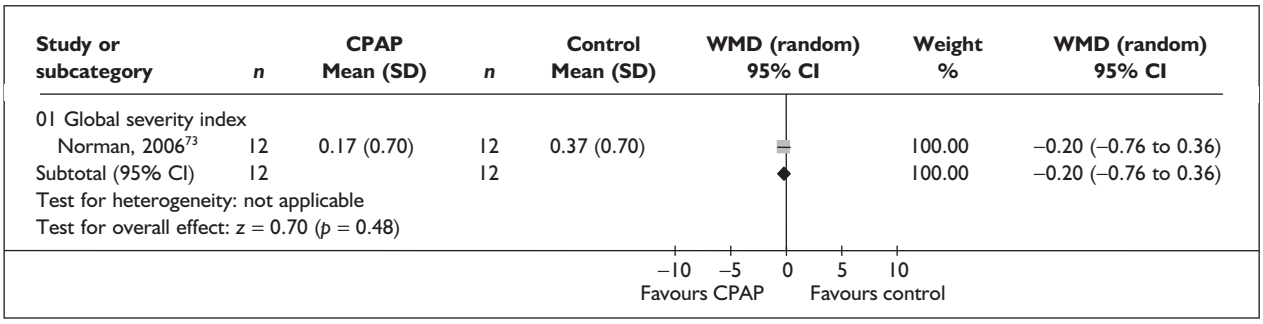

FIGURE 39 *Brief Symptom Inventory (CPAP versus placebo).*

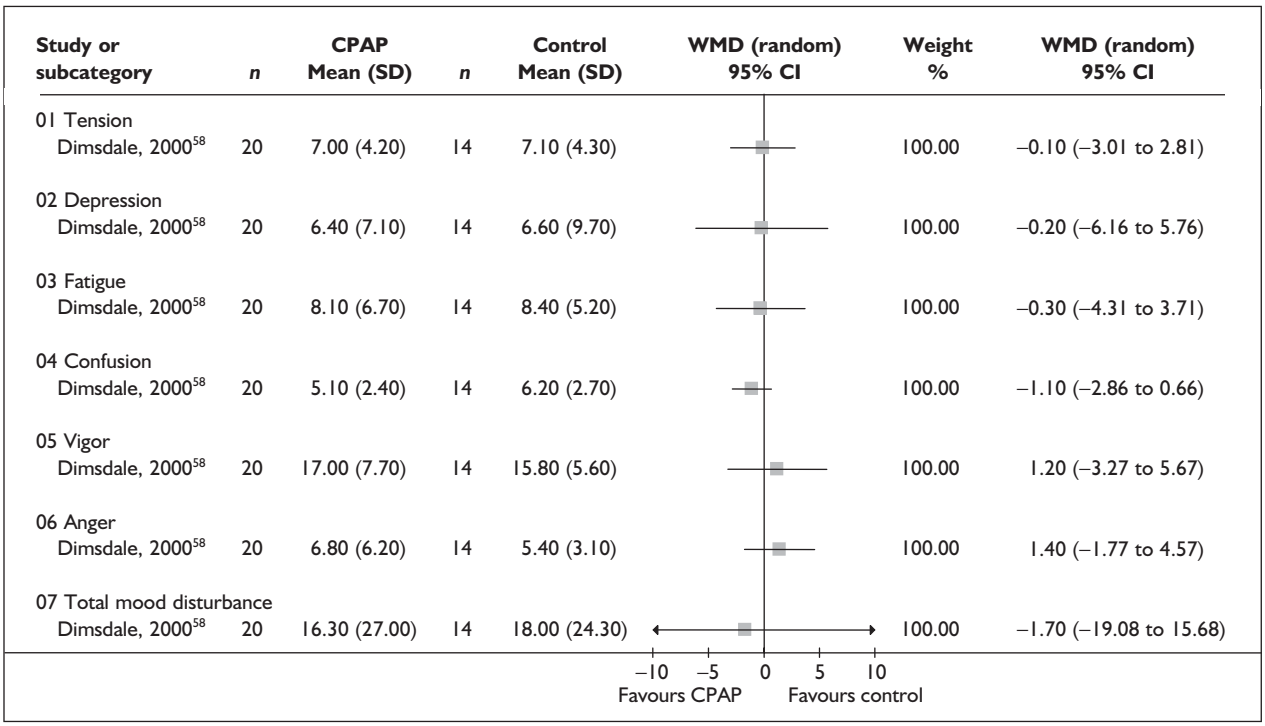

FIGURE 40 *Profile of Mood State (CPAP versus placebo).*

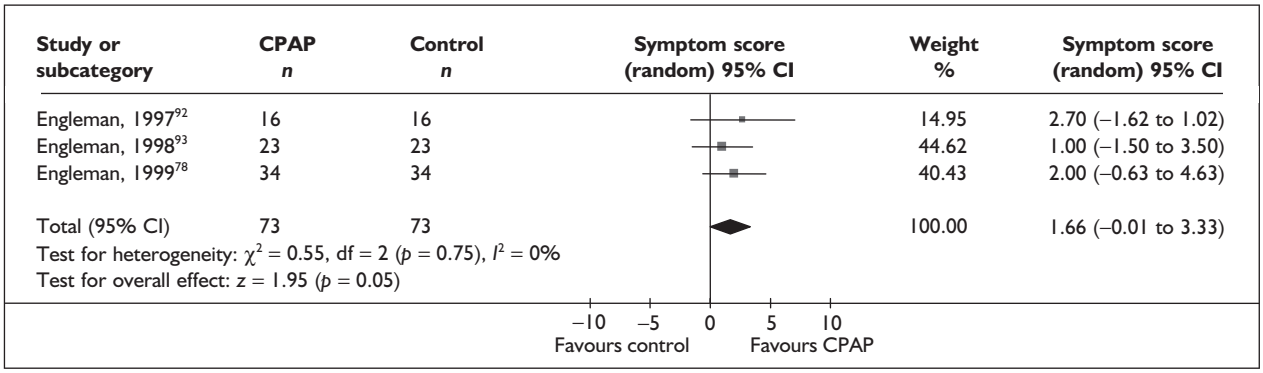

FIGURE 41 *UWIST Mood Adjective Checklist – energetic arousal score (CPAP versus control).*

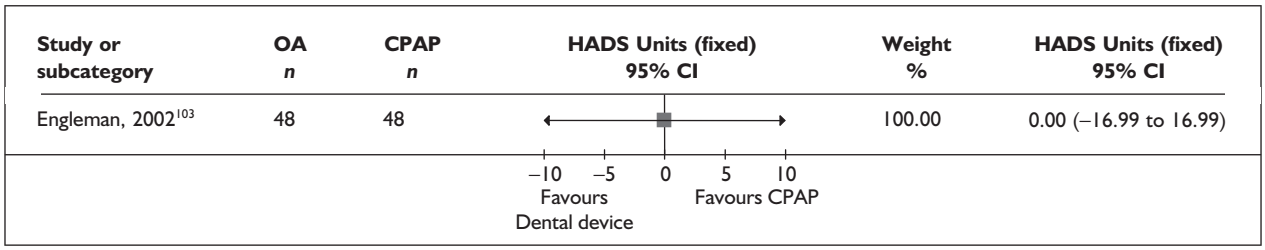

FIGURE 42 *Hospital Anxiety and Depression Scale – anxiety (CPAP versus dental devices).*

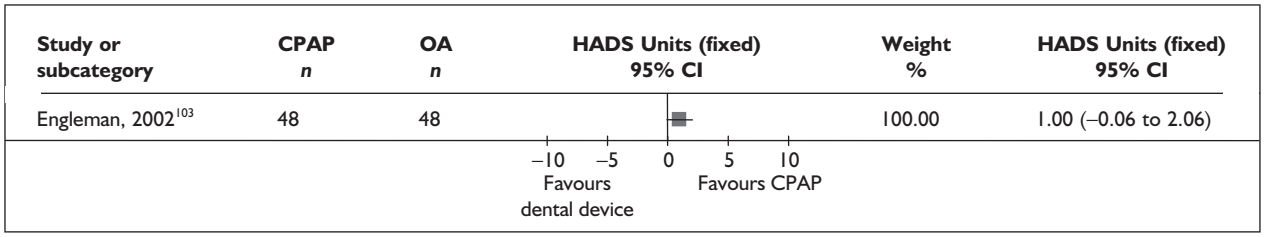

FIGURE 43 *Hospital Anxiety and Depression Scale – depression (CPAP versus dental devices).*

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Benton Visual Retention Test (direction of improvement +): This is a visuospatial memory test composed of 10 geometric designs; each design is exposed for 10 seconds, after which time the subject is required to reproduce the design from memory			
Crossover trials			
Engleman *et al.*, 1994[90]	CPAP: NR; OP: NR; both: NR	Data not reported because there was no statistically significant difference between CPAP and oral placebo	
Engleman *et al.*, 1997[92]	CPAP: NR; OP: NR; both: NR	CPAP: 7.3 (SE 0.6); OP: 7.3 (SE 0.6); MD (SD): 0, *p*-value: ns	
Engleman *et al.*, 1998[93]	CPAP: NR; OP: NR; both: 7.3 (SD 2.3), *n* = 23	CPAP: 7.7 (SD 1.5); OP: 7.7 (SD 1.7); MD (SD): 0, *p*-value: ns	
Parallel trials			
[a]Lojander *et al.*, 1999[113]	*Correct*	*Correct*	*Correct*
	CPAP: 8.5 (6–10), *n* = 10; CM: 7 (3–10), *n* = 17	CPAP: 8.5, *n* = 10; CM: 7, *n* = 16; *p*-value: ns	CPAP: 9.5, *n* = 9; CM: 5, *n* = 12; *p*-value: ns
	Delayed	*Errors*	*Errors*
	CPAP: 4 (4–4), *n* = 10; CM: 4 (1–4), *n* = 17	CPAP: 3, *n* = 10; CM: 5, *n* = 17; *p*-value: ns	CPAP: 1, *n* = 10; CM: 5, *n* = 17; *p*-value: ns
	Errors	*Delayed*	*Delayed*
	CPAP: 2 (0–9), *n* = 10; CM: 5 (0–9), *n* = 17	CPAP: 4, *n* = 10; CM: 4, *n* = 17; *p*-value: ns	CPAP: 4, *n* = 10; CM: 4, *n* = 17; *p*-value: ns
Brief Visuospatial Memory (direction of improvement +): The respondent is briefly shown a number of geometric figures presented on a single page and is asked to reproduce as many figures as possible in their correct location. After a delay, which includes primarily verbal activities, the task is repeated. The respondent is then asked to identify, from 12 figures, which were included in the six geometric figures originally presented. An optional copy trial may be administered.			
Parallel trials			
Norman *et al.*, 1996[73] (related paper[341])	*BVM-TR*	*BVM-TR*	
	CPAP: 26.4, *n* = 17; sham CPAP: 26.1, *n* = 14	CPAP: 29.7, *n* = 17; sham CPAP: 25.7 (SE 0.6); MD (SD): 4, *p*-value: 0.143	
	BVM-DL	*BVM-DL*	
	CPAP: 10.8, *n* = 17; sham CPAP: 10.5, *n* = 14	CPAP: 10.7, *n* = 17; sham CPAP: 9.4, *n* = 14; MD (SD): 1.3, *p*-value: 0.138	
		NB *p*-value based on treatment × time interaction (three treatment arms)	
Bourdon-Wiersma Test (direction of improvement +, except 'errors'): After scanning a series of rows containing groups of black dots, respondents are asked to strike out all groups of four dots.			
Parallel trials			
[a]Lojander *et al.*, 1999[113]	*Marked*	*Marked*	*Marked*
	CPAP: 128 (56–160), *n* = 10; CM: 120 (62–400), *n* = 17	CPAP: 118, *n* = 10; CM: 111, *n* = 16; *p*-value: ns	CPAP: 103, *n* = 9; CM: 116, *n* = 12; *p*-value: ns
	Errors	*Errors*	*Errors*
	CPAP: 11 (1–18), *n* = 10; CM: 4 (0–44), *n* = 17	CPAP: 12, *n* = 10; CM: 4, *n* = 16; *p*-value: ns	CPAP: 12, *n* = 9; CM: 4, *n* = 12; *p*-value: ns

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Concentration endurance test (direction of improvement +, except errors): This test of sustained attention and visual scanning consists of 14 lines with 47 characters in each line (each character consists of a letter, 'd' or 'p', marked with one, two, three or four small dashes). The respondent is required to scan the lines and cross out all occurrences of the letter 'd' with two dashes while ignoring all other characters.			
Crossover trials			
Jokic *et al*., 1999[108]	*Total score*	*Total score*	
	Both: 482.3 (SD 38.6), *n* = 13	CPAP: 532.3 (SD 73.5); CM: 530 (SD 55.6); MD (SD): 2.3, *p*-value: 2.36	
	% *Errors*	% *Errors*	
	Both: 7.4 (SD 3.1), *n* = 13	CPAP: 4.4 (SD 5.4); CM: 4.5 (SD 6.4); MD (SD): –0.1, *p*-value: 2.82	
Clock face drawing (direction of improvement –): Respondents are asked to draw the face of a clock and then add in a specified time.			
Parallel trials			
[a]Lojander *et al*., 1999[113]	CPAP: 1 (1–3), *n* = 10; CM: 1 (1–3), *n* = 17	CPAP: 1, *n* = 10; CM: 1, *n* = 16; *p*-value: ns (change)	CPAP: 1, *n* = 9; CM: 2, *n* = 12; *p*-value: ns (change)
Copying (direction of improvement –): Respondents are asked to reproduce a set of designs.			
Parallel trials			
[a]Lojander *et al*., 1999[113]	CPAP: 1 (1–3), *n* = 10; CM: 2 (1–4)	CPAP: 1, CM: 2; *p*-value: ns	CPAP: 1, CM: 2; *p*-value: ns
Complex figure test (direction of improvement +): The subject is required to make a pen/paper copy of a complex figure.			
Parallel trials			
Henke et al., 2001[85]	CPAP: NR; sham CPAP: NR	Data presented in graph only; no statistically significant difference between groups at follow-up	
Consonant trigram (direction of improvement +): In this distractor task respondents are asked to count backwards from a given number on hearing/seeing the stimulus item. When signalled to stop counting respondents are asked to report or identify the stimulus item.			
Crossover trials			
Jokic *et al*., 1999[108]	*3-second delay*	*3-second delay*	
	Both: 12.3 (SD 4.4), *n* = 13	CPAP: 13.2 (SD 1.5); CM other: 13.4 (SD 1.7); MD (SD): –0.2, *p*-value: 1.86	
	9-second delay	*9-second delay*	
	Both: 9.8 (SD 2.5), *n* = 13	CPAP: 10.5 (SD 1.5); CM other: 10.2 (SD 2.6); MD (SD): 0.3, *p*-value: 1.94	
	18-second delay	*18-second delay*	
	Both: 6.6 (SD 0.6), *n* = 13	CPAP: 8.0 (SD 3.6); CM other: 8.2 (SD 1.0); MD (SD): –0.2, *p*-value: 2.34	

continued

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
	Total correct position	*Total correct position*	
	Both: 34.3 (SD 7), $n = 13$	CPAP: 40.2 (SD 10.6); CM other: 41.5 (SD 11.6); MD (SD): –1.3, p-value: 2.88	
	Total correct sequence	*Total correct sequence*	
	Both: 38.9 (SD 9), $n = 13$	CPAP: 37.1 (SD 8.0); CM other: 38.4 (SD 11.1); MD (SD): –1.3, p-value: 0.77	
Controlled Oral Word Association Test (direction of improvement +): In these three word-naming trials respondents are asked to name words that begin with a specified set of letters in 60 seconds.			
Crossover trials			
Barnes *et al*., 2002[89]	CPAP: NR; OP: NR; both: 35.3 (SD 10.7), $n = 28$	*No. of words correct*	
		CPAP: 38.7; OP: 36.0; MD (SD): 2.7, p-value: 0.02 (difference in change)	
		NB After treatment × period interaction accounted for p = ns	
Barnes *et al*., 2004[82]	CPAP: NR; comparator: NR; both: 43.2 (SE 1.1), $n = 80$	CPAP: 46.5 (SE 1.2); OA: 46.3 (SE 1.1); OP: 46.3 (SE 1.0); CPAP/OA MD (SD): 0.2; CPAP/OP MD (SD): 0.2; p-value: ns	
Engleman *et al*., 1994[90]	CPAP: NR; OP: NR	Data not reported because there was no statistically significant difference between CPAP and oral placebo	
Engleman *et al*., 1997[92]	CPAP: NR; OP: NR; $n = 16$	*No. of words correct*	
		CPAP: 38.5 (SE 3.5); OP: 39.2 (SE 3.1); MD (SD): –0.7, p-value: ns	
Engleman *et al*., 1998[93]	CPAP: NR; OP: NR; both: 39 (SD 12), $n = 23$	*No. of words correct*	
		CPAP: 41 (SD 12); OP: 42 (SD 11); MD (SD): –1, p-value: ns	
Parallel trials			
Henke *et al*., 2001[85]	CPAP: NR; sham CPAP: NR	Data not reported; no statistically significant difference between groups at follow-up	
Digit ordering (direction of improvement +): Respondents are asked to recall digit sequences in ascending order.			
Parallel trials			
Dimsdale *et al*., 2000[58] (related paper[117])	*No. correct*	*No. correct*	
	CPAP: 87.8 (SE 1.9), $n = 20$; sham CPAP: 85.7 (SE 2.2), $n = 16$	CPAP: 90.6 (SE 1.7), $n = 20$; sham CPAP: 86.1 (SE 2.0), $n = 16$; MD (SD): 4.5, p-value: ns	
	No. of items	*No. of items*	
	CPAP: 4.3 (SE 0.7), $n = 20$; sham CPAP: 2.6 (SE 0.8), $n = 16$	CPAP: 4.9 (SE 0.7), $n = 20$; sham CPAP: 2.7 (SE 0.8), $n = 16$; MD (SD): 2.2, p-value: ns	

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Driving simulator test (direction of improvement –): Respondents are asked to steer an image of a car bonnet down the centre of a winding road as accurately as possible using a standard computer game steering wheel.			
Crossover trials			
Engleman *et al.*, 1994[90] (SteerClear)	*Obstacles hit* CPAP: NR; OP: NR; *n* = 32	*Obstacles hit* CPAP: 76 (SE 5); OP: 81 (SE 6); MD (SD): –5, *p*-value: 0.01	
Engleman *et al.*, 1997[92] (SteerClear)	*Obstacles hit* CPAP: NR; OP: NR; *n* = 16	*Obstacles hit* CPAP: 74.8 (SE 7.3); OP: 75.3 (SE 8.9); MD (SD): –0.5, *p*-value: ns	
Engleman *et al.*, 1998[93] (SteerClear)	*Obstacles hit* CPAP: NR; OP: NR; both: 100 (SD 63), *n* = 22	*Obstacles hit* CPAP: 63 (SD 27); OP: 71 (SD 40); MD (SD): –8, *p*-value: ns	
Engleman *et al.*, 1999[78] (SteerClear)	*Obstacles hit* CPAP: NR; OP: NR; both: 295 (SD 183), *n* = 34	*Obstacles hit* CPAP: 189 (SD 156); OP: 195 (SD 158); MD (SD): –6, *p*-value: ns	
Engleman *et al.*, 2002[103] (SteerClear)	*Obstacles hit* CPAP: NR; OA: NR; *n* = 48	*Obstacles hit* CPAP: 49 (SD 60); OA: 50 (SD 44); MD (SD): 1, *p*-value: 0.266	
Parallel trials			
Barbé *et al.*, 2001[83] (SteerClear)	*Obstacles hit (%)* CPAP: 5 (SE 1), *n* = 29; sham CPAP: 6 (SE 2), *n* = 25	*Obstacles hit (%)* CPAP: 4 (SE 1), *n* = 29; sham CPAP: 5 (SE 2), *n* = 25; MD (SD): –1, *p*-value: > 0.20 (difference in change)	
[b]Hoekema *et al.*, 2006[102] (related paper[117])	*Lapses of attention (total)* CPAP: 10.0 (1–16.8), *n* = 10; OA: 5.0 (2–14), *n* = 9 *Lapses of attention (0–5 minutes)* CPAP: 0.0 (0–0), *n* = 10; OA: 0.0 (0–1), *n* = 9 *Lapses of attention (6–10 minutes)* CPAP: 0.0 (0–1), *n* = 10; OA: 0.0 (0–1), *n* = 9 *Lapses of attention (11–15 minutes)* CPAP: 1.0 (0–2.5), *n* = 10; OA: 0.0 (0–5), *n* = 9 *Lapses of attention (16–20 minutes)* CPAP: 3.0 (0.8–7.8), *n* = 10; OA: 2.0 (0–5.5), *n* = 9	*Lapses of attention (total)* CPAP: 0.5 (0–5.3), *n* = 10; OA: 0.0 (0–2), *n* = 9; *p*-value: ns *Lapses of attention (0–5 minutes)* CPAP: 0.0 (0–0), *n* = 10; OA: 0.0 (0–0.5), *n* = 9; *p*-value: ns *Lapses of attention (6–10 minutes)* CPAP: 0.0 (0–0.3), *n* = 10; OA: 0.0 (0–0), *n* = 9; *p*-value: ns *Lapses of attention (11–15 minutes)* CPAP: 0.0 (0–1), *n* = 10; OA: 0.0 (0–0), *n* = 9; *p*-value: ns *Lapses of attention (16–20 minutes)* CPAP: 0.0 (0–0.5), *n* = 10; OA: 0.0 (0–0.5), *n* = 9; *p*-value: ns	

continued

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
	Lapses of attention (21–25 minutes)	*Lapses of attention (21–25 minutes*	
	CPAP: 4.0 (0.0–8.5), *n* = 10; OA: 2.0 (0–4), *n* = 9	CPAP: 0.0 (0.0–2.5), *n* = 10; OA: 0.0 (0–1), *n* = 9; *p*-value: ns	
[c]Jenkinson *et al.*, 1999[77] (other DST) (related paper[118])	*SD position on road*	*SD position on road*	
	CPAP: 0.36 (0.15–1.12), *n* = 26; sham CPAP: 0.35 (0.15–1.17), *n* = 33	CPAP: 0.21 (0.14–0.63), *n* = 26; sham CPAP: 0.30 (0.14–1.19), *n* = 33; MD (SD): –0.07, *p*-value: 0.08	
	SD deterioration (SD/hour)	*SD deterioration (SD/hour)*	
	CPAP: 0.18 (–1.14 to 30.3), *n* = 26; sham CPAP: 0.18 (–0.02 to 2.67), *n* = 33	CPAP: 0.06 (–1.02 to 0.40), *n* = 26; sham CPAP: 0.24 (–0.04 to 2.64), *n* = 33; MD (SD): –0.18, *p*-value: 0.007	
	Off-road events (no./hour)	*Off-road events (no./hour*	
	CPAP: 17.8 (0.4–149), *n* = 26; sham CPAP: 34.8 (0.9–149), *n* = 33	CPAP: 9 (0–76), *n* = 26; sham CPAP: 23 (0–150), *n* = 33; MD (SD): –14, *p*-value: 0.07	
	Length of drive (minutes)	*Length of drive (minutes)*	
	CPAP: 24.8 (7.6–30), *n* = 26; sham CPAP: 27.6 (10.9–30), *n* = 33	CPAP: 30 (17.6–30), *n* = 26; sham CPAP: 26.9 (9.1–30), *n* = 33; MD (SD): 3.1, *p*-value: 0.08	
	Reaction time (seconds)	*Reaction time (seconds)*	
	CPAP: 2.8 (1.8–4.9), *n* = 26; sham CPAP: 2.8 (1.7–5.5), *n* = 33	CPAP: 2.3 (1.5–3.5), *n* = 26; sham CPAP: 2.7 (1.6–4.0), *n* = 33; MD (SD): –0.4, *p*-value: 0.04	
Monasterio *et al.*, 2001[100] (SteerClear)	*Obstacles hit (%)*	*Obstacles hit (%)*	
	CPAP: 10 (SD 8), *n* = 66; CM: 10 (SD 3), *n* = 59	CPAP: 8 (SD 9), *n* = 66; CM: 8 (SD 10), *n* = 59; MD (SD): 0, *p*-value: 0.88	
Digit Vigilance Test (direction of improvement –): Respondents are asked to find and cross out either 6s (standard administration) or 9s (alternate administration), which appear randomly within 59 rows of single digits. These 59 rows of digits are printed in red on the first stimulus page and in blue on the second.			
Parallel trials:			
Dimsdale *et al.*, 2000[58] (related paper[117])	*Time (minutes)*	*Time (minutes)*	
	CPAP: 7.5 (SE 0.4), *n* = 20; sham CPAP: 6.4 (SE 0.4), *n* = 16	CPAP: 6.9 (SE 0.3), *n* = 20; sham CPAP: 6.6 (SE 0.4), *n* = 16; MD (SD): –0.3, *p*-value: ns	
	Errors	*Errors*	
	CPAP: 7.1 (SE 3.1), *n* = 20; sham CPAP: 18.3 (SE 3.7), *n* = 16	CPAP: 10.1 (SE 2.6), *n* = 20; sham CPAP: 12.3 (SE 3.1), *n* = 16; MD (SD): –2.2, *p*-value: ns	
Norman *et al.*, 2006[73] (related paper[341])	*Time (seconds)*	*Time (seconds)*	
	CPAP: 350.9, *n* = 17; sham CPAP: 326.4, *n* = 14	CPAP: 312.3, *n* = 17; sham CPAP: 303.1, *n* = 14; MD (SD): 9.2, *p*-value: 0.02	

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
	Errors	*Errors*	
	CPAP: 5.6, *n* = 17; sham CPAP: 14.1, *n* = 14	CPAP: 7.2, *n* = 20; sham CPAP: 10.6, *n* = 16; MD (SD): –2.4, *p*-value: 0.08 NB *p*-value based on treatment × time interaction (three treatment arms)	
Finger tapping task (direction of improvement +): Speed of finger tapping is measured for the index finger of the right and left hands separately; five times for a period of 10 seconds each.			
Parallel			
[a]Lojander *et al.*, 1999[113]	CPAP: 48 (42–55), *n* = 10; CM other: 44 (34–55), *n* = 17	CPAP: 48, *n* = 10; CM other: 44, *n* = 16; *p*-value: ns	CPAP: 45, *n* = 9; CM other: 43, *n* = 12; *p*-value: ns
IQ decrement (direction of improvement +): NART score minus WAIS-R subtests.			
Crossover			
Engleman *et al.*, 1994[90]	CPAP: NR; OP: NR; *n* = 32	CPAP: 4.0 (SE 2.1); OP: 7.2 (SE 2.0); MD (SD): –3.2, *p*-value: 0.04	
Engleman *et al.*, 1997[92]	CPAP: NR; OP: NR; *n* = 16	CPAP: 7.0 (SE 3.1); OP: 5.3 (SE 3.5); MD (SD): 1.7, *p*-value: ns	
Engleman *et al.*, 1998[93]	CPAP: NR; OP: NR; both: 6 (SD 12); *n* = 23	CPAP: 3.0 (SD 11); OP: 4.0 (SD 11); MD (SD): –1, *p*-value: ns	
Engleman *et al.*, 2002[103]	CPAP: NR; OA: NR; *n* = 34	CPAP: –1.0 (SD 14); OA: –2.0 (SD 14); MD (SD): 1, *p*-value: 0.549	
Hopkins Verbal Learning Task (direction of improvement +): Respondents are asked to verbally repeat a list of words (immediately and after a delay) and to identify the words from the list from a verbal presentation (including both the target words and the distractors).			
Parallel trials			
Norman *et al.*, 2006[73] (related paper[341])	*Immediate recall* CPAP: 24.7, *n* = 17; OA: 26.3, *n* = 14	*Immediate recall* CPAP: 24.2, *n* = 17; OA: 25.5, *n* = 14; MD (SD): –1.3, *p*-value: 0.486, *p*-value: 0.679 (difference in change)	
	Delayed recall CPAP: 8.9, *n* = 17; OA: 9, *n* = 14	*Delayed recall* CPAP: 8.8, *n* = 17; OA: 8.3, *n* = 14; MD (SD): 0.5, *p*-value: 0.641, *p*-value: 0.347 (difference in change) NB *p*-value based on treatment × time interaction (three treatment arms)	
Memory distractor task (direction of improvement –): This is a test of verbal and visual spatial memory using the Brown–Peterson technique.			
Parallel trials			
[a]Lojander *et al.*, 1999[113]	CPAP: 3 (1–3), *n* = 10; CM: 3 (1–5), *n* = 17	CPAP: 3; CM: 3; *p*-value: ns	CPAP: 3; CM: 3; *p*-value: ns

continued

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Paced Auditory Serial Addition Task (direction of improvement +): A series of single digits is presented at a set rate; the respondents are asked to add the numbers in pairs, such that each number is added to the one that immediately precedes it.			
Crossover trials			
Barnes *et al*., 2004[82]	*PASAT 1.2*	*PASAT 1.2*	
	CPAP: NR; comparator: NR; both: 3.4 (SE 0.2), *n* = 80	CPAP: 2.9 (SE 0.1); OA: 2.6 (SE 0.03);OP: 3.4 (0.1); CPAP/OA MD (SD): 0.3; CPAP/OP MD (SD): –0.5, *p*-value: ns	
	PASAT 2.4	*PASAT 2.4*	
	CPAP: NR; comparator: NR; both: 4.2 (SE 0.2), *n* = 80	CPAP: 3.8 (SE 0.2); OA: 3.7 (SE 0.1); OP: 3.7 (SE 0.1); CPAP/OA MD (SD): 0.1; CPAP/OP MD (SD): 0.1, *p*-value: ns	
Engleman *et al*., 1994[90]	*PASAT 2* CPAP: NR; OP: NR *PASAT 4* CPAP: NR; OP: NR	There was an improvement with CPAP but also an order effect. Data were analysed from first assessment only and no statistically significant difference between CPAP and placebo was found. Data were not reported because there was no statistically significant difference between CPAP and oral placebo	
Engleman *et al*., 1997[92]	*PASAT 2*	*PASAT 2*	
	CPAP: NR; OP: NR; *n* = 16	CPAP: 37.8 (SE 3.3); OP: 35.3 (SE 2.8); MD (SD): 2.5, *p*-value: ns	
Engleman *et al*., 1998[93]	*PASAT 2*	*PASAT 2*	
	CPAP: NR; OP: NR; both: 31 (SD 8), *n* = 23	CPAP: 37 (SD 11); OP: 35 (SD 11); MD (SD): 2, *p*-value: ns	
Engleman *et al*., 1999[78]	*PASAT 2*	*PASAT 2*	
	CPAP: NR; OP: NR; both: 31 (SD 12), *n* = 32	CPAP: 40 (SD 11); OP: 36 (SD 14); MD (SD): 4, *p*-value: 0.02	
Engleman *et al*., 2002[103]	*PASAT 2*	*PASAT 2*	
	CPAP: NR; OA: NR; both: NR, *n* = 48	CPAP: 40 (SD 11); OA: 39 (SD 10); MD (SD): 1, *p*-value: 0.064	
Parallel trials			
Barbé *et al*., 2001[83]	*PASAT 1*	*PASAT 1*	
	CPAP: 15 (SE 1), *n* = 29; sham CPAP: 14 (SE 1), *n* = 25	CPAP: 15 (SE 1); sham CPAP: 15 (SE 1); MD (SD): 0, *p*-value: > 0.20 (difference in change)	
	PASAT 2	*PASAT 2*	
	CPAP: 14 (SE 1), *n* = 29; sham CPAP: 15 (SE 1), *n* = 25	CPAP: 16 (SE 1); sham CPAP: 15 (SE 1); MD (SD): 1, *p*-value: 0.04 (difference in change)	
	PASAT 3	*PASAT 3*	
	CPAP: 10 (SE 1), *n* = 29; sham CPAP: 11 (SE 1), *n* = 25	CPAP: 12 (SE 1); sham CPAP: 12 (SE 1); MD (SD): 0, *p*-value: 0.09 (difference in change)	

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
	PASAT 4	*PASAT 4*	
	CPAP: 5 (SE 1), *n* = 29; sham CPAP: 4 (SE 1), *n* = 25	CPAP: 5 (SE 1); sham CPAP: 5 (SE 1); MD (SD): 0, *p*-value: > 0.20 (difference in change)	
Monasterio *et al.*, 2001[100]	*PASAT 1*	*PASAT 1*	
	CPAP: 4 (SD 3), *n* = 66; CM: 4 (SD 3), *n* = 59	CPAP: 5 (SD 4); CM: 5 (SD 3); MD (SD): 0, *p*-value: 0.32	
	PASAT 2	*PASAT 2*	
	CPAP: 10 (SD 4), *n* = 66; CM: 10 (SD 5), *n* = 59	CPAP: 12 (SD 4); CM: 12 (SD 4); MD (SD): 0, *p*-value: 0.12	
	PASAT 3	*PASAT 3*	
	CPAP: 14 (SD 5), *n* = 66; CM: 13 (SD 5), *n* = 59	CPAP: 15 (SD 4); CM: 15 (SD 4); MD (SD): 0, *p*-value: 0.20	
	PASAT 4	*PASAT 4*	
	CPAP: 13 (SD 5), *n* = 66; CM: 13 (SD 4), *n* = 59	CPAP: 14 (SD 4); CM: 16 (SD 4); MD (SD): –2, *p*-value: 0.20	
		NB Reduced version with 20 items for each condition. It is unclear whether the score is for number correct or percentage correct.	
Purdue Pegboard (direction of improvement +): This is a test of manual dexterity. Following standard instructions the subject places pegs onto a pegboard.			
Crossover trials			
Jokic et al., 1999[108]	*Dominant hand (no. correct)*	*Dominant hand (no. correct)*	
	CPAP: NR; CM other: NR; both: 13 (SD 3.6), *n* = 13	CPAP: 15.3 (SD 1.7); CM other: 14.3 (SD 1.7); MD (SD): 1, *p*-value: 0.25	
	Non-dominant hand (no. correct)	*Non-dominant hand (no. correct)*	
	CPAP: NR; CM other: NR; both: 13 (SD 1.5), *n* = 13	CPAP: 14.1(SD 2.3); CM other: 12.8 (SD 2.3); MD (SD): 1.3, *p*-value: 0.16	
	Both hands (no. correct)	*Both hands (no. correct)*	
	CPAP: NR; CM other: NR; both: 10.8 (SD 1.5), *n* = 13	CPAP: 11.1(SD 1.0); CM other: 11.5 (SD 1.0); MD (SD): –0.4, *p*-value:1.41	
	Right/left/both hands (no. correct)	*Right/left/both hands (no. correct)*	
	CPAP: NR; CM other: NR; both: 36.8 (SD 6.7), *n* = 13	CPAP: 39.6 (SD 10.7); CM other: 38.6 (SD 4.9); MD (SD): 1, *p*-value: 1.47	
	Assembly	*Assembly*	
	CPAP: NR; CM other: NR; both: 34.6 (SD 5.7), *n* = 13	CPAP: 35.1(SD 7.6); CM other: 35.4 (SD 8.1); MD (SD): –0.3, *p*-value: 2.05	

continued

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Psychomotor Vigilance Test (direction of improvement –): This is a test of sustained attention. Typically it requires the subject to respond as quickly as possible to a specific stimulus while maintaining accuracy (e.g. pressing a button on seeing a dot/light on the computer screen).			
Crossover trials			
Barnes *et al*., 2002[89]	*Inverse of mean of slowest 10%*	*Inverse of mean of slowest 10%*	
	CPAP: NR; OP: NR; both: 2.7 (SE 0.5), *n* = 28	CPAP: 2.6; OP: 2.6; MD (SD): 0, *p*-value: ns (difference in change)	
Barnes *et al*., 2004[82]	*Inverse of mean of slowest 10%*	*Inverse of mean of slowest 10%*	
	CPAP: NR; comparator: NR; both: 2.7 (SE 0.1), *n* = 80	CPAP: 2.7 (SE 0.1); OA: 2.7 (SE 0.1); OP: 2.6 (SE 0.1); CPAP/OA MD (SD): 0; CPAP/OP MD (SD): 0.1, *p*-value: ns	
	Lapses (> 500 milliseconds RT)	*Lapses (> 500 milliseconds RT)*	
	CPAP: NR, comparator: NR Both: 2.5 (SE 0.3), *n* = 80	CPAP: 2.1 (SE 0.2); OA: 2.2 (SE 0.2); OP: 2.7 (SE 0.3); CPAP/OA MD (SD): –0.1; CPAP/OP MD (SD): –0.6, *p*-value: < 0.05	
	Errors	*Errors*	
	CPAP: NR, comparator: NR Both: 7.4 (SE 0.8), *n* = 80	CPAP: 7.4 (SE 0.7); OA: 7.5 (SE 0.8); OP: 7.8 (SE 0.8); CPAP/OA MD (SD): –0.1; CPAP/OP MD (SD): –0.4, *p*-value: ns	
Cibele *et al*., 2006[72]	NR	NR	
Marshall *et al*., 2005[79]	*Mean RT (milliseconds)*	*Mean RT (milliseconds)*	
	CPAP: NR; sham CPAP: NR; both: 264 (SE 5), *n* = 29	CPAP: 266 (SE 5); sham CPAP: 259 (5); MD (SD): 7, *p*-value: NR	
	Lapses (> 500 milliseconds RT)	*Lapses (> 500 milliseconds RT)*	
	CPAP: NR; sham CPAP: NR; both: 1.3 (SE 0.3), *n* = 29	CPAP: 1.3 (SE 0.4); sham CPAP: 1.0 (SE 0.4); MD (SD): 0.3, *p*-value: NR	
	Errors	*Errors*	
	CPAP: NR; sham CPAP: NR; both: 2.8 (SE 0.5), *n* = 29	CPAP: 3.2 (SE 0.7); sham CPAP: 3.3 (SE 0.7); MD (SD): –.01, *p*-value: NR	
Reaction time, milliseconds (direction of improvement –): This is the elapsed time between the presentation of a sensory stimulus and the subsequent behavioural response.			
Crossover trials			
Engleman *et al*., 1994[90]	CPAP: NR; OP: NR	Data not reported because there was no statistically significant difference between CPAP and oral placebo	
Engleman *et al*., 1997[92]	CPAP: NR; OP: NR; *n* = 16	CPAP: 365 (SE 16); OP: 356 (SE 14); MD (SD): 9, *p*-value: ns	
Engleman *et al*., 1998[93]	CPAP: NR; OP: NR; both: 346 (SD 57), *n* = 23	CPAP: 327 (SD 46); OP: 325 (SD 38); MD (SD): 2, *p*-value: ns	

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Rapid Visual Information Processing Task (direction of improvement +): Single digits are presented in quick succession on a computer screen, and respondents are asked to identify (button press) target sequences of numbers.			
Crossover trials			
Engleman *et al.*, 1994[90]	CPAP: NR; OP: NR	Data not reported because there was no statistically significant difference between CPAP and oral placebo	
Engleman *et al.*, 1997[92]	CPAP: NR; OP: NR; *n* = 16	*No. correct* CPAP: 36.9 (SE 3.2); OP: 34.8 (SE 3.2); MD (SD): 2.1, *p*-value: ns	
Engleman *et al.*, 1998[93]	CPAP: NR; OP: NR; both: 28 (SD 10), *n* = 23	*No. correct* CPAP: 34 (SD 15); OP: 35 (SE 13); MD (SD): –1, *p*-value: ns	
STROOP colour and word test (direction of improvement +): Respondents are asked to name colour-words printed in different colours, name the printed colours, or read a set of colour-words while naming colours of another set of colour-words.			
Crossover trials			
Barnes *et al.*, 2004[82]	CPAP: NR; comparator: NR; both: 4.8 (SE 0.8), *n* = 80	CPAP: 9.3 (SE 0.9); OA: 10.3 (SE 0.9); OP: 9.2 (SE 0.9); CPAP/OA MD (SD): –1; CPAP/OP MD (SD): 0.1, *p*-value: ns	
Parallel trials			
Dimsdale *et al.*, 2000[58] (related paper[117])	*Naming (no. correct)* CPAP: 73.6 (SE 2.5), *n* = 20; sham CPAP: 77.7 (SE 2.9), *n* = 16	*Naming (no. correct)* CPAP: 80.3 (SE 2.7), *n* = 20; sham CPAP: 82.2 (SE 3.2), *n* = 16; MD (SD): 1.9, *p*-value: ns	
	Naming (errors) CPAP: 0.3 (SE 0.2), *n* = 20; sham CPAP: 0.2 (SE 0.2), *n* = 16	*Naming (errors)* CPAP: 0.1 (SE 0.1), *n* = 20; sham CPAP: 0.3 (SE 0.1), *n* = 16; MD (SD): –0.2, *p*-value: ns	
	Reading (no. correct) CPAP: 93.1 (SE 1.9), *n* = 20; sham CPAP: 92.4 (SE 2.2), *n* = 16	*Reading (no. correct)* CPAP: 95.6 (SE 2.0), *n* = 20; sham CPAP: 92.8 (SE 2.3), *n* = 16; MD (SD): 2.8, *p*-value: ns	
	Reading (errors) CPAP: 0.2 (SE 0.2), *n* = 20; sham CPAP: 0.2 (SE 0.2), *n* = 16	*Reading (errors)* CPAP: 0.1 (SE 0.1), *n* = 20; sham CPAP: 0.01 (SE 0.1), *n* = 16; MD (SD): 0.19, *p*-value: ns	
	Inference (no. correct) CPAP: 40 (SE 1.6), *n* = 20; sham CPAP: 38.5 (SE 1.9), *n* = 16	*Inference (no. correct)* CPAP: 44.2 (SE 1.8), *n* = 20; sham CPAP: 41 (SE 2.1), *n* = 16; MD (SD): 3.2, *p*-value: ns	

continued

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
	Inference (errors)	*Inference (errors)*	
	CPAP: 0.5 (SE 0.3), *n* = 20; sham CPAP: 0.4 (SE 0.3), *n* = 16	CPAP: 0.3 (SE 0.3), *n* = 20; sham CPAP: 0.8 (SE 0.3), *n* = 16; MD (SD): –0.5, *p*-value: ns	
Norman *et al.*, 2006[73] (related paper[341])	*Colour*	*Colour*	
	CPAP: 67.7, *n* = 17; sham CPAP: 73.7, *n* = 14	CPAP: 72.3, *n* = 17; sham CPAP: 77.9, *n* = 14; MD (SD): –5.6, *p*-value: 0.532	
	Colour-word ratio	*Colour-word ratio*	
	CPAP: 37.7, *n* = 17; sham CPAP: 37.9, *n* = 14	CPAP: 37.3, *n* = 17; sham CPAP: 41.9, *n* = 14; MD (SD): –4.6, *p*-value: 0.061	
		NB *p*-value based on treatment × time interaction (three treatment arms)	
Trail Making Task (direction of improvement –): This is a complex attention task in which respondents are asked to draw lines to connect consecutively numbered circles on one sheet (Part A), and then connect the same number of consecutively numbered and lettered circles on another sheet by alternating between the two sequences (Part B).			
Crossover trials			
Engleman *et al.*, 1994[90]	*Part A/Part B*	*Part A*	
	CPAP: NR; OP: NR; *n* = 32	Data not reported because there was no statistically significant difference between CPAP and oral placebo	
		Part B	
		CPAP: 66 (SE 5); OP: 76 (SE 5); MD (SD): –9, *p*-value: 0.02	
Engleman *et al.*, 1997[92]	*Part B*	*Part B*	
	CPAP: NR; OP: NR; *n* = 16	CPAP: 64.1 (SE 5.5); OP: 77.7 (SE 9.2); MD (SD): –13.6, *p*-value: 0.02	
Engleman *et al.*, 1998[93]	*Part B*	*Part B*	
	CPAP: NR; OP: NR; both: 84 (SD 41), *n* = 23	CPAP: 69 (SD 32); OP: 68 (SD 32); MD (SD): 1, *p*-value: ns	
Engleman *et al.*, 1999[78]	*Part A*	*Part A*	
	CPAP: NR; OP: NR; both: 34 (SD 12), *n* = 34	CPAP: 26 (SD 11); OP: 29 (SD 11); MD (SD): –3, *p*-value: 0.06	
	Part B	*Part B*	
	CPAP: NR; OP: NR; both: 76 (SD 36), *n* = 34	CPAP: 63 (SD 33); OP: 65 (SD 27); MD (SD): –2, *p*-value: ns	
Engleman *et al.*, 2002[103]	*Part B*	*Part B*	
	CPAP: NR; OA: NR; *n* = 34	CPAP: 59 (SD 21); OA: 64 (SD 28); MD (SD): –5, *p*-value: 0.106	
Barnes *et al.*, 2002[89]	*Part A*	*Part A*	
	CPAP: NR; OP: NR; both: 28.2 (SD 9), *n* = 28	CPAP: 28.1; OP: 27.6; MD (SD): 0.5, *p*-value: ns	

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
	Part B	*Part B*	
	CPAP: NR; OP: NR; both: 65.3 (SD 30.2), *n* = 28	CPAP: 60.1; OP: 65.2; MD (SD): –5.1, *p*-value: ns	
Barnes *et al.*, 2004[82]	*Part B*	*Part B*	
	CPAP: NR; OA:NR; OP: NR; all: 85.9 (SE 4.4), *n* = 80	CPAP: 73.3 (SE 3.3); OA: 76.0 (SE 3.7); OP: 74.2 (SE 3.6); CPAP/OA MD (SD): –2.7; CPAP/OP MD (SD): –0.9, *p*-value: ns	
Jokic *et al.*, 1999[108]	*Part A*	*Part A*	
	CPAP: NR; CM other: NR; both: 28.1 (SD 2.1), *n* = 13	CPAP: 20.5 (SD 3.2); CM other: 21.9 (SD 7.9); MD (SD): –1.4, *p*-value: 1.17	
	Part B	*Part B*	
	CPAP: NR; CM other: NR; both: 73.8 (SE 34.7), *n* = 13	CPAP: 56.5 (SD 7); CM other: 57.7 (SD 6.6); MD (SD): –1.2, *p*-value: 2.18	
Parallel trials			
Barbé *et al.*, 2001[83]	*Part A (seconds)*	*Part A (seconds)*	
	CPAP: 49 (SE 4), *n* = 29; sham CPAP: 49 (SE 4), *n* = 25	CPAP: 47 (SE 3), *n* = 29; sham CPAP: 47 (SE 3), *n* = 25; MD (SD): 0, *p*-value: > 0.2 (difference in change)	
	Part B (seconds)	*Part B (seconds)*	
	CPAP: 122 (SE 16), *n* = 29; sham CPAP: 108 (SE 11), *n* = 25	CPAP: 96 (SE 6), *n* = 29; sham CPAP: 110 (SE 10), *n* = 25; MD (SD): –14, *p*-value: 0.1 (difference in change)	
Dimsdale *et al.*, 2000[58] (related paper[117])	*Part A*	*Part A*	
	CPAP: 33.3 (SE 2.2), *n* = 20; sham CPAP: 32.4 (SE 2.7), *n* = 16	CPAP: 27.4 (SE 1.6), *n* = 20; sham CPAP: 27.4 (SE 2), *n* = 16; MD (SD): 0, *p*-value: ns	
	Part A (errors)	*Part A (errors)*	
	CPAP: 0.2 (SE 0.1), *n* = 20; sham CPAP: 0.1 (SE 0.1), *n* = 16	CPAP: 0.03 (SE 0.1), *n* = 20; sham CPAP: 0.2 (SE 0.1), *n* = 16; MD (SD): –0.17, *p*-value: ns	
	Part B	*Part B*	
	CPAP: 81.1 (SE 8), *n* = 20; sham CPAP: 88.3 (SE 9.8), *n* = 16	CPAP: 71.2 (SE 7.1), *n* = 20; sham CPAP: 87 (SE 8.7), *n* = 16; MD (SD): –14.5, *p*-value: ns	
	Part B (errors)	*Part B (errors)*	
	CPAP: 1.2 (SE 0.3), *n* = 20; sham CPAP: 0.8 (SE 0.4), *n* = 16	CPAP: 0.5 (SE 0.2), *n* = 20; sham CPAP: 1.1 (SE 0.3), *n* = 16; MD (SD): –0.6, *p*-value: ns	

continued

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Henke *et al.*, 2001[85]		*Part A/Part B* Data presented as graph. No statistically significant difference between groups at follow-up	
[a]Lojander *et al.*, 1999[113]	*Part B* CPAP: 111 (65 to 180), *n* = 10; CM: 83 (50 to 290), *n* = 17	*Part B* CPAP: 128; CM: 82; *p*-value: ns	*Part B* CPAP: 130; CM: 75; *p*-value: ns
Monasterio *et al.*, 2001[100]	*Part A* CPAP: 56 (SD 26), *n* = 66; CM: 54 (SD 18), *n* = 59 *Part B* CPAP: 121 (SD 44), *n* = 66; CM other: 125 (SD 47), *n* = 59	*Part A (seconds)* CPAP: 49 (SD 19), *n* = 66; CM: 49 (SD 20), *n* = 59; MD (SD): 0, *p*-value: 0.76 *Part B (seconds)* CPAP: 106 (SD 42), *n* = 66; CM: 100 (SD 39), *n* = 59; MD (SD): 6, *p*-value: 0.15	
Norman *et al.*, 2006[73] (related paper[341])	*Part A* CPAP: 32.4, *n* = 17; sham CPAP: 25.5, *n* = 14 *Part B* CPAP: 70.8, *n* = 17; sham CPAP: 70.3, *n* = 14	*Part A* CPAP: 26.5, *n* = 17; sham CPAP: 21.7, *n* = 14; MD (SD): 4.8, *p*-value: 0.494 *Part B* CPAP: 63.4, *n* = 17; sham CPAP: 59.6, *n* = 14; MD (SD): 3.8, *p*-value: 0.823 NB *p*-value based on treatment × time interaction (three treatment arms)	
Verbal fluency test (direction of improvement +): This is a word-naming task.			
Parallel trials			
Dimsdale *et al.*, 2000[58] (related paper[117])	*No. correct* CPAP: 40.6 (SE 2.9), *n* = 20; sham CPAP: 35.9 (SE 3.4), *n* = 16 *Perseveration* CPAP: 1.1 (SE 0.4), *n* = 20; sham CPAP: 0.9 (SE 0.5), *n* = 16 *Intrusions* CPAP: 0.2 (SE 0.1), *n* = 20; sham CPAP: 0.5 (SE 0.1), *n* = 16 *Variations* CPAP: 0.5 (SE 0.3), *n* = 20; sham CPAP: 0.7 (SE 0.3), *n* = 16	*No. correct* CPAP: 44.5 (SE 2.7), *n* = 20; sham CPAP: 37.3 (SE 3.2), *n* = 16; MD (SD): 7.2, *p*-value: ns *Perseveration* CPAP: 0.8 (SE 0.3), *n* = 20; sham CPAP: 1.2 (SE 0.3), *n* = 16; MD (SD): –0.4, *p*-value: ns *Intrusions* CPAP: 0.1 (SE 0.1), *n* = 20; sham CPAP: 0.4 (SE 0.2), *n* = 16; MD (SD): –0.3, *p*-value: ns *Variations* CPAP: 0.6 (SE 0.2), *n* = 20; sham CPAP: 0.8 (SE 0.3), *n* = 16; MD (SD): –0.2, *p*-value: ns	

TABLE 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
Monasterio *et al.*, 2001[100]	*Score: percentile* CPAP: 69 (SD 29), *n* = 66; CM: 66 (SD 28), *n* = 59	*Score: percentile* CPAP: 69 (SD 27), *n* = 66; CM: 70 (SD 29), *n* = 59; MD (SD): –1, *p-value*: 0.53	
Norman *et al.*, 2006[73] (related paper[341])	*Total score* CPAP: 38.4, *n* = 17; sham CPAP: 42.3, *n* = 14	*Total score* CPAP: 40.9, *n* = 17; sham CPAP: 45.5, *n* = 14; MD (SD): –4.6, *p*-value: 0.149 NB *p*-value based on treatment × time interaction (three treatment arms)	
Wechsler Adult Intelligence Scale (direction of improvement +): This is a neuropsychological test battery. The full-scale IQ test is broken down into 14 subtests comprising the verbal (seven subtests) and performance (seven subtests) scales.			
Crossover trials			
Barnes *et al.*, 2002[89]	*DSST* CPAP: NR; OP: NR; both: 46.5 (SD 4.0), *n* = 28	*DSST* CPAP: 47.3; OP: 48.0; MD (SD): –0.7, *p*-value: 0.07 (difference in change)	
Barnes *et al.*, 2004[82]	*DSST* CPAP: NR; OA: NR; OP: NR; all: 46.4 (SE 0.4), *n* = 80	*DSST* CPAP: 47.3 (SE 0.4); OA: 47.5 (SE 0.4); OP: 46.8 (SE 0.4); CPAP/OA MD (SD): –0.2; CPAP/OP MD (SD): 0.5; *p*-value: ns	
	Digit backwards CPAP: NR; OA: NR; OP: NR; all: 4.4 (SE 0.1), *n* = 80	*Digit backwards* CPAP: 4.6 (SE 0.1); OA: 4.6 (SE 0.1); OP: 4.8 (SE 0.1); CPAP/OA MD (SD): 0; CPAP/OP MD (SD): –0.2; *p*-value: ns	
Engleman *et al.*, 1994[90]	*DSST* CPAP: NR; OP: NR; *n* = 32	*DSST* CPAP: 52.0 (SE 2.0); OP: 51.0 (SE 2.0); MD (SD): 1, *p*-value: 0.05	
	Block design CPAP: NR; OP: NR; *n* = 32	*Block design* Data not reported because there was no statistically significant difference between CPAP and oral placebo	
Engleman *et al.*, 1998[93]	*DSST* CPAP: NR; OP: NR; both: 48.0 (SD 12.0), *n* = 23	*DSST* CPAP: 52.0 (SD 13.0); OP: 52.0 (SD 14.0); MD (SD): 0, *p*-value: ns	
	Block design CPAP: NR; OP: NR; both: 29.0 (SD 11.0), *n* = 23	*Block design* CPAP: 33.0 (SD 9.0); OP: 31.0 (SD 8.0); MD (SD): 2, *p*-value: ns	
Engleman *et al.*, 1999[78]	*DSST* CPAP: NR; OP: NR; both: 54.0 (SD 12.0), *n* = 34	*DSST* CPAP: 59.0 (SD 12.0); OP: 57.0 (SD 14.0); MD (SD): 2, *p*-value: 0.0004	

continued

Table 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
	Block design	*Block design*	
	CPAP: NR; OP: NR; both: 29.0 (SD 10.0), *n* = 34	CPAP: 31.0 (SD 12.0); OP: 32.0 (SD 10.0); MD (SD): –1, *p*-value: ns	
Parallel trials			
Barbé *et al*., 2001[83]	*Digit symbols*	*Digit symbols*	
	CPAP: 42.0 (SE 2.0), *n* = 29; OP: 44.0 (SE 4.0), *n* = 25	CPAP: 43.0 (SE 3.0), *n* = 29; OP: 47 (SE 4.0), *n* = 25; MD (SD): –4, *p*-value: > 0.20 (difference in change)	
	Block design	*Block design*	
	CPAP: 33.0 (SE 1.0), *n* = 29; OP: 32.0 (SE 2.0), *n* = 25	CPAP: 34.0 (SE 1.0), *n* = 29; OP: 33.0 (SE 2.0), *n* = 25; MD (SD): 1, *p*-value: > 0.20 (difference in change	
	Digit forwards	*Digit forwards*	
	CPAP: 9.0 (SE 0.3), *n* = 29; OP: 10.0 (SE 0.4), *n* = 25	CPAP: 9.0 (SE 0.3), *n* = 29; OP: 10.0 (SE 1.0), *n* = 25; MD (SD): –1, *p*-value: > 0.20 (difference in change)	
Dimsdale *et al*., 2000[73] (related paper[117])	*Digit symbols*	*Digit symbols*	
	CPAP: 51.3 (SE 2.3), *n* = 20; sham CPAP: 52.9 (SE 2.8), *n* = 16	CPAP: 53.2 (SE 2.5), *n* = 20; sham CPAP: 53.5 (SE 3.0), *n* = 16; MD (SD): –0.3, *p*-value: ns	
	Digit forwards	*Digit forwards*	
	CPAP: 8.1 (SE 0.7), *n* = 20; sham CPAP: 8.6 (SE 0.8), *n* = 16	CPAP: 8.6 (SE 0.6), *n* = 20; sham CPAP: 8.7 (SED 0.7), *n* = 16; MD (SD): –0.1, *p*-value: ns	
	Digit forwards and backwards	*Digit forwards and backwards*	
	CPAP: 14.7 (SE 1.1), *n* = 20; sham CPAP: 14.7 (SE 1.2), *n* = 16	CPAP: 16.2 (SE 1.1), *n* = 20; sham CPAP: 15.1 (SE 1.3), *n* = 16; MD (SD): 1.1, *p*-value: ns	
Henke *et al*., 2001[85]	*Digit symbols and digit backwards*	Data presented as graphs. Rather than assess change scores a binary variable was created of improved or not improved and the two groups were compared based on this. No significant difference between groups	
[a]Lojander *et al*., 1999[113]	*Verbal intelligence quotient*	*Verbal intelligence quotient*	*Verbal intelligence quotient*
	CPAP: 121 (110–148), *n* = 10; CM: 111 (91–140), *n* = 17	CPAP: 115, *n* = 10; OP: 104, *n* = 16; *p*-value: ns	CPAP: 114, *n* = 9; OP: 105, *n* = 12; *p*-value: ns
	Performance quotient	*Performance quotient*	*Performance quotient*
	CPAP: 115 (110–143), *n* = 10; CM: 114 (84–147), *n* = 17	CPAP: 123, *n* = 10; OP: 109, *n* = 16; *p*-value: ns	CPAP: 106, *n* = 9; OP: 109, *n* = 12; *p*-value: ns

Table 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	**Follow-up 1**	**Follow-up 2**
Monasterio *et al.*, 2001[100]	*Digit symbols*	*Digit symbols (scaled score)*	
	CPAP: 9 (SD 3), *n* = 66; CM: 9 (SD 3), *n* = 59	CPAP: 9.0 (SD 3.0), *n* = 66; CM: 9.0 (SD 2.0), *n* = 59; MD (SD): 0, *p*-value: 0.97 (difference in change)	
	Block design	*Block design (scaled score)*	
	CPAP: 10 (SD 3), *n* = 66; CM: 10 (SD 3), *n* = 59	CPAP: 11.0 (SD 3.0), *n* = 66; CM: 11.0 (SD 3.0), *n* = 59; MD (SD): 0, *p*-value: 0.82 (difference in change)	
	Digit forwards and backwards	*Digit forwards and backwards (scaled score: mean 10, SD 3)*	
	CPAP: 10 (SD 2), *n* = 66; CM: 10 (SD 3), *n* = 59	CPAP: 11.0 (SD 3.0), *n* = 66; CM: 11.0 (SD 2.0), *n* = 59; MD (SD): 0, *p*-value: 0.56 (difference in change)	
Norman *et al.*, 2006[73] (related paper[341])	*Digit symbols*	*Digit symbols (no. correct)*	
	CPAP: 65.8, *n* = 17; sham CPAP: 67.6, *n* = 14	CPAP: 73.8, *n* = 17; CM: 68.7, *n* = 14; MD (SD): 5.1, *p*-value: 0.256	
	Digit forwards	*Digit forwards (total score)*	
	CPAP: 18.6, *n* = 17; sham CPAP: 21.2, *n* = 14	CPAP: 26.4, *n* = 17; CM: 22.5, *n* = 14; MD (SD): 3.9, *p*-value: 0.378	
	Letter sequencing	*Letter sequencing*	
	CPAP: 11.0, *n* = 17; sham CPAP: 11.7, *n* = 14	CPAP: 11.9, *n* = 17; CM: 12.9, *n* = 14; MD (SD): –1, *p*-value: 0.827	
	Symbol search	*Symbol search (no. correct)*	
	CPAP: 31.8, *n* = 17; sham CPAP: 32.1, *n* = 14	CPAP: 33.8, *n* = 17; CM: 37.7, *n* = 14; MD (SD): –3.9, *p*-value: 0.614	
		NB p-value based on treatment × time interaction (three treatment arms)	
Wechsler Memory Scale (direction of improvement +): This is a battery of memory tests.			
Crossover trials			
Barnes *et al.*, 2002[89]	*Visual reproduction*	*Visual reproduction*	
	CPAP: NR; OP: NR; both: 33.5 (SD 5.4), *n* = 28	CPAP: 34.7; OP: 35.1; MD (SD): –0.4, *p*-value: ns	
Jokic *et al.*, 1999[108]	No baseline data; *n* = 13	*Visual reproduction*	
		CPAP: 10.6 (SD 4.4); CM other: 10.3 (SD 2); MD (SD): 0.3, *p*-value: 0.72	
		Orientation	
		CPAP: 5.0 (SD 0); CM other: 5.0 (SD 0); MD (SD): 0, *p*-value: 1	

continued

Table 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
		Information	
		CPAP: 5.5 (SD 1.2); CM other: 5.9 (SD 0); MD (SD): –0.4, *p*-value: 0.14	
		Mental control	
		CPAP: 7.3 (SD 2.1); CM other: 7.4 (SD 1.2); MD (SD): –0.1, *p*-value: 0.9	
		Logical memory	
		CPAP: 11.4 (SD 3.3); CM other: 12.0 (SD 3.8); MD (SD): –0.6, *p*-value: 0.42	
		Associate learning	
		CPAP: 14. 8 (SD 1.0); CM other: 16.6 (SD 4.2); MD (SD): –1.8, *p*-value: 0.06	
		Digit forwards	
		CPAP: 6.5 (SD 2.1); CM other: 6.5 (SD 1.5); MD (SD): 0, *p*-value: 1	
		Digit backwards	
		CPAP: 4.9 (SD 2.1); CM other: 5.0 (SD 1.7); MD (SD): –0.1, *p*-value: 0.86	
		Recall (logical memory)	
		CPAP: 9.0 (SD 5.0); CM other: 9.5 (SD 3.5); MD (SD): –0.5, *p*-value: 0.52	
		Recall (visual reproduction)	
		CPAP: 9.2 (SD 4.5); CM other: 9.9 (SD 2.1); MD (SD): –0.7, *p*-value: 0.15	
		Recall (associate learning)	
		CPAP: 6.1 (SD 3.1); CM other: 6.3 (SD 3.3); MD (SD): –0.2, *p*-value: 0.54	
		Memory quotient	
		CPAP: 122.2 (SD 24.7); CM other: 122.8 (SD 20.2); MD (SD): –0.6, *p*-value: 0.83	
Parallel trials			
Barbé *et al*., 2001[83]	*Mental control*	*Mental control*	
	CPAP: 6.0 (SE 0.4), $n = 29$; sham CPAP: 6.0 (SE 1.0), $n = 25$	CPAP: 6.0 (SE 0.4), $n = 29$; sham CPAP: 7.0 (SE 0.4); MD (SD): –1, *p*-value: > 0.20 (difference in change)	
	Verbal paired associate	*Verbal paired associate*	
	CPAP: 14 (SE 1.0), $n = 29$; sham CPAP: 15 (SE 1.0), $n = 25$	CPAP: 15.0 (SE 1.0), $n = 29$; sham CPAP: 15.0 (SE 1.0), $n = 25$; MD (SD): 0, *p*-value: > 0.20 (difference in change)	

Table 53 *Summary of neurocognitive outcomes for individual studies*

	Baseline	Follow-up 1	Follow-up 2
[a]Lojander *et al.*, 1999[113]	*Memory quotient* CPAP: 128 (105 to 151), *n* = 10; CM: 118 (99 to 150), *n* = 17	*Memory quotient* CPAP: 129 *n* = 10; CM: 115, *n* = 16; *p*-value: ns	*Memory quotient* CPAP: 121 *n* = 9; CM: 120, *n* = 12; *p*-value: ns
Monasterio *et al.*, 2001[100]	*No baseline data reported*	*Mental control (percentile)* CPAP: 51.0 (SD 274), *n* = 66; CM: 53.0 (SD 27.0), *n* = 59; MD (SD): –2, *p*-value: 0.08 (difference in change) *Verbal paired associate (percentile)* CPAP: 41.0 (SD 30.0), *n* = 66; CM: 43.0 (SD 32.0), *n* = 59; MD (SD): –2, *p*-value: 0.63 (difference in change) *Verbal paired associate (percentile)* CPAP: 61.0 (SD 24.0), *n* = 66; CM: 63.0 (SD 25.0), *n* = 59; MD (SD): –2, *p*-value: 0.06 (difference in change)	
Word Paired Memory Recall (direction of improvement +): Respondents were asked to learn a series of word-pair associates; this was followed by a retention period, after which respondents were asked to recall target words.			
Crossover trials			
Barnes *et al.*, 2002[89]	CPAP: NR; OP: NR; both: 1.5 (SD 1.2), *n* = 28	CPAP: 1.9; OP: 1.55; MD (SD): 0.35, *p*-value: ns	

BVM-DL, Brief Visuospatial Memory (delayed learning); BVM-TR, Brief Visual Memory (total recall); CM, conservative management; DSST, Digit Symbol Substitution Test; DST, Driver Simulator Test; NART, National Adult Reading Test; NR, not reported; OA, oral appliance; OP, oral placebo; PASAT, Paced Auditory Serial Addition Task; RT, reaction time; WAIS-R, Wechsler Adult Intelligence Scale-Revised.
a Values presented are median (range).
b Values are median (interquartile range).
c Values presented are median (5th–95th percentile).

Table 54 *Test procedures for neurocognitive trials*

Study	Time of day	Caffeine/medication	Test order	Environment	Special exclusion criteria	Test–retest
Barbé *et al.*, 2001[83]	NR	Drug intake and alcohol consumption were assessed at each test period	NR	NR	Cognitive deterioration of any cause, illicit drugs or excessive alcohol use	NR
Barnes *et al.*, 2002[89]	The NAB was administered three times during the day of the MSLT and a mean score was computed to account for time of day effects. Other NC tests were only administered during the first session	NR	NR	NR	Fluency of English language, no history of cerebrovascular disease, closed head injury associated with loss of consciousness > 15 minutes, psychiatric illness, or drug or alcohol abuse	Participants attended a familiarisation session 1 week prior to baseline assessment and performed an abbreviated version of the neurocognitive tests
Barnes *et al.*, 2004[82]	NR	Clinically significant depression was present in 40% of the OSAHS participants (as measured by the BDI)	NR	NR	Fluency of English language, no history of cerebrovascular disease, closed head injury associated with loss of consciousness > 15 minutes, psychiatric illness, or drug or alcohol abuse	Participants attended a familiarisation session 1 week prior to baseline assessment and performed an abbreviated version of the neurocognitive tests
Cibele *et al.*, 2006[72]	NR	NR	NR	NR	NR	NR
Bardwell *et al.*, 2000[117]	Tests were administered early afternoon	NR	NR	NR	No major illness other than OSA, hypertension medication tapered before participation	Alternate forms were used for the word fluency test (considered to be the most likely test to show a learning effect)
Engleman *et al.*, 1994[90]	Cognitive function was assessed in between MSLT naps across the course of a day	Participants were asked to avoid caffeine-containing drinks before attending assessments and were offered only decaffeinated drinks during the assessment day	Tests were conducted on the last day of each treatment period and were administered in a standardised order at the same time of day	NR	NR	Participants attended a familiarisation session with the psychometric battery prior to baseline assessment. Alternate forms of two neurocognitive tests were used at follow-up assessment

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Table 54 *Test procedures for neurocognitive trials*

Study	Time of day	Caffeine/medication	Test order	Environment	Special exclusion criteria	Test–retest
Engleman *et al.*, 1997[92]	Assessments were conducted throughout the day	NR	Tests were conducted on the last day of each treatment period and were administered in a standardised order	NR	Individuals with co-existing neurological disorders were excluded	Participants attended a familiarisation session with the psychometric battery prior to baseline assessment. Alternate forms of two neurocognitive tests were used at follow-up assessment
Engleman *et al.*, 1998[93]	NR	NR	Tests were administered in a standardised order	NR	Individuals with co-existing neurological disorders were excluded	NR
Engleman *et al.*, 1999[78]	Afternoon, during 'post-lunch dip' in performance	NR	Tests were administered in a standardised order	NR	NR	Participants attended a familiarisation session with the psychometric battery prior to baseline assessment
Engleman *et al.*, 2002[103]	NR	NR	NR	NR	NR	NR
Henke *et al.*, 2001[85]	Tests were administered between 2 p.m. and 6 p.m.	NR	NR	NR	NR	Participants attended a familiarisation session with the psychometric battery prior to baseline assessment. Four parallel test packets were administered on a randomised counterbalanced schedule
Hoekema *et al.*, 2006[102,114]	Between noon and 2 p.m	Participants were instructed to avoid stimulating products, such as caffeine, up to 3 hours before testing and not to smoke in the 30 minutes before testing	The test was administered at the same time of day in subsequent sessions	Room conditions: lights were dimmed, noise was excluded, and room temperature was kept at 22°C. Participants were alone during testing	Individuals without a driving licence, or who were involved in shift work or night-time work, were excluded	A practice session immediately prior to baseline assessment was provided

continued

Study	Time of day	Caffeine/medication	Test order	Environment	Special exclusion criteria	Test–retest
Jenkinson *et al.*, 1999[77,118]	Three 30-minute drives (11 a.m, 12 p.m. and 2 p.m)	NR	The tests were performed at the same time of day on each occasion	NR	Individuals considered too mentally impaired to provide reliable informed consent were excluded	An initial training drive was administered prior to the first drive on each day
Jokic *et al.*, 1999[108]	Cognitive tests were administered after the third MSLT test, which was conducted 2 hours after waking and given at 2-hourly intervals	Participants were asked to avoid caffeine-containing drinks before attending assessments and were offered only decaffeinated drinks during the assessment day. A urine toxicology screen was performed on day 15 of each study limb for use of any drugs that might affect sleep quality or daytime function	Each test was administered at the same time of day on each study limb. The order was balanced throughout the study	NR	NR	Participants attended a familiarisation session with the psychometric tests prior to baseline assessment
Lojander *et al.*, 1999[113]	Tests were performed in the morning	NR	NR	NR	Individuals with other diseases and daytime hypoxaemia were excluded	NR
Marshall *et al.*, 2005[79]	PVT was administered twice a day with a 1-minute practice session before each 10-minute data collection session at 2.30 p.m. and 4.30 p.m. on each of the four study days (beginning and end of each treatment period)	NR	Testing procedures were time of day fixed	NR	Individuals who performed shift work, had extreme somnolence requiring immediate treatment, had a chronic sleep restriction, were taking sedatives, had an alcohol intake > 3 standard units/24 hours or had a caffeine dependency were excluded	NR

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Table 54 *Test procedures for neurocognitive trials*

Study	Time of day	Caffeine/medication	Test order	Environment	Special exclusion criteria	Test–retest
Monasterio *et al.*, 2001[100]	Tests were administered at 9 a.m.	NR	Testing procedures were administered at the same time each session	NR	Individuals with hazardous jobs (drivers or those handling dangerous machinery), with conditions that might affect cognition or quality of life (severe neurological disease, psychiatric disease, severe chronic disease or illiteracy) were excluded	NR
Norman *et al.*, 2006[73,341]	Tests were administered at 1 p.m.	NR	NR	NR	Individuals were excluded if they had a history of heart, liver or renal disease, diabetes, psychosis, narcolepsy, current drug or alcohol abuse, severe asthma or cerebrovascular disease, were pregnant, or were taking prescription medications except hypertensive medication. Those taking hypertensive medication underwent a 3-week washout period before study entry	Employed alternate forms for tests

BDI, Beck Depression Inventory; MSLT, Multiple Sleep Latency Test; NAB, neuropsychological assessment battery; NC, neurocognitive; NR, not reported; OSA, obstructive sleep apnoea; OSAHS, obstructive sleep apnoea–hypopnoea syndrome; PVT, Psychomotor Vigilance Test.

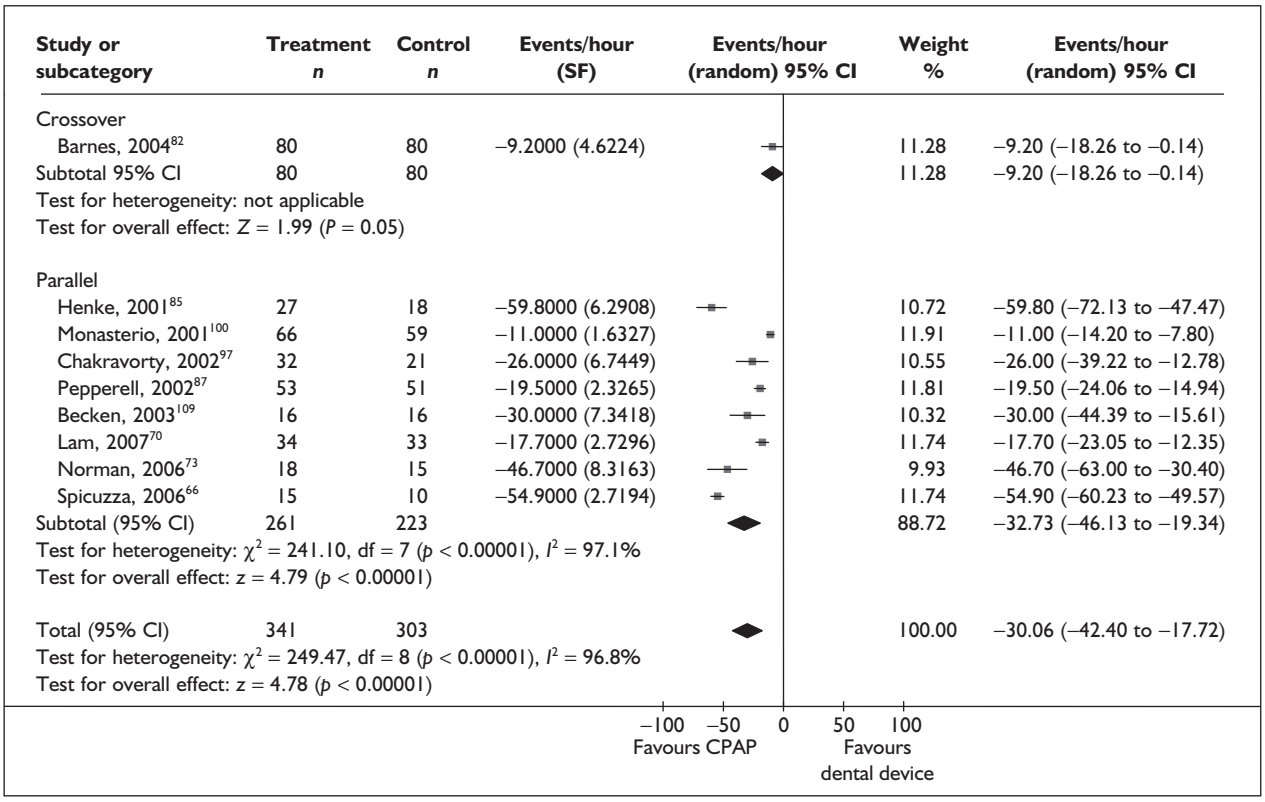

FIGURE 44 *Apnoea–hypopnoea index (CPAP versus placebo/usual care).*

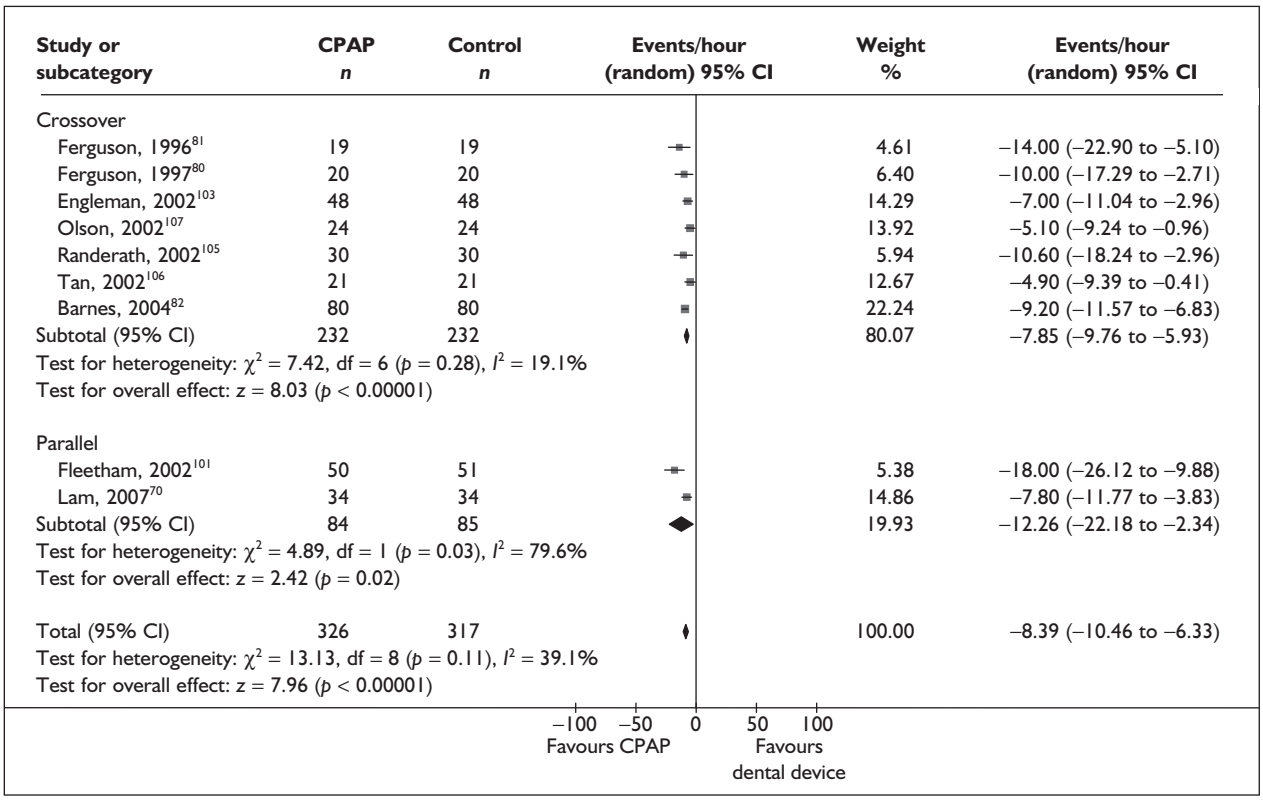

FIGURE 45 *Apnoea–hypopnoea index (CPAP versus dental devices).*

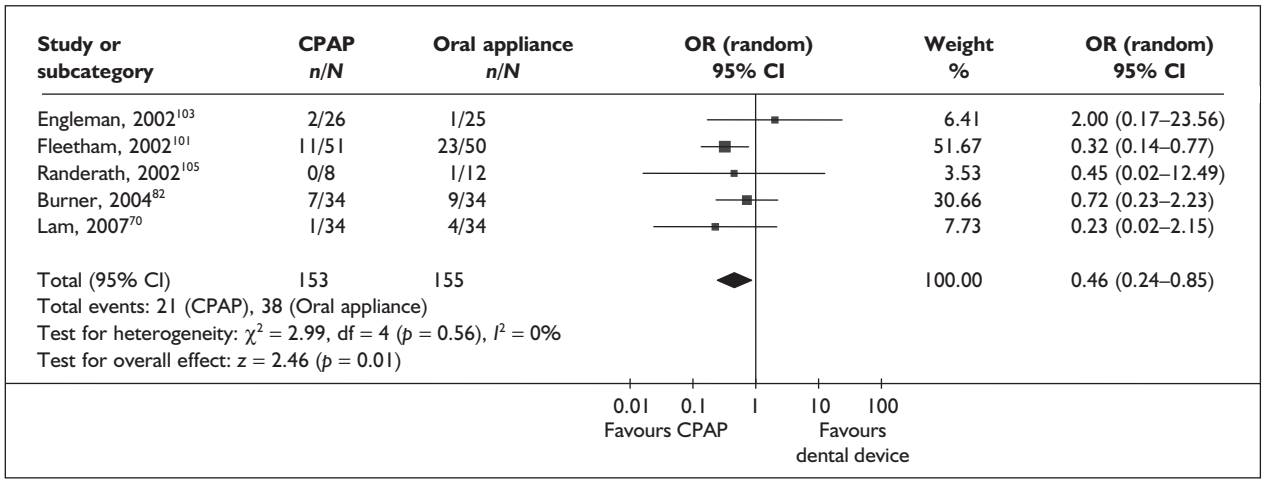

FIGURE 46 *Withdrawals (CPAP versus dental devices).*

Appendix 5

Data extraction for clinical effectiveness trials

Study details	Intervention	Participants
Arias et *al*., 2005[56] (related papers[301–304])	*CPAP* (following full-night titration using an automated pressure setting device to set the pressure)	*Number randomised*. Total: 27 [baseline data for BP are presented for completers ($n = 25$)]
Setting. Spain	*Comparator*. Sham nCPAP	*Number of withdrawals*. Total: 2 (CPAP: 2, comparator: 0)
Design. Crossover study.		*Reasons for withdrawals*. Participants were not included in analysis because of insufficient use of CPAP
Duration. Two × 12 weeks (no washout period)		*Baseline characteristics*
Inclusion criteria. Men with OSAHS.		
Exclusion criteria. Obstructive or restrictive lung disease demonstrated on pulmonary function testing, current use of cardioactive medication, cardiac rhythm disturbances, hypertension or 24-hour mean BP of 135 and/or ≥85 mmHg, left ventricular ejection fraction < 50%, ischaemic or valvular heart disease, hypertrophic restrictive or infiltrative cardiomyopathy, pericardial disease or stroke, diabetes mellitus, morbid obesity, daytime hypoxaemia or hypercapnia		*Additional information*. 24-hour BP, urinary catecholamines, heart rate and echocardiographic parameters. Outcomes were assessed at study entry, after first treatment period and after second treatment period. BP was measured every 30 minutes from 8 a.m. to 11 p.m. and every 60 minutes from 11 p.m. to 8 a.m. using a cuff.

	Total	**CPAP**	**Comparator**
Age (years)	52 (SD 13)		
Sex	Male ($n = 27$)		
AHI	29.0 (SD 26.9)		
ESS	Not assessed		
BMI (kg/m^2)	30.5 (SD 4.0)		
BP (mmHg)			
Daytime SBP	127 (SD 9)		
Daytime DBP	79 (SD 5)		
Night-time SBP	118 (SD 11)		
Night-time DBP	71 (SD 7)		

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Study details	Intervention	Participants
Arias et *al*., 2006[63] *Setting*. Spain *Design*. Crossover trial (outcome data appeared to be from the first sequence and data were treated as parallel data) *Duration*. Two × 12 weeks (no washout period) *Inclusion criteria*. Individuals with OSA (AHI > 9 and ESS > 9), and in whom pulmonary artery systolic pressure could be estimated *Exclusion criteria*. Obstructive or restrictive lung disease demonstrated on pulmonary function test, connective tissue or chronic thromboembolic diseases, current cardioactive medication, cardiac rhythm disturbances, known hypertension or 24-hour mean BP of 135 and/or ≥ 85 mmHg, left ventricular ejection fraction < 50%, ischaemic or valvular heart disease, cardiomyopathy, pericardial disease or stroke, diabetes, morbid obesity, day-time hypoxaemia or hypercapnia, history of cocaine or antidepressant drug use	*CPAP* (following full-night titration using an automated pressure setting device to set the pressure). Adherence: 6.2 hours/night (SD 1.1) *Comparator*. Sham CPAP. Adherence: 5.8 hours/night (SD 1.4)	*Number randomised*. Total: 23 (CPAP: NR, comparator: NR) *Number of withdrawals*. Total: 2 (CPAP: NR, comparator: NR) *Reasons for withdrawals*. Two participants not included in the analyses because of insufficient (< 3.5 hour/night) CPAP use *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: 51 (SD 13) Sex: Male (*n* = 22), female (*n* = 1) AHI: 44.1 (SD 29.3) ESS: Not assessed BMI: 30.9 (SD 4) BP Daytime SBP: 127 (SD 10) Daytime DBP: 79 (SD 5) Night-time SBP: 118 (SD 12) Night-time DBP: 71 (SD 7) *Additional information*. 24-hour BP, heart rate, echocardiographic parameters, urinary catecholamines and levels of pulmonary artery pressure were assessed at study entry and after each 12-week treatment period. Ambulatory BP monitoring was performed using an oscillometric method.

continued

Study details	Intervention	Participants
Ballester *et al.*, 1999[96] *Setting*. Spain *Design*. Parallel *Duration*. 12 weeks *Notes*. Two patients randomised to CPAP group for every one randomised to control group; nine patients excluded *Inclusion criteria*. Men and women with severe symptoms and AHI > 15 or mild to moderate symptoms and AHI > 10	*CPAP* (following full-night titration using an automated pressure setting device) and *conservative treatment*. Adherence: 5.2 hours/night (± 2). Adequate compliance (defined as > 4.5 hours/night) was achieved in 73% of participants *Comparator*. Conservative treatment (postural advice, avoid sedatives and alcohol, lose weight)	*Number randomised*. Total: *n* = 105 (CPAP: *n* = 68, comparator: *n* = 37) *Number of withdrawals*. Total: unclear (CPAP: *n* = 0, comparator: NR) *Reasons for withdrawals*. No record of dropouts recorded for control group *Baseline characteristics*

	Total	**CPAP**	**Comparator**
Age	53 (SD 10)	53 (SE 1.3)	54 (SE 1.5)
Sex	Male (*n* = 92), female (*n* = 13)	Male, *n* = 60; female, *n* = 8	Male, *n* = 32; female, *n* = 5
AHI	56 (SD 20)	55 (SE 2.7)	58 (SE 3)
ESS	12 (SD5)	12.1 (SE 0.6)	11.4 (SE 1)
BMI	32 (SD 6)	32 (SE 0.6)	34 (SE 1.2)
BP	Not assessed	–	–
Sleep questionnaire		23.2 (SE 0.8)	21.0 (SE 1.2)
Associated symptoms		43.4 (SE 0.8)	41.8 (SE 1.1)
Daytime function		33.9 (SE 1.3)	32.3 (SE 1.7)
NHP			
Emotional reactions		28.4 (SE 3.3)	29.4 (SE 5.0)
Sleep		30.1 (SE 3.3)	23.1 (SE 3.8)
Physical		24.2 (SE 2.6)	25.0 (SE 3.6)
Social isolation		14.2 (SE 2.3)	13.2 (SE 3.0)
Pain		20.5 (SE 3.3)	20.6 (SE 4.0)
Energy		34.3 (SE 4.7)	23.2 (SE 4.6)

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Study details	Intervention	Participants
Barbé *et al.*, 2001[83] *Setting*. Spain *Design*. Parallel *Duration*. 6 weeks *Inclusion criteria*. Men and women with AHI > 30, ESS ≤ 10 and with no or mild symptoms of daytime sleepiness. *Exclusion criteria*. Severe cardiac disease	*CPAP* (following full-night titration). Adherence: 5 hours/night *Comparator*. Sham CPAP (no pressure added) following mock titration Adherence was not reported for the control group. However, adherence was reported to be similar in both groups	*Number randomised*. Total: 55 (CPAP: 29, comparator: 26) *Number of withdrawals*. Total: 1 (CPAP: 0, comparator: 1) *Reasons for withdrawals*. Loss to follow-up due to change in residence *Baseline characteristics* (baseline data are presented for completers, $n = 54$)

	Total	CPAP	Comparator
Age		54 (SD 2)	52 (SD 2)
Sex	Male ($n = 49$), female ($n = 5$)	Male ($n = 26$), female ($n = 3$)	Male ($n = 23$), female ($n = 2$)
AHI		54 (SD 3)	57 (SD 4)
ESS		7 (SE 0.4)	7 (SE 0.4)
BMI		29 (SD 1)	29 (SD 0.4)
BP			
24-Hour SBP		126 (SE 2)	123 (SE 2)
Diurnal SBP		130 (SE 2)	127 (SE 2)
Nocturnal SBP		118 (SE 2)	118 (SE 3)
24-Hour DBP		79 (SE 1)	77 (SE 2)
Diurnal DBP		82 (SE 1)	80 (SE 2)
Nocturnal DBP		73 (SE 1)	73 (SE 2)
SF-36			
PCS score		49 (SE 1)	48 (SE 1)
MCS score		51 (SE 2)	50 (SE 2)
FOSQ		102 (SE 3)	107 (SE 3)
MSLT (minutes)		12 (SE 1)	10 (SE 1)

Additional information. Outcomes: ESS, FOSQ, BP, AHI, MSLT, SF-36, and cognitive function (see *Table 53*).

continued

Study details	Intervention	Participants
Barnes et *al.*, 2002[89] *Setting*. Australia *Design*. Crossover *Duration*. Two periods of 8 weeks (no washout period) *Inclusion criteria*. Men and women with AHI 5–30 with symptoms of sleep-disordered breathing *Exclusion criteria*. Excessive daytime sleepiness requiring urgent treatment	*CPAP*. Adherence: 3.53 hours/night ($n = 23$) *Comparator*. Oral placebo (lactose tablet)	*Number randomised*. Total: $n = 42$ *Number of withdrawals*. Total: $n = 14$ (CPAP: NR, comparator: NR) *Reasons for withdrawals*. Work commitments ($n = 6$), intolerance of CPAP ($n = 5$), unrelated surgery ($n = 1$), subsequent diagnosis of periodic limb movement syndrome ($n = 1$) and loss of interest ($n = 1$) *Baseline characteristics* **Additional information**. Seven participants were hypertensive at study entry (defined as BP > 140 mmHg, or a mean 24-hour DBP > 90 mmHg). Outcomes: ESS, FOSQ, AHI, MSLT, symptoms, and cognitive function (see *Table 53*).

	Total	CPAP	Comparator
Age	45.5 (SD 10.7)		
Sex	Male ($n = 35$), female ($n = 7$)		
AHI	12.9 (SD 4.24)		
ESS	11.2 (SD 5)		
BMI	30.2 (SD 4.8)		
BP	Not assessed		
MSLT (minutes)	12.5 (SD 4.8)		
Symptom questionnaire			
Sleepiness	26.3 (SD 9.4)		
Sleep fragmentation	21.9 (SD 9.5)		
Personality change	8.6 (SD 6.1)		
Morning confusion	6.4 (SD 5.3)		
Total score	63.2 (SD 21.7)		
FOSQ			
General productivity	3.3 (SD 0.6)		
Social outcome	3.2 (SD 1.0)		
Activity level	3.1 (SD 0.6)		
Vigilance	3.0 (SD 0.7)		
Intimate relationships	3.0 (SD 1.3)		
Total score	0.8 (SD 0.1)		

DOI: 10.3310/hta13040

Study details	Intervention	Participants
Barnes et *al.*, 2004[82] *Setting*. Australia *Design*. Three-way crossover trial *Duration*. Three × 12 weeks (2-week washout period between each treatment). *Notes*. Authors report that 80 participants completed all three treatment arms *Inclusion criteria*. Patients with mild to moderate OSA	*CPAP*. Adherence (machine usage): 3.6 hours/night (± 0.3) and 4.2 nights/per week (± 0.3) *Comparator*. Mandibular advancement splint. Mean mandibular advancement was 10.3 mm (range 1–13 mm). MAS was advanced weekly during a wash-in period as tolerated by the participant until the maximum comfortable protrusion was reached. The screw was sealed. Adherence (self-reported): 5.5 hours/night (± 0.3) and 5.3 nights/per week (± 0.3) *Placebo* (dummy pill). Adherence (pill count): tablets taken for 94.3% (± 1.2) of treatment nights	*Number randomised*. Total: unclear (at least 99 randomised). *Number of withdrawals*. Total: 30 (CPAP: 8, MAS: 14, oral: 8) *Reasons for withdrawals*. CPAP: time commitments ($n = 5$), relocated ($n = 1$), intolerant to CPAP ($n = 1$), illness ($n = 1$). MAS: teeth unsuitable for MAS ($n = 5$), time commitments ($n = 2$), did not tolerate MAS ($n = 2$), unrelated illness ($n = 1$), lost weight and felt better ($n = 1$), lost to follow-up ($n = 1$). Placebo: time commitments ($n = 6$), wanted CPAP treatment ($n = 1$), illness ($n = 1$) *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: 47 (SE 0.9) Sex: Male (79.8%), female ($n = 16$) AHI: 21.3 (SE 1.3) ESS: 10.7 (SE 0.4) BMI: 31.1 (SE 0.5) BP 24-Hour SBP: 126.5 (SE 1.0) 24-Hour DBP: 76.3 (SE 0.8) Night-time DBP: 69.4 (SE 1.3) FOSQ, mean score: 3.1 (SE 0.1) SASQ: 64.7 (SE 1.7) POMS, total mood disorder: 15.5 (SE 2.0) BDI: 9.2 (SE 0.5) SF-36: 69.4 (SE 1.3) *Additional information*. 16 participants were hypertensive (defined as: SBP > 140 and/or DBP > 90 mmHg). Outcomes were measured at baseline and at the end of each intervention period: ESS, FOSQ, ODI 4%, AHI, MWT, SF-36 and cognitive function (see *Table 53*).

continued

Study details	Intervention	Participants
Becker *et al.*, 2003[109] (related papers[84,305]) *Setting*. Germany *Design*. Parallel placebo controlled trial *Duration*. 9 weeks *Notes*. A maximum of four patients per week could be included in the study. If more than one patient was eligible on 1 day, the patient with the most pronounced sleep apnoea was invited to participate first *Inclusion criteria*. Men and women with OSA (AHI ≥ 5 and excessive daytime sleepiness) *Exclusion criteria*. Predominantly central sleep apnoea, respiratory failure, heart failure, myocardial infarction 3 months before the study, relevant cardiac arrhythmia and professional driver	*CPAP* (following overnight manual titration). Adherence: 5.5 hours/night (SD 2.0) *Comparator*. Sham CPAP (pressure 3 or 4 cmH_2O). Adherence: 5.4 hours/night (SD 2.2)	*Number randomised*. Total: 60 (CPAP: 30, comparator: 30) *Number of withdrawals*. Total: 28 (CPAP: 14, comparator: 14) *Reasons for withdrawals*. CPAP: refused to continue ($n = 3$), technical fault with BP device ($n = 6$), antihypertensive medication change ($n = 3$), other ($n = 2$). Comparator: refused to continue ($n = 2$), technical fault with BP device ($n = 5$), antihypertensive medication change ($n = 4$), other ($n = 3$) *Baseline characteristics* (presented for completers only)

	Total	CPAP	Comparator
Age		54.4 (SD 8.9)	52.3 (SD 8.4)
Sex	Male ($n = 29$), female ($n = 3$)	Male ($n = 15$), female ($n = 1$)	Male ($n = 14$), female ($n = 2$)
AHI		62.5 (SD 17.8)	65.0 (SD 26.7)
ESS		14.4 (SD 2.5)	14.1 (SD 3.2)
BMI		33.3 (SD 5.1)	33.5 (SD 6.0)
BP			
24-Hour BP		100.4 (SD 15.9)	99.5 (SD 12.3)
24-Hour SBP		135.9 (SD 17.5)	136.2 (SD 13.1)
24-Hour DBP		83.4 (SD 15.9)	81.1 (SD 12.3)
Daytime BP		103.6 (SD 16.1)	103.5 (SD 12.1)
Daytime SBP		140.1 (SD 17.6)	141.0 (SD 13.8)
Daytime DBP		86.4 (SD 16.1)	85.4 (SD 12.3)
Night-time BP		96.2 (SD 17.6)	93.6 (SD 15.2)
Night-time SBP		129.9 (SD 20.0)	129.2 (SD 16.9)
Night-time DBP		79.1 (SD 17.0)	75.4 (SD 15.2)

Additional information. 8/16 in CPAP group were hypertensive; 13/16 in control group were hypertensive. Outcomes were measured at baseline and at 9 weeks: daytime MAP, night-time MAP, ESS, AHI, REM (%), minimum SaO_2. BP was measured using a cuff (recording time was limited to 20 hours). During the diagnostic period participants spent 7.2 hours in bed; night-time BP was calculated for this time period. Daytime BP was recorded for the remaining 12 hours.

DOI: 10.3310/hta13040

Study details	Intervention	Participants
Campos-Rodriguez *et al.*, 2006[65] *Setting*. Spain. *Design*. Parallel group trial *Duration*. 4 weeks. *Inclusion criteria*. Adults with OSAHS and hypertension (defined as > 140/90 mmHg in three independent measurements *Exclusion criteria*. Greater than 30% central sleep apnoea, respiratory failure, heart failure, ischaemic heart disease, cardiac arrhythmia, neoplastic or systemic diseases, patients with secondary hypertension, or professional driver. Participants were also excluded if their antihypertensive medication was changed during the course of the trial	*CPAP* (following a full-night titration). Adherence not reported *Comparator*. Sham CPAP (pressure < 2 cmH_2O) (following a mock titration night)	*Number randomised*. Total: 72 (CPAP: 36, comparator: 36) *Number of withdrawals*. Total: 4 (CPAP: 2, comparator: 2) *Reasons for withdrawals*. CPAP: one participant changed treatment, and one did not attend follow-up. Comparator: one did not tolerate placebo and one changed antihypertensive treatment *Baseline characteristics. n = 68* **Total** / **CPAP** / **Comparator** Age: 55.3 (SD 9.6) / 58.0 (SD 7.0) Sex: Male (*n* = 41), female (*n* = 27) / NR / NR AHI: 58.3 (SD 24.6) / 59.5 (SD 21.7) ESS: 15.0 (SD 3.9) / 13.6 (SD 3.6) BMI: 35.7 (SD 5.6) / 33.8 (SD 6.3) BP 24-Hour BP: 97.7 (SD 10.7) / 96.2 (SD 10.1) 24-Hour SBP: 131.9 (SD 13.5) / 130.4 (SD 15.9) 24-Hour DBP: 78.4 (SD 10.3) / 77.6 (SD 8.7) Daytime BP: 100.8 (SD 10.7) / 98.9 (SD 10.0) Night-time BP: 94.6 (SD 11.1) / 93.5 (SD11.4) *Additional information*. ESS, AHI and 24-hour BP. Participants were assessed at trial entry and after 4 weeks of treatment. BP was measured using cuff inflation every 30 minutes for 24 hours. All participants were naïve to CPAP treatment.

continued

Study details	Intervention	Participants
Chakravorty et *al*., 2002[97] (related paper[306]) *Setting*. UK *Design*. Parallel group trial *Duration*. 12 weeks *Inclusion criteria*. Participants with AHI ≥ 15	*CPAP* (following home-based titration using an automated pressure setting device). Adherence not reported *Comparator*. Conservative management (verbal advice, leaflet listing strategies for sleep hygiene, quitting smoking, reducing alcohol consumption, and controlling stress, verbal and written advice on ideal body weight, weight reduction and exercise)	*Number randomised*. Total: 71 (CPAP: 37, comparator: 34) *Number of withdrawals*. Total: 18 (CPAP: 5, comparator: 13) *Reasons for withdrawals*. CPAP: failed to tolerate CPAP ($n = 4$), subsequently underwent surgery ($n = 1$). Comparator: excluded due to health reasons ($n = 5$), preferred surgery ($n = 2$), other ($n = 6$) *Baseline characteristics* (based on completers only)

	Total	CPAP	Comparator
Age	50 (SD 11)	49 (SD 11)	52 (SD 9.6)
Sex	NR	NR	NR
AHI	49 (SD 28)	55 (SD 28.7)	35 (SD 19.1)
ESS	14 (SD 5)	16 (SD 5.6)	14 (SD 4.2)
BMI	37 (SD 12)	40 (SD 14.5)	32.3 (SD 5.5)
BP	Not assessed	–	–
EuroQol (0–100)		59 (SD 19.8)	68 (SD 16.8)
Ueq[a]		0.73 (SD 0.18)	0.77 (SD 0.12)
Usg[b]		0.32 (SD 0.17)	0.31 (SD 0.13)

a EuroQol-derived utility.
b Standard gamble utility.

Additional information. Outcomes include ESS, AHI, quality of life and utility.

Study details	Intervention	Participants
Cibele *et al.*, 2006[72] *Setting*. Brazil *Design*. Crossover trial *Duration*. 1 month OA or OA placebo and then 1 month nCPAP (1-week washout period between OA devices and CPAP treatment) *Notes*. Conference abstract – insufficient outcome data available *Inclusion criteria*. Adults with moderate to severe OSA (AHI ≥20)	*CPAP*. Adherence not reported *Comparator*. OA (repositioning mandibular appliance with progressive adjustment) or placebo OA (splint at lower arch)	*Number randomised*. Total: 13 *Number of withdrawals*. The authors do not report any losses to follow-up *Reasons for withdrawals*. NA *Baseline characteristics* **Additional information**. Outcomes include: ESS, SF-36, PVT (see *Table 53*), and oxidative stress. Outcomes were assessed before treatment and at each treatment phase.

	Total	**CPAP**	**Comparator**
Age	44 (SD 8)		
Sex	Male (n = 12), female (n = 1)		
AHI	45.5 (SD 28)		
ESS	10.6 (SD 4)		
BMI	27.4 (SD 5)		
BP	Not assessed		

continued

<table>
<tr><th>Study details</th><th>Intervention</th><th>Participants</th></tr>
<tr>
<td>Coughlin et al., 2007[62] (related paper[307])

Setting. UK

Design. Crossover trial

Duration. Two × 6 weeks (no washout period)

Notes. Participants spent significantly more each night on the therapeutic CPAP machine than on the sham CPAP machine ($p < 0.01$). No evidence of a carryover effect for any outcome variable

Inclusion criteria. Untreated male patients with OSAHS

Exclusion criteria. Any abnormality identified on baseline ECG, or if there was evidence of diabetes, renal liver or cardiac disease, or if participants had symptoms of peripheral neuropathy or waking blood pressure ≥ 180/110 mmHg, or a level of blood pressure requiring treatment</td>
<td>CPAP (following titration in sleep laboratory using automated pressure setting device). Adherence (machine running time): 3.9 hours/night (range 0–7.4)

Comparator. Sham CPAP (pressure < 1 cmH_2O). Adherence (machine running time): 2.6 hours/night (range 0–7.5)</td>
<td>Number randomised. Total: 35

Number of withdrawals. Total: 1 (CPAP: 1, comparator: 0)

Reasons for withdrawals. One participant withdrew during the first treatment period (CPAP limb) for personal reasons

Baseline characteristics (based on 34 participants)
<table>
<tr><th></th><th>Total</th><th>CPAP</th><th>Comparator</th></tr>
<tr><td>Age</td><td>49.0 (SD 8.3)</td><td></td><td></td></tr>
<tr><td>Sex</td><td>Male ($n = 34$)</td><td></td><td></td></tr>
<tr><td>RDI</td><td>39.7 (SD 13.8)</td><td></td><td></td></tr>
<tr><td>ESS</td><td>13.8 (SD 4.9)</td><td></td><td></td></tr>
<tr><td>BMI</td><td>36.1 (SD 7.6)</td><td></td><td></td></tr>
<tr><td>BP</td><td>NR</td><td></td><td></td></tr>
</table>
Additional information. 27 participants (79%) were hypertensive (resting blood pressure of 140/90 mmHg). Outcomes included ESS, waking BP, fasting glucose, baroreceptor sensitivity, fasting insulin, cholesterol and incidence of metabolic syndrome. Outcomes were assessed at baseline and after each intervention period. Waking BP was measured from 8 a.m. to 11 a.m. in a supine position after a 5-minute rest. It was recorded as the mean of three measurements taken at 1-minute intervals.</td>
</tr>
</table>

Study details	Intervention	Participants
Cross *et al.*, 2005[308] (related paper[88]) *Setting*. UK *Design*. Crossover trial *Duration*. Two × 6 weeks (washout period not reported) *Notes*. Conference abstract *Inclusion criteria*. Adults with severe OSA (two major symptoms of OSAHS, > 20 of 4% nocturnal desaturation/hour)	*CPAP*. Adherence: 5.5 hours/night (1.2) *Comparator*. Sham CPAP. Adherence: 3.3 hours/night (2.2)	*Number randomised*. Total: 31 *Number of withdrawals*. Total: NR (CPAP: NR, comparator: NR) *Reasons for withdrawals*. NA *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: 51 (SD 5) Sex: Male (*n* = 30), female (*n* = 1) AHI: 63 (SD 26) ESS: Not assessed BMI: 40.1 (SD 8.4) BP: NR *Additional information*. Outcomes include bilateral forearm blood flow (measured using venous occlusion plethysomography with unilateral intrabrachial infusions).

continued

Study details	Intervention	Participants
Dimsdale *et al.*, 2000[58] (related papers[117,309–314]) *Setting*. USA *Design*. Parallel group trial *Duration*. 1 week *Notes*. Patients were treatment naïve *Inclusion criteria*. Adults (aged 30–65 years), within 100–170% of ideal weight and RDI > 15 *Exclusion criteria*. Major ongoing illness other than sleep apnoea and hypertension (> 140/90 mmHg but < 180/110 mmHg)	*CPAP* (following manual overnight titration). Compliance was reported to be > 5 hours/night *Comparator*. Sham CPAP (pressure: 2 cmH_2O) (following mock titration). Adherence was reported to be > 5 hours/night	*Number randomised*. Unclear: 39 participants completed the study, but related papers indicate that a greater number of participants may have originally been randomised (n = 38–48) [CPAP (n = 21), comparator (n = 18)] *Number of withdrawals*. The authors do not report any withdrawals for BP or QoL outcomes. The papers report that POMS had 34 participants [CPAP (n = 20)] *Reasons for withdrawals*. NR *Baseline characteristics*

	Total	CPAP	Comparator
Age		47.7 (SD 8.1)	48.9 (SD 9.9)
Sex		Male (n = 15), female (n = 6)	Male (n = 16), female (n = 2)
AHI	Not assessed	–	–
ESS	Not assessed	–	–
BMI		32.7 (SD 4.9)	28.5 (SD 5.0)
BP			
Mean screening SBP		128 (SD 15)	123 (SD 12)
Mean screening DBP		82 (SD 8)	78 (SD 9)
RDI		53.6 (SD 23.2)	41.7 (SD 25.6)
POMS			
Tension		10.9 (SD 7.1)	9.9 (SD 5.5)
Depression		12.5 (SD 15.1)	12.7 (SD 10.1)
Fatigue		13.3 (SD 8.2)	11.6 (SD 6.6)
Confusion		7.6 (SD 5.0)	8.3 (SD 3.5)
Vigour		15.3 (SD 7.7)	15.3 (4.7)
Anger		14.3 (SD 11.9)	9.2 (SD 6.5)
Total mood disturbance		43.2 (SD 48.5)	36.5 (SD 28.4)

Additional information. Ten participants were hypertensive (CPAP 6, sham CPAP 4). Participants receiving antihypertensive medication had their medication tapered and their BP status confirmed after a 3-week washout. Outcomes included BP and RDI. Participants wore an ambulatory BP monitor for a 24-hour period on three occasions: before randomisation, after 1 day of treatment and after 1 week of treatment. BP was taken every 15 minutes 6 a.m. to 10 p.m. and every 30 minutes 10 p.m. to 6 a.m. Related papers report QoL (MOS) (Profant[309]), mood (POMS; Yu[313]), and cognitive outcomes (Bardwell[117]) (see *Table 53*); assessed before treatment and after 1 week of treatment.

Study details	Intervention	Participants
Drager et *al*., 2006[69] *Setting*. Brazil *Design*. Parallel group trial *Duration*. 12 weeks *Notes*. Conference abstract – insufficient outcome data available *Inclusion criteria*. Normotensive participants with OSA	*CPAP*. Adherence not reported *Comparator*. Usual care	*Number randomised*. Total: 16 (CPAP: NR, comparator: NR) *Number of withdrawals*. Total: no reported dropouts *Reasons for withdrawals*. NA *Baseline characteristics*

	Total	**CPAP**	**Comparator**
Age		45 (SE 3)	47 (SE 4)
Sex	NR	NR	NR
AHI		54 (SE 8)	65 (SE 13)
ESS	Not assessed	–	–
BMI		31 (SE 1)	30 (SE 1)
BP			
Mean SBP		118 (SE 4)	125 (SE 5)

Additional information. Outcomes included BP, carotid–femoral pulse wave velocity, cholesterol level and heart rate. Participants were assessed at baseline and after 3 months.

continued

<table>
<tr><th>Study details</th><th>Intervention</th><th>Participants</th></tr>
<tr><td>Engleman et al., 1994[90]

Setting. UK

Design. Crossover trial

Duration. Two × 2 weeks (no washout period)

Notes. Significant learning effect on some outcome measures, especially cognitive tests

Inclusion criteria. Men and women with AHI ≥5 and at least two symptoms of obstructive sleep apnoea. Included consecutive patients referred for investigation of OSA

Exclusion criteria. No co-existing disorder causing excessive sleepiness and lives within 50 miles of the laboratory.</td><td>CPAP (following overnight titration). Adherence: 3.7 hours/night

Comparator. Oral placebo (inactive ranitidine)</td><td>Number randomised. Total: 35

Number of withdrawals. Total: 3 (CPAP: NR, comparator: NR)

Reasons for withdrawals. Pressure at work (n = 1), relocation (n = 1), reluctance to use CPAP (n = 1)

Baseline characteristics (based on completers only)

<table>
<tr><th></th><th>Total</th><th>CPAP</th><th>Comparator</th></tr>
<tr><td>Age</td><td>49 (SE 1.5)</td><td></td><td></td></tr>
<tr><td>Sex</td><td>Male (n = 26), female (n = 6)</td><td></td><td></td></tr>
<tr><td>AHI (median)</td><td>28</td><td></td><td></td></tr>
<tr><td>ESS</td><td>Not assessed</td><td></td><td></td></tr>
<tr><td>BMI</td><td>33 (1.6)</td><td></td><td></td></tr>
<tr><td>BP</td><td>Not assessed</td><td></td><td></td></tr>
</table>

Additional information. These outcomes were measured on the last day of each treatment period: MSLT, cognitive function (NART, WAIS, TMT A and B, SteerClear, RVIPT, PASAT, Borkowski Test, BVRT-R) (see Table 53), in-house symptom score, HADS, GHQ, NHP, energetic arousal score compliance, patient preference.</td></tr>
</table>

Study details	Intervention	Participants
Engleman *et al.*, 1996[91] *Setting*. UK *Design*. Crossover trial *Duration*. Two × 4 weeks (no washout period) *Inclusion criteria*. Men and women with AHI ≥5 and at least two symptoms of obstructive sleep apnoea	*CPAP*. Adherence: 4.3 hours/night (SE 0.6) *Comparator*. Oral placebo (inactive ranitidine)	*Number randomised*. Total: 16 *Number of withdrawals*. Total: 3 (CPAP: NR, comparator: NR) *Reasons for withdrawals*. Equipment unavailability ($n = 1$), poor ambulatory BP ($n = 1$) and non-attendance ($n = 1$) *Baseline characteristics* (completers only, $n = 13$) *Additional information*. Five participants were classified as hypertensive (24-hour BP > 134 and DBP > 84 mmHg), and four participants were taking antihypertensive medication; medication did not change throughout the trial period. Outcome was 24-hour ambulatory BP. BP was recorded every 30 minutes for a 24-hour period with a cuff.

	Total	CPAP	Comparator
Age	51 (SE 3)		
Sex	Male ($n = 11$), female ($n = 2$)		
AHI	49 (SE 9)		
ESS	Not assessed		
BMI	36 (SE 2.6)		
BP	NR		

continued

Study details	Intervention	Participants
Engleman *et al.*, 1997[92] *Setting*. UK *Design*. Crossover trial *Duration*. Two × 4 weeks (no washout period) *Notes*. No tests reported for differential carryover for period or washout effect. Ten patients refused to participate in the study *Inclusion criteria*. Patients with mild sleep apnoea (AHI 5–14.9) and at least two symptoms of obstructive sleep apnoea	*CPAP* (following titration study). Adherence (machine usage): 3.2 hours/night (SE 0.7) *Comparator*. Oral placebo (inactive ranitidine)	*Number randomised*. Total: 18 *Number of withdrawals*. Total: 2 (CPAP: 2, comparator: 0) *Reasons for withdrawals*. Relocated ($n = 1$), intolerant of noise from CPAP unit and declined to complete treatment limb ($n = 1$) *Baseline characteristics* (based on completers)

	Total	CPAP	Comparator
Age	52 (SE 2)		
Sex	Male ($n = 12$), female ($n = 4$)		
AHI	11 (SE 1)		
ESS	14 (SE 1)		
BMI	29.8 (SE 1.8)		
BP	Not assessed		

Additional information. Outcomes were measured on the last day of each treatment: MSLT, cognitive function (NART, WAIS, TMT A and B, SteerClear, RVIPT, PASAT, Borkowski Test, BRVT-R) (see *Table 53*), in-house symptom score, HADS, GHQ, NHP, energetic arousal score, compliance, patient preference.

DOI: 10.3310/hta13040

Study details	Intervention	Participants
Engleman *et al.*, 1998[93] *Setting*. UK *Design*. Crossover trial *Duration*. Two × 4 weeks (no washout period) *Inclusion criteria*. Patients with AHI of at least 15 and two or more symptoms of sleep-disordered breathing *Exclusion criteria*. Lung disease, neurological disorders, co-existing sleep disorder and individuals who lived more than 50 miles from the Scottish National Sleep Centre	*CPAP* (following overnight titration). Adherence: 3.2 hours/night *Comparator*. Oral placebo	*Number randomised*. Total: 23 *Number of withdrawals*. Total: 1 (CPAP: 1, comparator: 0) *Reasons for withdrawals*. Myocardial infarction during CPAP limb. Participant position refilled by next available recruit *Baseline characteristics* *Additional information*. Outcomes were measured on the last day of each treatment: ESS, AHI, NHP, MSLT, HADS, GHQ-28, UMACL, cognitive function (see *Table 53*), preference.

	Total	CPAP	Comparator
Age	47 (SD 12)		
Sex	Male ($n = 21$), female ($n = 2$)		
AHI	43 (SD 37)		
ESS	12.0 (SD 4)		
BMI	BMI 30 (SD 7)		
BP	Not assessed		
UMACL, energetic arousal score	21 (SD 5)		
Symptom score, total	5.1 (SD 1.5)		
HADS			
Anxiety	8.3 (SD 4.4)		
Depression	5.7 (SD 4.4)		
GHQ-28	6.6 (SD 6.5)		
NHP part 2	8.0 (SD 5.0)		

continued

Study details	Intervention	Participants
Engleman *et al.*, 1999[78] *Setting*. UK *Design*. Crossover trial *Duration*. Two × 4 weeks (no washout period) *Inclusion criteria*. New outpatient attendees with at least two symptoms of OSA including sleepiness (ESS ≥8) and mild sleep apnoea (AHI 5–14.9/hour)	*CPAP* (following overnight titration). Heated humidified nCPAP. Adherence (machine usage): 3.2 hours/night (SD 2.4) *Comparator*. Oral placebo	*Number randomised*. Total: 37 *Number of withdrawals*. Total: 3 (CPAP: NR, comparator: NR) *Reasons for withdrawals*. Unwilling to persist with CPAP treatment ($n = 1$), failed to attend final assessment ($n = 1$), travel to centre too demanding (final CPAP limb) ($n = 1$) *Baseline characteristics* (based on completers only)

	Total	**CPAP**	**Comparator**
Age	44 (SD 8)		
Sex	Male ($n = 21$), female ($n = 13$)		
AHI	10 (SD 3)		
ESS	13 (SD 3)		
BMI	30 (SD 5)		
BP	Not assessed		
Symptoms (total score)	22 (SD 6)		
UMACL, energetic arousal score	18 (SD 5)		
HADS			
Anxiety	9.0 (SD 4.2)		
Depression	7.4 (SD 4.1)		
NHP part 2	10.5 (SD 4.8)		
SF-36			
Health transition	3.1 (SD 0.6)		
Physical function	75 (SD 27)		
Role – physical	58 (SD 36)		
Role – emotional	62 (SD 38)		
Bodily pain	68 (SD 31)		
Mental health	64 (SD 19)		
Social function	60 (SD 27)		
General health	68 (SD 21)		
Vitality	33 (SD 19)		

Additional information. Outcomes included MWT, ESS, UMACL, symptom questionnaire, HADS, NHP part 2, SF-36, WAIS-R, cognitive function (see *Table 53*).

Study details	Intervention	Participants
Engleman *et al.*, 2002[103] (related papers[112,315]) *Setting*. UK *Design*. Crossover trial *Duration*. Two × 8 weeks (no washout period) *Inclusion criteria*. Patients aged 18–70 years with AHI ≥5 and two symptoms of OSAHS *Exclusion criteria*. Individuals with fewer than four teeth remaining in either arch, co-existing narcolepsy, periodic limb movement of more than 10/hour, major medical illness, shift work, or living more than 50 miles away from Edinburgh	*CPAP* (following all-night titration). Adherence: 6.1 hours/night (± 1.9) *Comparator*. Oral appliance. Participants were randomised to receive one of two oral devices: (1) two mouth guards providing complete occlusal coverage constructed by an ethylenemethylacrylate/polystyrene material and the two units sealed in protrusion; (2) device manufactured from less flexible 1MEDL™ dual laminate material, without occlusal coverage. Both were individually fitted to produce 80% of maximal comfortable mandibular protrusion, with 2–4 mm of interdental clearance. Adherence: 5.6 hours/night (± 2.0)	*Number randomised*. Total: 51 *Number of withdrawals*. Total: 3 (CPAP: 2, comparator: 1) *Reasons for withdrawals*. Uncontactable (first CPAP limb) ($n = 1$), unable to spare time due to starting a new job (during first CPAP and first OA limb) *Baseline characteristics* ($n = 48$) **Total** / **CPAP** / **Comparator** Age: 46 (SD 9) Sex: Male ($n = 36$), female ($n = 12$) AHI: 31 (SD 26) ESS: 14 (SD 4) BMI: NR BP: Not assessed *Additional information*. Outcomes were measured on the last day of each treatment: SF-36, ESS, MWT, HADS, AHI, FOSQ, PASAT, cognitive function (see *Table 53*), preference.

continued

<table>
<tr><th>Study details</th><th>Intervention</th><th>Participants</th></tr>
<tr><td>Faccenda et al., 2001[94] (related papers[316, 317])

Setting. UK

Design. Crossover trial.

Duration. Two × 4 weeks (no washout period)

Inclusion criteria. Patients that exhibit two symptoms of sleep apnoea/hypopnoea syndrome and an AHI ≥ 15

Exclusion criteria. Individuals taking hypotensive medication</td><td>CPAP (following full-night titration using an automated pressure setting device). Adherence: 3.3 hours/night (range 0–8.1)

Comparator. Oral placebo. Adherence (capsule counting): a median of 0 tablets (95th percentile, 1.4 tablets) were missed over the 1-month period</td><td>Number randomised. Total: 71

Number of withdrawals. Total: 3 (CPAP: 2, comparator: 1)

Reasons for withdrawals. NR

Baseline characteristics (n = 68)

<table>
<tr><th></th><th>Total</th><th>CPAP</th><th>Comparator</th></tr>
<tr><td>Age</td><td>50 (29–72)</td><td></td><td></td></tr>
<tr><td>Sex</td><td>Male (n = 55), female (n = 13)</td><td></td><td></td></tr>
<tr><td>AHI</td><td>35 (15–129)</td><td></td><td></td></tr>
<tr><td>ESS</td><td>15 (6–24)</td><td></td><td></td></tr>
<tr><td>BMI</td><td>30 (21–53)</td><td></td><td></td></tr>
<tr><td>BP</td><td>NR</td><td></td><td></td></tr>
</table>
Data presented as median (range) unless otherwise stated

Additional information. Outcomes were measured on the last day of each 1-month period treatment: ESS; AHI; BP. BP was measured via arm cuff, programmed to record every 30 minutes for a 48-hour period. Data for second 24-hour period used (6 p.m.–6 p.m.).</td></tr>
</table>

DOI: 10.3310/hta13040

Study details	Intervention	Participants
Ferguson et *al.*, 1996[81] *Setting*. Canada *Design*. Crossover trial *Duration*. Two × 16 weeks (2-week washout period) *Notes*. Patients randomised after 2-week wash-in period. Unclear about patient preference – only provided results for seven patients who were treatment successes with both treatments. No evidence of carryover effect between treatment periods *Inclusion criteria*. Patients with mild to moderate sleep apnoea and at least 10 teeth in each of the mandibular and maxillary arches.	*CPAP* (following overnight titration). The use of a humidifier was optional, but encouraged. Intranasal corticosteroids and/or anticholinergic medications to relieve nasal symptoms caused by CPAP use were used. Adherence (% of the night treatment used): 10 patients used CPAP 100%, four patients used CPAP > 75%, three patients used CPAP 25–75%, four patients used CPAP < 25% Adherence (% of the night treatment used): nine patients used CPAP 100%, five patients used CPAP > 75%, three patients used CPAP 25–75%, four patients used CPAP < 25% *Comparator*. Oral appliance. OA was constructed to position the mandible 3 mm posterior to the position of maximal acceptable advance and with a 7 mm opening between the upper and lower incisors. Material was added to increase the vertical dimension of the appliance in a few participants. Oral device was constructed of an acrylic polymer Adherence (% nights treatment used): 15 patients used OA 100%, nine patients used OA > 75%, one patient used OA 25–75% Adherence (% nights treatment used): 12 patients used OA 100%, eight patients used OA > 75%, four patients used OA 25–75%, one patient used OA < 25%	*Number randomised*. Total: 26 *Number of withdrawals*. Total: 1 (CPAP: 0, comparator: 1) *Reasons for withdrawals*. Relocated (*n* = 1) *Baseline characteristics* (*n* = 27, based on number recruited for washout period before randomisation) **Total** / **CPAP** / **Comparator** Age: 46.2 (SD 10.9) Sex: Male (*n* = 24, female *n* = 3) AHI: 24.5 (SD 8.8) ESS: Not assessed BMI: 30.4 (SD 4.8) BP: Not assessed *Additional information*. Outcomes were measured at end of each 4-month period: sleep variables, symptom questionnaire, patient preference, side effects.

continued

Study details	Intervention	Participants
Ferguson et *al*., 1997[80] *Setting*. Canada *Design*. Crossover trial *Duration*. Two × 16 weeks (2-week washout period) *Notes*. Patients randomised after 2-week wash-in period. No evidence of carryover effect *Inclusion criteria*. Patients with symptomatic mild to moderate sleep apnoea (AHI 15–55), and at least 10 teeth in each of the mandibular and maxillary arches	*CPAP*. Participants used a variety of airway access devices based on their own preference. The use of a cold flow-by humidifier was optional but encouraged. Intranasal corticosteroids and/or anti-cholinergic medications were used to relieve nasal symptoms *Comparator*. Oral appliance. The amount of mandibular advancement was initially set at 70% of maximal mandibular advancement. The amount of mandibular advancement was increased over the treatment period by a mean of 1.8 mm (SD 1.2) until snoring stopped and symptoms improved, or until participants could not tolerate further advancement	*Number randomised*. Total: 24 [baseline data for ESS are presented for completers ($n = 20$)] *Number of withdrawals*. Total: 4 (CPAP: NR, comparator: NR) *Reasons for withdrawals*. Refused follow-up assessments ($n = 1$), refused to cross over from OA to CPAP ($n = 3$) *Baseline characteristics* **Additional information**. Outcomes were measured at the end of each treatment period: sleep variables, symptom questionnaire, patient preference, side effects.

	Total	**CPAP**	**Comparator**
Age	44 (SD 11)		
Sex	Male ($n = 19$), female ($n = 5$)		
AHI	27 (SD 12)		
ESS	NR	11 (SD 3.8)	10.3 (SD 3.1)
BMI	32 (SD 8)		
BP	Not assessed		

Study details	Intervention	Participants
Fleetham *et al.*, 2002[50] (unpublished data from Giles *et al.*, 2006) (related papers[101,119,218]) *Setting*. Canada *Design*. Parallel group trial *Duration*. 12 weeks *Inclusion criteria*. AHI > 10	*CPAP*. Adherence: NR *Comparator*. Adjustable oral appliance	*Number randomised*. Total: 101 (CPAP: NR, comparator: NR) *Number of withdrawals*. Total: NR *Reasons for withdrawals*. NA *Baseline characteristics* **Additional information**. Outcomes included: AHI, ESS, minimum SaO_2, quality of life index.

	Total	CPAP	Comparator
Age		49.0 (± 9.4)	6.2 (± 11.3)
Sex	Male ($n = 96$), female ($n = 5$)		
AHI		37.6 (± 22.8)	38.7 (± 22.2)
ESS		12.8 (± 4.1)	11.1 (± 4.9)
BMI		32.0 (± 5.5)	1.4 (± 5.7)
BP	Not assessed	–	–
SAQLI		4.2 (± 1.1)	4.2 (± 1.0)
Minimum SaO_2		75.8 (± 12.7)	73.6 (± 1.8)

continued

Study details	Intervention	Participants
Henke *et al.*, 2001[85] *Setting*. USA *Design*. Partial crossover trial *Duration*. Six weeks (no washout period). Sham-CPAP group received treatment for 15 days then crossed over and received CPAP for rest of treatment period. CPAP received treatment for entire period *Notes*. Only data from the first sequence were used, thus data were treated as parallel data *Inclusion criteria*. Males and females with diagnosed symptoms of sleep apnoea/hypopnoea syndrome with AHI > 10 plus daytime sleepiness or AHI > 20 without daytime sleepiness *Exclusion criteria*. Oxygen saturation < 85% for > 50% of sleep time, clinical signs of right-sided congestive heart failure, claustrophobia or nasal obstruction preventing use of nasal CPAP	*CPAP* (following laboratory titration). Adherence (hours/night): first limb 5.9 (SD 1.8); second limb 5.8 (SD 2.0) *Comparator*. Sham CPAP. Adherence (hours/night): first limb 5.2 (SD 2.2); second limb 4.9 (SD 2.4)	*Number randomised*. Total: 45 (CPAP: 27, comparator: 18) *Number of withdrawals*. Total: 4 (T3 parallel analysis) (CPAP: NR, comparator: NR) *Reasons for withdrawals*. Baseline polysomnography was mistakenly performed on effective CPAP rather than ineffective CPAP for four participants from placebo group; data were not included in the analysis *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: NR / 50.2 (SD 10.4) / 50.6 (SD 9.7) Sex: Male ($n = 25$), female ($n = 20$) / NR / NR AHI: NR / 62.1 (SD 27.4) / 68.1 (SD 25.2) ESS: 16 / 16.4 (SD 5.6) / 16.0 (SD 4.8) BMI: NR / 42.7 (SD 10.5) / 42.2 (SD 11.9) BP: Not assessed / – / – Additional information. Outcomes were measured on the last day of each treatment: ESS, AHI, ODI, minimum SaO_2, SteerClear (see *Table 53*).

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Study details	Intervention	Participants
Hoekema *et al.*, 2006[102] (related papers[71,111,114,300]) *Setting*. Netherlands *Design*. Parallel group trial *Duration*. 8 weeks *Notes*. Abstract only for main efficacy data. Data for driving simulator test come from related paper (Hoekema *et al.*, 2006[114]). Data for sexual dysfunction (GRISS) taken from related paper (Hoekema *et al.*, 2006[111]). *Duration* (for the two related papers). 8–12 weeks. After 8 weeks of treatment participants were assessed with a second polysomnographic study; for participants with AHI ≥ 5, treatment was adjusted if possible to improve effectiveness, and in these participants the follow-up period was extended for another 4 weeks. Adjustment sequence was continued until AHI < 5 or until adjustments become uncomfortable *Inclusion criteria*. Adults with OSAHS (AHI > 5)	*CPAP*. Adherence: NR *Comparator*. Oral appliance *Related papers*. The oral appliance was a two-part adjustable appliance set at 5 degrees of patients' maximum advancement to begin with; patients could adjust the amount of mandibular advancement in increments of 0.2 degrees and were instructed to adjust by 0.2–0.4 degrees in weeks 2–8 until symptoms abated or any further advancement was uncomfortable	*Number randomised*. Total: 103 (CPAP: 52, comparator: 51) *Number of withdrawals*. NR *Reasons for withdrawals*. NR *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: NR Sex: NR AHI (median): NR ESS: Not assessed BMI: Not assessed BP: Not assessed Driving simulator test ($n = 19$) Lapses of attention, median: 10 (IQR 1.0–16.8) / 5.0 (IQR 2.0–14.0) GRISS ($n = 47$) Erectile dysfunction: 9.5 (SD 4.2) / 7.9 (SD 3.5) Premature ejaculation: 9.0 (SD 2.7) / 9.5 (SD 3.5) Non-sensuality: 5.8 (SD 2.1) / 5.4 (SD 2.0) Avoidance: 4.0 (IQR 4.0–5.5) / 4.0 (IQR 4.0–5.0) Sexual dissatisfaction: 10.2 (SD 4.3) / 8.5 (SD 3.9) Infrequency of sexual contact: 7.0 (SD 1.7) / 5.9 (SD 2.0) Non-communication: 4.6 (SD 1.8) / 4.0 (SD 1.9) *Additional information*. Primary outcome for main paper: AHI. Primary outcomes for related papers: driving simulator test and sexual dysfunction. Participants undertaking the driving simulator test were assessed between noon and 2 p.m. Room conditions: lights were dimmed, noise was excluded and room temperature was kept at 22 °C. The driving test was completed alone. Participants were instructed to refrain from stimulating products such as caffeine in the 3 hours before testing and not to smoke for 30 minutes before testing. Outcomes were assessed at baseline and after 8 weeks of treatment. In some participants final assessment occurred at a later stage [median final review was 81 days (IQR 72–93) in the OA group and 79 days (IQR 63–102) in the CPAP group].

continued

Study details	Intervention	Participants
Hui et *al.*, 2006[64] (related paper[318]) *Setting*. Hong Kong *Design*. Parallel group trial *Duration*. 3 months *Inclusion criteria*. CPAP-naïve adults with OSA. Participants with hypertension were eligible as long as there was no change in antihypertensive medication *Exclusion criteria*. Individuals with problems staying awake during driving, professional drivers, shift workers, recent myocardial infarction, unstable angina or underlying malignancy	*CPAP* (following overnight titration using an automated pressure setting device). Adherence (machine running time): 5.1 hours/night (SE 0.4) *Comparator*. Sham CPAP (pressure: 4 cmH_2O). Adherence (machine running time): 2.6 hours/night (SE 0.4)	*Number randomised*. Total: 56 (CPAP: 28, comparator: 28) *Number of withdrawals*. Total: 10 (CPAP: 5, comparator: 5) *Reasons for withdrawals*. CPAP: defaulted ambulatory BP measurement ($n = 3$), ambulatory BP recording failed to record ($n = 2$); Comparator: discomfort with treatment ($n = 5$) *Baseline characteristics* *Additional information*. 28 participants had hypertension (previously documented BP > 140/90 mmHg on at least two occasions or receiving antihypertensive medication). There were no changes in antihypertensive medication during the study. Outcomes included ESS, change in 24-hour arterial BP, change in SBP and DBP, change in mean BP awake and asleep. Outcomes were assessed at baseline and 48 hours before end of treatment (BP) or 3 months after treatment (ESS). BP was measured every 30 minutes for 48 hours using cuff inflation; the second 24 hours of data were used.

	Total	**CPAP**	**Comparator**
Age	50.8 (SE 1.7)	50.3 (SE 1.6)	51.2 (SE 1.8)
Sex	Male ($n = 43$), female ($n = 13$)	Male ($n = 22$), female ($n = 6$)	Male ($n = 21$), female ($n = 7$)
AHI	31.2 (SE 2.2)	32.9 (SE 3.2)	29.5 (SE 3.1)
ESS	11.1 (SE 0.7)	10.7 (SE 1.0)	11.6 (1.0)
BMI	27.2 (SE 0.5)	27.5 (SE 0.6)	26.9 (SE 0.7)
BP			
24-hour SBP	123.7 (SE 1.8)	125.4 (SE 2.6)	122.0 (SE 2.7)
24-hour DBP	80.9 (SE 1.2)	81.8 (SE 1.9)	80.0 (SE 1.7)
24-hour MAP	95.2 (SE 1.3)	96.2 (SE 1.8)	94.1 (SE 2.0)
Wake time SBP	127.8 (SE 1.8)	128.6 (SE 2.6)	127.2 (SE 2.7)
Wake time DBP	83.6 (SE 1.2)	83.7 (SE 1.9)	83.7 (SE 1.7)
Wake time MAP	98.1 (SE 1.5)	98.3 (SE 1.8)	97.9 (SE 1.9)
Sleep time SBP	115.7 (SE 2.0)	117.7 (SE 2.9)	113.9 (SE 3.0)
Sleep time DBP	74.8 (SE 1.4)	75.8 (SE 2.1)	74.1 (SE 2.0)
Sleep time MAP	89.1 (SE 1.5)	90.6 (SE 2.1)	87.8 (SE 2.3)

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Study details	Intervention	Participants
Jenkinson *et al.*, 1999[77] (related papers[118,319–324]) *Setting*. UK *Design*. Parallel group trial *Duration*. 4 weeks *Inclusion criteria*. Men aged 30–75 years with ESS ≥ 10 and ODI (SaO_2) > 4%	*CPAP* (autotitrating). Adherence: 5.4 (2.2–7.4) hours/night *Comparator*. Sham CPAP (pressure: approx. 1 cmH_2O). Adherence: 4.6 (0.7–8.5) hours/night	*Number randomised*. Total: 107 (CPAP: 54, comparator: 53) *Number of withdrawals*. Total: 6 (CPAP: 2, comparator: 4) *Reasons for withdrawals*. CPAP: did not use nCPAP and failed to reattend ($n = 2$); Comparator: did not use nCPAP and failed to reattend ($n = 3$), unexplained collapse ($n = 1$) *Baseline characteristics*

	Total	CPAP	Comparator
Age	49 (34–70)	50 (33–71)	48 (36–68)
Sex	Male ($n = 107$)	Male ($n = 54$)	Male ($n = 53$)
AHI	Not assessed	–	–
ESS	NR	16.0 (10.7–21.7)	17 (10.0–23.0)
BMI	35 (26–50)	35.1 (25.8–44.3)	35.0 (26.9–51.4)
BP			
4% SaO_2 (dips per hour)	31 (13–65)	32.9 (15.5–63.4)	28.5 (10.7–68.7)
MWT		22.5 (7.6–40.0)	20.0 (3.5–40.0)
SF-36*			
Mental component		44.8 (SD 10.4)	43.5 (SD 10.7)
Physical component		43.7 (SD 11.6)	42.6 (SD 10.1)
General health perception		59.2 (SD 18.4)	59.5 (SD 20.4)
Physical functioning		80.9 (SD 22.7)	78.6 (SD 22.1)
Social functioning		73.5 (SD 26.1)	73.0 (SD 26.1)
Physical role		62.0 (SD 37.2)	58.7 (SD 37.0)
Mental role		73.7 (SD 33.2)	68.7 (SD 36.3)
Bodily pain		82.1 (SD 23.8)	76.2 (SD 25.5)
Mental health		73.2 (SD 16.8)	68.7 (SD 18.2)
Energy and vitality		35.4 (SD 22.4)	33.9 (SD 17.5)

*With exception of mean (SD) data are median (5th–95th centiles)

Additional information. Outcomes include ESS, MWT, daytime saturation, SF-36. Related paper reports cognitive outcomes (Hack *et al.*, 2000[118]) (see *Table 53*).

continued

Study details	Intervention	Participants
Jokic *et al.*, 1999[108] *Setting*. Canada *Design*. Crossover trial *Duration*. Two × 2 weeks (no washout period) *Notes*. Unclear how many originally eligible *Inclusion criteria*. Outpatients referred with daytime sleepiness. Postural OSA (AHI during supine sleep that was two or more times AHI during sleep in the lateral position; AHI < 15 in lateral position; daytime sleepiness)	*CPAP* (following manual titration) *Comparator*. Postural therapy with backpack with soft ball inside to prevent subjects from sleeping supine	*Number randomised*. Total: 14 participants completed study *Number of withdrawals*. Total: 1 (exclusion) (CPAP: NR, comparator: NR) *Reasons for withdrawals*. NR *Baseline characteristics. n = 13* *Additional information*. Outcomes include MWT, ESS, HADS, UMACL, NHP, TMT A and B, GHQ, SDMT, WMS I and II, and cognitive outcomes (see *Table 53*).
L'Estrange *et al.*, 1999[104] *Setting*. UK *Design*. Crossover trial *Duration*. Two × 2 months (washout period not reported) *Notes*. Conference abstract – insufficient outcome information *Inclusion criteria*. Patients with severe OSAHS (AHI > 50)	*CPAP*. Adherence: NR *Comparator*. Oral appliance (mandibular advancement splint)	*Number randomised*. Total: 15 *Number of withdrawals*. Total: unclear, appears that six participants were not included in the analysis *Reasons for withdrawals*. Two participants failed to tolerate CPAP and four participants failed to complete OA treatment period *Baseline characteristics* *Additional information*. Outcomes include ESS and AHI.

	Total	CPAP	Comparator
Age	51 (SD 9)		
Sex	Male (*n* = 12), female (*n* = 1)		
AHI	17 (SD 8)		
ESS	13 (SD 1.3)		
BMI	30 (SD 4)		
BP	Not assessed		

	Total	CPAP	Comparator
Age	52.9 (± 6.3)		
Sex	NR		
AHI	63.7 (± 10.0)		
ESS	17.2 (± 3.8)		
BMI	34.2 (± 7.2)		
BP	Not assessed		

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Study details	Intervention	Participants
Lam et *al.*, 2007[70] (related papers[325,326]) *Setting*. Hong Kong *Design*. Parallel group trial *Duration*. 10 weeks *Inclusion criteria*. Patients with mild to moderate OSA *Exclusion criteria*. Sleepiness which may present a risk to self or others, unstable medical disease, co-existence of sleep disorders other than OSA, previous surgery to upper airway (except for nasal problems) and pregnant women	*CPAP* (at a pre-titrated pressure) and *conservative management* (advice on sleep hygiene and attendance at a weight control programme if overweight) *plus CPAP* Adherence to active treatment: 4.2 (SEM 0.1) hours/night and 4.4 (SEM 0.1) nights/week *Comparator*. CM (advice on sleep hygiene and attendance at a weight control programme if overweight using Asian criteria of BMI ≥23 kg/m^2); CM plus OA: tailor-made non-adjustable device made of dental acrylic from a functional activator (Harvold type) Adherence to active treatment (self-reported): 6.4 (SEM 0.2) hours/night and 5.2 (SEM 0.3) nights/week	*Number randomised*. Total: 101 (CPAP: 34, OA: 34, CM: 33) *Number of withdrawals*. Total: 10 (CPAP: 1, OA: 4, CM: 5) *Reasons for withdrawals*. CPAP: intolerance of device ($n = 1$), OA: gum problems ($n = 4$), CM: refused final PSG ($n = 5$) *Baseline characteristics* **CPAP** / **OA** / **CM** Age: 45 (SE 1) / 45 (SE 2) / 47 (SE 2) Sex: Male ($n = 27$), female ($n = 7$) / Male ($n = 26$), female ($n = 8$) / Male ($n = 26$), female ($n = 7$) AHI: 23.8 (SE 1.9) / 20.9 (SE 1.7) / 19.3 (SE 1.9) ESS: 12 (SE 1) / 12 (SE 1) / 12 (SE 1) BMI: 27.6 (SE 0.6) / 27.3 (SE 0.6) / 27.3 (SE 0.6) BP Morning SBP: 127.9 (SE 2.3) / 127.1 (SE 2.6) / 125.5 (SE 3.5) Morning DBP: 77.0 (SE 1.8) / 76.2 (SE 2.1) / 74.2 (SE 2.4) Evening SBP: 130.9 (SE 2.4) / 131.9 (SE 3.1) / 127.2 (SE 3.2) Evening DBP: 78.0 (SE 1.9) / 77.8 (SE 2.2) / 73.5 (SE 1.9) *Additional information*. 19 participants were hypertensive and on treatment [CPAP ($n = 7$), OA ($n = 4$), CM ($n = 8$)]. There was no change in antihypertensive medications during the study period. Outcomes included AHI, ESS, QoL (SF-36, SAQLI), morning BP (8–9 a.m.), evening BP (8–9 p.m.), treatment adherence (assessed at 4 weeks and 10 weeks) and adverse events. BP was the average of three readings taken at 1-minute intervals.

continued

Study details	Intervention	Participants
Lim 2005[110] *Setting*. USA *Design*. Parallel group trial *Duration*. 4 weeks *Notes*. Abstract – insufficient outcome data *Inclusion criteria*. Adults with chronic daily headache and AHI ≥5	*CPAP*. Adherence :NR *Comparator*. Conservative management	*Number randomised*. Total: 23 (CPAP: 12, comparator: 11) *Number of withdrawals*. No dropouts were reported *Reasons for withdrawals*. NA *Baseline characteristics*

	Total	CPAP	Comparator
Age	NR		
Sex	Male ($n = 5$), female ($n = 18$)		
AHI	NR		
ESS	Not assessed		
BMI	Not assessed		
BP	Not assessed		

Additional information. There were no changes in medication throughout the study period.

DOI: 10.3310/hta13040

Study details	Intervention	Participants
Lojander *et al.*, 1996[99] (related paper[113]) *Setting*. Finland *Design*. Parallel group trial *Duration*. 52 weeks *Notes*. Patients were reviewed by a panel of experts and allocated to two groups: candidates for UPP surgery ($n = 23$) and candidates for CPAP ($n = 27$). The latter group was randomly allocated to CPAP or conservative follow-up *Inclusion criteria*. Patients with OSA and BMI of < 40 kg/m^2	*CPAP*. Nasal CPAP (initiated in the hospital). Adherence: 9 out of 10 participants complied with CPAP use (a minimum of 4 hours/night for at least five nights/week) *Comparator*. Conservative management (avoidance of alcohol at bedtime and weight reduction)	*Number randomised*. Total: 27 (CPAP: 10, comparator: 17) *Number of withdrawals*. Total: 9 (CPAP: unclear, comparator: unclear) *Reasons for withdrawals*. Refused to attend follow-up visits due to relocation or other personal reason ($n = 5$). Four participants randomised to CM were put on CPAP ($n = 3$) or operated on ($n = 1$) due to a worsening of symptoms *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: 50 (41–60) / 51 (43–65) Sex: NR / NR / NR AHI: Not assessed / – / – ESS: Not assessed / – / – BMI: 31 (25–38) / 33 (26–41) BP: Not assessed / – / – ODI 4%: 31 (10–67) / 26 (11–96) Daytime somnolence (VAS): 31 (21–80) / 58 (8–90) Data are median (range) *Additional information*. Follow-up at 3 and 12 months: ODI 4%, ODI 10%, VAS for sleepiness, frequency and loudness of snoring questionnaire. Cognitive outcomes were also reported (see *Table 53*).

continued

Study details	Intervention	Participants
Marshall *et al.*, 2005[79] (related papers[327,328]) *Setting*. New Zealand *Design*. Crossover trial *Duration*. Two × 3 weeks (2-week washout period) *Inclusion criteria*. AHI 5–30, age ≥18 years; daytime symptoms of sleepiness/ESS ≥ 8, CPAP naïve, English-speaking	*CPAP*. Humidified CPAP (following manual titration overnight). Adherence (machine running time): 4.9 hours/night (range 0–8.4) *Comparator*. Humidified sham CPAP (pressure: < 1 cmH_2O). Adherence (machine running time): 4.9 hours/night (range 0–8.32)	*Number randomised*. Total: 31 *Number of withdrawals*. Total: 2 (CPAP: 1, comparator: 1) *Reasons for withdrawals*. Non-fatal MI during sham treatment ($n = 1$), and CPAP intolerant ($n = 1$) *Baseline characteristics* (completers only, $n = 29$)

	Total	**CPAP**	**Comparator**
Age range	26–67		
Sex	Male ($n = 22$), female ($n = 7$)		
AHI	22 (14.5)		
ESS	12.5 (SE 0.8)		
BMI	Not assessed		
BP	Not assessed		
MWT	20.9 (SE 2.5)		
SF-36			
Mental health	75 (SE 3)		
Bodily pain	73 (SE 4)		
Social functioning	79 (SE 4)		
Vitality	44 (SE 3)		
Role – emotional	78 (SE 7)		
Role – physical	63 (SE 8)		
Physical functioning	82 (SE 3)		
General health	74 (SE 3)		
HADS			
Anxiety	6.8 (SE 0.7)		
Depression	4.2 (SE 0.5)		
FOSQ			
Total	12.6 (SE 0.3)		
Activity	3.0 (SE 0.1)		
Social outcomes	3.2 (SE 0.1)		
Vigilance	3.0 (SE 0.1)		
General product	3.3 (SE 0.1)		

Additional information. Outcomes: ESS, FOSQ, SF-36, HADS (anxiety), HADS (depression), MWT and cognitive function (see *Table 53*).

DOI: 10.3310/hta13040

Study details	Intervention	Participants
McArdle and Douglas, 2001[95] *Setting*. UK *Design*. Crossover trial *Duration*. Two × 4 weeks. No washout phase described *Inclusion criteria*. Men and women with AHI> 15 and at least two symptoms of obstructive sleep apnoea *Exclusion criteria*. Shift workers, those with driving problems due to sleepiness, consumption of > 21 g alcohol/week, medication/ comorbidity likely to disturb sleep quality	*CPAP*. Adherence: NR *Comparator*. Oral placebo (lactose capsule)	*Number randomised*. Total: 23 *Number of withdrawals*. Total: 1 (CPAP: 1, comparator: 0) *Reasons for withdrawals*. Refused to continue with CPAP treatment *Baseline characteristics* *Additional information*. Outcomes: ESS; sleep efficiency.

	Total	CPAP	Comparator
Age	53 (SD 11)		
Sex	Male ($n = 20$), female ($n = 3$)		
AHI (median)	40 (IQR 25–65)		
ESS (median)	14 (IQR 10–17)		
BMI	31 (SD 5)		
BP	Not assessed		

continued

Study details	Intervention	Participants
Monasterio *et al.*, 2001[100] (related paper[329]) *Setting*. Spain. *Design*. Parallel group trial *Duration*. 24 weeks *Inclusion criteria*. Men and women with AHI 10–30 and absence of severe daytime sleepiness *Exclusion criteria*. Apnoea index > 20, hazardous jobs, notable cardiovascular disease and conditions that may affect cognitive or quality of life evaluation (severe neurological or psychiatric disorder, severe chronic disease or illiteracy)	*CPAP*. CPAP plus CM. Adherence: 4.8 hours/night (SD 2.2) at 6 months; at 6 months 64% of participants used CPAP for > 4 hours/night *Comparator*. CM: weight loss programme following home diet if BMI > 27, avoidance of sedatives and alcohol consumption, supine position during sleep and adequate hours of sleep every night	*Number randomised*. Total: 142 (CPAP: 77, comparator: 65) *Number of withdrawals*. Total: 17 (CPAP: 11, comparator: 7) *Reasons for withdrawals*. NR *Baseline characteristics* *Additional information*. Outcomes were measured at study entry and after 3 months and 6 months of treatment. Outcomes included symptom measures (SAHS symptom questionnaire), sleepiness (ESS, MSLT), quality of life (NHP, FOSQ) and cognitive function (see *Table 53*).

	Total	**CPAP**	**Comparator**
Age	54 (SD 9)	53 (SD 9)	54 (SD 9)
Sex (%)	Male (86%)	Male (81%)	Male (91%)
AHI	20 (SD 6)	20 (SD 6)	21 (SD 6)
ESS	12.6 (SD 4.6)	12.1 (SD 4.9)	13.2 (SD 4.3)
BMI	29 (SD 4)	29.4 (SD 3.7)	29.5 (SD 3.3)
BP			
SBP		126 (SD 17)	132 (SD 17)
DBP		81 (SD 12)	84 (SD 11)
FOSQ		101 (SD 18)	100 (SD 15)
NHP		21 (SD 20)	20 (SD 16)
MSLT (minutes)		10 (SD 5)	11 (SD 5)
SAHS-related symptoms		21 (SD 4)	21 (SD 3)

DOI: 10.3310/hta13040

Study details	Intervention	Participants
Montserrat *et al.*, 2001[86] *Setting*. Spain *Design*. Partial crossover trial *Duration*. 6 weeks *Notes*. CPAP group had 6 weeks study period using the intervention; sham CPAP group trialled 6 weeks on each intervention. 10-day washout period *Inclusion criteria*. Patients previously diagnosed with AHI > 10 and excessive daytime somnolence *Exclusion criteria*. Severe or unstable cardiovascular disease or hazardous job (professional driver or handling dangerous machinery)	*CPAP* (following overnight manual titration). Adherence: 4.25 hours/night *Comparator*. Sham CPAP All participants were encouraged to follow a diet and sleep regimen regardless of treatment group assigned	*Number randomised*. Total: 48 (CPAP: 24, comparator: 24) [baseline data for age, AHI and BMI ($n = 45$), other outcomes ($n = 46$)] *Number of withdrawals*. Total: 2 (first treatment period), 1 (crossover) [CPAP: 2 ($n = 1$ first treatment period, $n = 1$ crossover), comparator: 1) *Reasons for withdrawals*. NR *Baseline characteristics*

	Total	CPAP	Comparator
Age		55.65 (SD 9.41)	52.59 (SD 10.93)
Sex	NR	NR	NR
AHI		50.52 (SD 19.83)	57.14 (SD 21.14)
ESS		16.13 (SD 1.03)	16.86 (SD 1.20)
BMI		30.31 (SD 4.49)	33.73 (SD 6.62)
BP	Not assessed	–	–
SF-36			
PCS		46.53 (SD 1.92)	45.54 (SD 2.17)
MCS		48.21 (SD 2.06)	48.73 (SD 2.49)
Physical functioning		76.96 (SD 5.66)	78.18 (SD 4.80)
Role – physical		71.74 (SD 8.79)	78.41 (SD 8.11)
Bodily pain		75.26 (SD 5.26)	58.32 (SD 7.27)
General health		60.48 (SD 3.05)	61.55 (SD 5.61)
Vitality		56.52 (SD 5.93)	58.03 (SD 6.23)
Social functioning		82.61 (SD 3.91)	82.39 (SD 5.37)
Role – emotional		84.06 (SD 7.52)	75.76 (SD 8.55)
Mental health		71.83 (SD 3.93)	77.45 (SD 3.67)
FOSQ			
General productivity		19.18 (SD 1.06)	20.25 (SD 0.89)
Social		18.96 (SD 1.26)	18.00 (SD 1.66)
Activity level		16.71 (SD 0.81)	17.21 (SD 1.23)
Vigilance		13.66 (SD 1.16)	14.17 (SD 1.48)
Intimacy		16.40 (SD 1.57)	17.43 (SD 1.63)
Total score		84.45 (SD 4.63)	86.16 (SD 5.96)
SAHS-related symptoms		39.70 (SD 1.14)	38.86 (SD 1.14)

Additional information. Outcomes were measured on the last day of each treatment: ESS, SF-36, FOSQ.

continued

Study details	Intervention	Participants
Norman *et al.*, 2006[73] (related papers [116,302,330–335])	*CPAP*. Humidified CPAP (following manual titration) plus an oxygen concentrator that provided room air. Adherence: 6.7 hours/night (SE 1.2)	*Number randomised*. Total: 46 (CPAP: 18, sham CPAP: 15, oxygen: 13)
Setting. USA	*Comparator*. Sham CPAP (0–0.5 cmH_2O) following mock titration plus an oxygen concentrator that provided room air. Adherence: 6.0 hours/night (SE 2.4)	*Number of withdrawals*. No withdrawals reported
Design. Parallel group trial	*Supplemented oxygen* (3 l/m oxygen concentrator) plus sham CPAP. Adherence: 6.7 hours/night (SE 1.2)	*Reasons for withdrawals*. NA
Duration. 2 weeks		*Baseline characteristics*
Notes. At time of initial screening, CPAP group had a higher baseline SBP than sham CPAP group ($p = 0.042$). Participants whose BP was > 170/105 mmHg were excluded and re-started on BP medication		*Additional information*. Outcomes: BP (mean 24-hour ambulatory BP, daytime SBP and DBP, night-time SBP and DBP), AHI and various polysomnographic parameters. BP was taken every 15 minutes between 6 a.m. and 10 p.m. (daytime) and every 30 minutes between 10 p.m. and 6 a.m. (night-time) using a cuff. Related papers report psychological symptoms (Bardwell *et al.*, 2007[334]) and cognitive outcomes (Lim *et al.*, 2005[116]) (see *Table 53*).
Inclusion criteria. Men and women between 25 and 65 years within 100–170% of their ideal body weight, with AHI > 15		
Exclusion criteria. Major ongoing illness other than sleep apnoea and hypertension. Individuals who had had previous treatment with CPAP or undergone pharyngeal surgery for OSA were also excluded		

	Total	CPAP	Sham CPAP
Age		49.7 (SE 2.5)	49.3 (SE 2.7)
Sex		Male ($n = 15$), female ($n = 3$)	Male ($n = 13$), female ($n = 2$)
AHI		66.1 (SD 29.1)	53.9 (SD 29.8)
ESS		12.0 (SE 1.3)	12.0 (SE 1.7)
BMI		31.5 (SE 1.4)	29.9 (SE 1.3)
BP			
SBP		135.1 (SE 3.8)	122.5 (SE 3.3)
DBP		79.6 (SE 1.7)	75.6 (SE 2.5)
MAP		98.1 (SE 2.5)	91.2 (SE 2.5)

Study details	Intervention	Participants
Olson *et al.*, 2002[107] (unpublished data from Giles *et al.*, 2006) *Setting*. NR *Design*. Crossover trial *Duration*. Two × 6 weeks (2-week washout period) *Inclusion criteria*. AHI > 15, or apnoea index > 5, or AHI > 5 and arousal index > 15 *Exclusion criteria*. Poor dentition, temporomandibular joint pain, or previous treatment with oral appliances or CPAP	*CPAP*. Adherence: NR *Comparator*. Oral appliance	*Number randomised*. Total: unclear, 24 participants included *Number of withdrawals*. NR *Reasons for withdrawals*. NA *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: NR Sex: NR AHI (range): 8.1–36.9 ESS: NR BMI: NR BP: NR *Additional information*. Outcomes: total sleep time, sleep efficiency, % REM sleep, AHI, arousal index, SAQLI.

continued

Study details	Intervention	Participants
Pepperell *et al.*, 2002[87] (related papers[336,337]) *Setting*. UK *Design*. Parallel group trial *Duration*. 4 weeks *Notes*. A specialist nurse helped all participants with advice by telephone, and masks were further adjusted if necessary *Inclusion criteria*. Men with > 10 episodes/hour of > 4% drop in SaO_2 and ESS ≥ 10 *Exclusion criteria*. Required urgent CPAP therapy, were about to lose their job as a result of sleepiness, declined to participate, preferred alternative treatment, unable to give informed consent	*CPAP* (following overnight titration using an automated pressure setting device). Adherence: 4.5 hours/night (SD 2.4) *Comparator*. Subtherapeutic CPAP (pressure < 1 cmH_2O). Adherence: 4.9 hours/night (SD 204)	*Number randomised*. Total: 118 (CPAP: 59, comparator: 59) *Number of withdrawals*. Total: 14 (CPAP: 6, comparator: 8) *Reasons for withdrawals*. CPAP: discontinued CPAP ($n = 2$), did not attend post-treatment BP ($n = 4$); Sham CPAP: discontinued CPAP ($n = 2$), did not attend post-treatment BP ($n = 6$). In addition, post-BP recordings were inadequate in 10 participants ($n = 5$ per treatment arm) *Baseline characteristics* **Additional information**. 22 participants (11 in each group) were taking medication for hypertension. Outcomes: BP, withdrawal, ESS, AHI. BP was recorded every 30 minutes for a 24-hour period, and measured with a cuff.

	Total	**CPAP**	**Comparator**
Age		50.1 (SD 10.4)	51.0 (SD 9.8)
Sex	Male ($n = 118$)		
AHI	Not assessed		
ESS		16.3 (SD 3.3)	16.0 (SD 3.1)
BMI		34.6 (SD 8.5)	35.3 (SD 6.0)
BP			
SBP		132.5 (SD 15.3)	134.9 (SD 18.7)
DBP		85.1 (SD 8.7)	85.1 (SD 8.9)
24-Hour mean BP		101.0 (SD 9.8)	101.7 (SD 10.8)
Sleep period BP		93.7 (SE 1.6)	96.2 (SE 1.6)
Wake period BP		104.3 (SE 1.3)	104.2 (SE 1.4)

Study details	Intervention	Participants
Randerath *et al.*, 2002[105] (related paper[338]) *Setting*. Germany *Design*. Crossover trial *Duration*. Two × 6 weeks *Inclusion criteria*. Patients with AHI 5–30 and clinical symptoms of OSAS *Exclusion criteria*. AHI > 30, temporomandibular joint disorders, bruxism, participants with gaps in their teeth preventing fitting of device	*CPAP*. Adherence (self-reported): > 8 hours/night, 9%; 6–7 hours/night, 27%; 4–5 hours/night, 64%; 2–3 hours/night, 0%. All participants used CPAP on at least five nights/week *Comparator*. Oral appliance (two thin thermoplastic plates, worn on the upper and lower jaws connected by two adjustable telescopic guide rods). The maximum forward protrusion of the mandible was measured and this amount reduced to about two-thirds before mounting the casts. Adherence (self-reported): > 8 hours/night, 33%; 6–7 hours/night, 53%; 4–5 hours/night, 7%; 2–3 hours/night, 7%. All participants used OA on at least five nights/week	*Number randomised*. Total: 20 *Number of withdrawals*. No dropouts reported *Reasons for withdrawals*. NA *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: 56.5 (SD 10.2) Sex: Male (*n* = 16), female (*n* = 4) AHI: 17.5 (SD 7.7) ESS: Not assessed BMI: 31.2 (SD 6.4) BP: Not assessed *Additional information*. Outcomes: AHI; snoring (epochs/hour); SaO_2 (%); TST (minutes); wake after sleep onset; sleep stages 1, 2, 3, 4; REM sleep; arousals/hour; respiration-induced arousals per hour of TST.

continued

Study details	Intervention	Participants
Redline *et al.*, 1998[59] *Setting*. USA *Design*. Parallel group trial *Duration*. 8–16 weeks *Inclusion criteria*. Adults, aged 25–65 years, with mild to moderate sleep disordered breathing (RDI 5–30) without subjective pathological sleepiness *Exclusion criteria*. Any severe or unstable medical disease documented in previous 3 months, neurological disease, alcohol or drug abuse, regular use of medications that impair sensorium and < 8 years of education	*CPAP*. CPAP plus CM (advice on sleep, posture and sleep hygiene. Weight reduction and counselling was provided to patients with a BMI > 29 kg/m^2 and nasal steroid spray for those with nasal congestion). Adherence (machine usage): 44% (SD 34) of the time subjects were estimated to be asleep (3.1 hours) *Comparator*. Conservative treatment. Control patients were also given a supply of nasal dilators. Use of mechanical nasal dilators: 82% (SD 28) of intervention nights	*Number randomised*. Total: 111 (CPAP: 59, comparator: 52) *Number of withdrawals*. Total: 14 (CPAP: 8, comparator: 6) *Reasons for withdrawals*. CPAP: three withdrew due to problems in using CPAP and five due to an inability to schedule all-day testing battery; Comparator: all withdrew due to an inability to schedule all-day testing battery *Baseline characteristics* (presented for completers only, *n* = 97)

	Total	CPAP	Comparator
Age		48.1 (SD 9.2)	49.2 (SD 10.5).
Sex		Male (*n* = 30), female (*n* = 21)	Male (*n* = 20), female (*n* = 26)
AHI	Not assessed	–	–
ESS		10.4 (SD 4.3)	10.6 (SD 5.6)
BMI		33.4 (SD 6.9)	32.0 (SD 8.5)
BP	Not assessed	–	–
RDI		14.6 (SD 9.8)	11.8 (SD 9.6)
MSLT (minutes)		9.9 (SD 4.8)	10.3 (SD 5.0)
POMS			
Fatigue score		44.2 (SD 8.2)	41.8 (SD 7.6)
SF-36			
Fatigue/energy		51.7 (SD 19.8)	58.3 (SD 19.0)
General health perception		66.4 (SD 18.2)	69.8 (SD 19.5)
Social role functioning		88.4 (SD 18.3)	91.4 (SD 14.0)
Role limitations – physical		70.6 (SD 34.5)	88.1 (SD 22.5)
Role limitation – emotional		85.6 (SD 26.9)	82.8 (SD 31.1)
PANAS			
Positive affect		32.9 (SD 7.3)	32.3 (SD 6.8)
Negative affect		16.3 (SD 5.4)	16.0 (SD 6.0)

Additional information. Polysomnographic parameters and daytime test battery: mood (POMS, PANAS, well-being and functional status (SF-36) and objective measure of sleepiness (MSLT). Participants were evaluated at baseline and at 8–16 weeks, and after at least 2 weeks following any intercurrent illness. Change on these measures was used to calculate an overall treatment response score. ESS was also assessed. Three participants were re-tested after the 16-week period (two at 17 weeks and 1 at 19 weeks).

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Study details	Intervention	Participants
Robinson et *al.*, 2006[68] (related paper[339]) *Setting*. UK *Design*. Crossover trial *Duration*. Two × 4 weeks (2-week washout period) *Inclusion criteria*. Adults with moderate to severe OSA (without hypersomnolence) and hypertension. Hypertension was defined as BP > 140/90mmHg, or currently using hypertensive medication *Exclusion criteria*. Respiratory failure	*CPAP* (following titration using an automated pressure device). Adherence (mean machine usage): 5.2 hours/night (SD 2.1) *Comparator*. Sham CPAP (pressure < 1 cmH_2O). Adherence (mean machine usage): 4.3 hours/night (SD 2.4)	*Number randomised*. Total: 35 *Number of withdrawals*. Total: 3 (CPAP: 3, comparator: 0) *Reasons for withdrawals*. CPAP arm: two before completing first month's treatment period (one due to intolerance of BP cuff and one due to inadequate BP data), and one during the second treatment period due to intolerance of BP cuff *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: 54 (SD 8) Sex: Male ($n = 31$), female ($n = 4$) AHI: Not assessed ESS (median): 5.3 (IQR 3.0–7.0) BMI: 33.2 (SD 5.3) BP 24-hour BP (mmHg): NR / 103.4 (SD 11.6) / 105.1 (SD 12.1) 24-hour SBP: 140.3 (SD 16.1) / 143.0 (SD 17.33) 24-hour DBP: 85.3 (SD 11.2) / 86.7 (SD 11.1) Wake BP: 106.1 (SD 13.6) / 108.8 (SD 13.0) Sleep BP: 96.0 (SD 11.5) / 98.0 (SD 14.8) Osler test [minutes (median)]: 40 (IQR 40–40) Dips in SaO_2 of > 4%/hour sleep (median): 28.1(IQR 18.0–38.0) *Additional information*. 77% (27) of participants were receiving medication for hypertension; these participants were instructed not to change their antihypertensive medication during the study period. Outcomes: oxygen saturation, ESS and 24-hour BP. Outcomes were assessed before and after each treatment period. BP was measured every 30 minutes over 24 hours using an arm cuff.

continued

Study details	Intervention	Participants
Skinner et *al*., 2004[60] *Setting*. New Zealand *Design*. Crossover trial *Duration*. Two × 4 weeks (1-week washout period) *Inclusion criteria*. Men and women with OSA (AHI 10–60 and symptoms of daytime somnolence) *Exclusion criteria*. History of cardiovascular, neurological and/or psychological disorders affecting sleep; known cervical, shoulder or thoracic wall abnormalities and/or chronic pain; or previous treatment for OSA	*CPAP* (the pressure was set following 3–5 nights on an automated titrating device). Adherence (machine recorded): 4.7 hours/night (SD 2.6) *Comparator*. Shoulder–head elevation pillow (SHEP): designed to keep the patient in an upright posture (60°) during sleep. Adherence (self-reported): 6.3 hours/night (SD 1.6)	*Number randomised*. Total: 14 *Number of withdrawals*. Total: 1 (CPAP: 1, comparator: 0) *Reasons for withdrawals*. Declined to use portable sleep monitor at end of CPAP treatment phase *Baseline characteristics* *Additional information*. Outcomes: ESS, AHI, FOSQ, SF-36 and Scottish SHS were assessed at study entry and at the end of each treatment period. In addition, adverse events were assessed using a questionnaire at the end of each treatment period; a questionnaire comprising 19 adverse events most likely to be associated with SHEP was administered and a similar questionnaire was completed after CPAP.

	Total	**CPAP**	**Comparator**
Age	54 [SD 10 (range 39–69)]		
Sex	Male ($n = 12$), female ($n = 2$)		
AHI	27 (SD 12)		
ESS	11.9 (SD 4.6)		
BMI	34 (SD 7)		
BP	Not assessed		
SHS (%)	53.6 (SD 13.7)		
SF-36			
Physical score	42.6 (SD 11.3)		
Mental score	47.9 (SD 12.3)		
FOSQ	12.1 (SD 1.9)		

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Study details	Intervention	Participants
Skinner et *al*., 2004[61] *Setting*. New Zealand *Design*. Crossover trial *Duration*. Two × 4 weeks (no report of washout period) *Inclusion criteria*. Men and women with AHI 10–60 and mild to moderate obstructive sleep apnoea *Exclusion criteria*. History of cardiovascular, neurological or psychological disorders affecting sleep, known cervical or temporomandibular joint dysfunction and/or pain	*CPAP* (the pressure was set following 3–5 nights on an automated titrating device). Adherence: 68% (SD 24%) of available study nights, mean nightly duration 4.4 hours (SD1.2) *Comparator*. Cervicomandibular collar (designed to retain head in natural head position and prevent jaw opening during sleep). Adherence: 89% (SD 23%) of total available study nights, mean nightly duration 5.2 hours (SD 1.2)	*Number randomised*. Total: 10 *Number of withdrawals*. None *Reasons for withdrawals*. NA *Baseline characteristics* *Additional information*. Outcomes: sleep parameters, ESS, SF-36, FOSQ and SHS were assessed before treatment and after each treatment period. Adverse effects of treatment were also assessed at the end of each treatment period (self-reported diary and questionnaire). Mean scores were annotated from responses to 19 self-reported questions (score 0–3). Overall benefit of each treatment was assessed at the end of the study.

	Total	**CPAP**	**Comparator**
Age	48.6 (SD 14.8).		
Sex	Male ($n = 8$), female ($n = 2$)		
AHI	29.4 (SD 13.4)		
ESS	13.2 (SD 4.9)		
BMI	34.1 (SD 5.6)		
BP	Not assessed		
SF-36			
Physical score	45.3 (SD 10.4)		
Mental score	43.8 (SD 13.1)		
FOSQ	12.2 (SD 3.1)		
SHS	59.7 (SD 11.9)		

continued

Study details	Intervention	Participants
Spicuzza et *al*., 2006[66] *Setting*. Italy *Design*. Parallel group trial *Duration*. 4 weeks *Inclusion criteria*. Men and women with moderate to severe obstructive sleep apnoea *Exclusion criteria*. Presence of hypertension and/or other cardiovascular diseases, diabetes, thyroid disorders, chronic obstructive/restrictive lung diseases or respiratory failure, and smokers	*CPAP* (following overnight titration). Adherence (machine usage): 6.0 hours (SD 1.1) *Comparator*. Sham CPAP (pressure 1–2 cmH_2O). Adherence (machine usage): 6.5 hours (SD 2.4)	*Number randomised*. Total: 25 (CPAP: 15, comparator: 10) *Number of withdrawals*. The authors do not report withdrawals *Reasons for withdrawals*. NA *Baseline characteristics* *Additional information*. Outcomes: AHI and ventilatory control measures. Outcomes were assessed at baseline and at the end of the study.

	Total	**CPAP**	**Comparator**
Age		55.9 (SD 9.4)	55.1 (SD 9.3)
Sex	Male ($n = 20$), female ($n = 5$)		
AHI		55.3 (SD 11.9)	59.2 (SD 17.3)
ESS	Not assessed		
BMI		31.1 (SD 4.2)	33.5 (SD 5.5)
BP			
SBP		145.4 (SD 4.7)	149.5 (SD 7.2)
DBP		87.9 (SD 4.6)	85.0 (SD 3.8)

DOI: 10.3310/hta13040

Study details	Intervention	Participants
Tan et *al.*, 2002[106] (related papers[340–342]) *Setting*. UK *Design*. Crossover trial *Duration*. Two × 8 weeks (2-week washout) *Notes*. Baseline: O_2 desaturation: 7.1 ± 2.7. Arousals/hour: 19.3 ± 9.6 *Inclusion criteria*. Men and women with AHI < 50, with adequate dentition and periodontal status for support and retention of oral appliance *Exclusion criteria*. Temporomandibular joint dysfunction, medical contraindications, significant heart disease, co-existent chronic obstructive pulmonary disease, regular hypnotic use, epilepsy, arterial oxygen saturation < 60% during initial sleep study, ability to give informed consent	*CPAP*. Two different models of nCPAP compressor were used. Nasal corticosteroid sprays were prescribed to relieve nasal congestion where necessary. Adherence: NR *Comparator*. Oral appliance. A soft one-piece MAS was used for the first 10 participants. A two part semi-rigid MAS was used for the remainder of the study; this appliance permitted some mandibular opening during sleep. Adherence: NR	*Number randomised*. Total: 24 *Number of withdrawals*. Total: 3 (CPAP: 2, comparator: 1) *Reasons for withdrawals*. Two participants did not tolerate nCPAP, one participant did not tolerate MAS *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: 50.9 (SD 10.1) Sex: Male (*n* = 20), female (*n* = 4) AHI: 22.2 (SD 9.6) ESS: 13.4 (4.6) BMI: 31.9 (SD 6.8) BP: Not assessed *Additional information*. Outcomes were measured on the last day of each treatment: ESS, AHI, ODI, REM %, sleep efficacy, preference.

continued

Study details	Intervention	Participants
West *et al.*, personal communication[151] (unpublished data supplied by the author) (related papers[67]) *Setting*. UK *Design*. Parallel group trial *Duration*. 12 weeks *Notes*. One participant in the active treatment group received a defective machine which delivered minimal pressure and was analysed with sham CPAP group *Inclusion criteria*. Men with OSA (> 10 SaO_2 dips of greater than 4% per hour) and type 2 diabetes *Exclusion criteria*. Urgent CPAP required or unstable diabetes requiring an escalation in treatment. Primary care physicians were requested not to change participants' medications, unless essential	*CPAP*. CPAP (autotitrating). Adherence (machine usage): 3.6 hours/night (SD 2.8) *Comparator*. Sham CPAP (pressure < 1 cmH_2O and > 0 cmH_2O). Adherence (machine usage): 3.3 hours/night (SD 3.0)	*Number randomised*. Total: 42 (CPAP: 20, comparator: 22) *Number of withdrawals*. Total: 2 (CPAP: 2, comparator: 0) *Reasons for withdrawals*. Unrelated surgery ($n = 1$), unwilling to continue using CPAP ($n = 1$) *Baseline characteristics* **Total** / **CPAP** / **Comparator** Age: – / 57.8 (SD 10.4) / 54.5 (SD 9.4) Sex: – / Male ($n = 21$) / Male ($n = 21$) AHI: Not assessed / – / – ESS: – / 14.7 (SD 3.5) / 13.5 (SD 3.5) BMI: – / 36.6 (SD 4.9) / 36.8 (SD 4.6) BP: Not assessed / – / – > 4% SaO_2 dips/hour: – / 33.1 (SD 21.6) / 39.1 (SD 24.8) MWT (minutes): – / 21.9 (SD 12.8) / 32 (SD 10.8) SAQLI: – / 4.3 (SD 1.1) / 4.4 (SD 0.9) *Additional information*. Outcomes: ESS, MWT (Osler), SAQLI, change in HbA1c, insulin sensitivity and adverse events. Outcomes were assessed at baseline and at end of treatment.

AHI, apnoea–hypopnoea index; BDI, Beck Depression Inventory; BMI, body mass index; BP, blood pressure; BVRT-R, Benton Visual Retention Test-Revised; DBP, diastolic blood pressure; ESS, Epworth Sleepiness Scale; FOSQ, Functional Outcomes of Sleep Questionnaire; GHQ, General Health Questionnaire; GRISS, Golombok Rust Inventory of Sexual Satisfaction; HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; MAP, mean arterial pressure; MAS, mandibular advancement splint; MCS, mental component summary; MOS, Medical Outcomes Survey; MSLT; Multiple Sleep Latency Test; MWT, Maintenance of Wakefulness Test; nCPAP, nasal continuous positive airway pressure; NA, not applicable; NART, National Adult Reading Test; NHP, Nottingham Health Profile; NR, not reported; OA, oral appliance; ODI, oxygen desaturation index; OSA, obstructive sleep apnoea; OSAHS, obstructive sleep apnoea–hypopnoea syndrome; PANAS, Positive and Negative Affect Scale; PASAT, Paced Auditory Serial Addition Test; PCS, physical component summary; POMS, Profile of Mood State; PSG, polysomnography; PVT, Psychomotor Vigilance Test; QoL, quality of life; RDI, respiratory disturbance index; REM, rapid eye movement; RVIPT, Rapid Visual Information Processing Test; SAHS, sleep apnoea-hypopnoea syndrome; SAQLI, sleep apnoea quality of life index; SBP, systolic blood pressure; SDMT, Symbol Digit Modalities Test; SEM, standard error of the mean; SF-36, Medical Outcomes Survey Short Form; SHS, Sleep Health Symptom questionnaire; TMT, Trail Making Task; TST, total sleep time; UMACL, University of Wales Institute of Science and Technology Mood Adjective Checklist; UPP, uvulopalatal pharyngoplasty; VAS, visual analogue scale; WAIS, Wechsler Adult Intelligence Scale; WMS, Wechsler Memory Scale.

Appendix 6

Economic evaluation data extraction

	Ayas *et al.*, 2006[122]	Mar *et al.*, 2003[123]
Type of economic evaluation	Cost–utility analysis	Cost–utility analysis
Currency used, year	US$, 2003	Euros (converted from Spanish pesetas), 2000
Study design	Markov model using effectiveness estimates from one study and adjusting these for the impact of RTAs, based on a random-effects meta-analysis of eight before and after studies	Semi-Markov model using effectiveness estimates from a before and after study
Perspective	Third-party payer. Societal perspective	Health-care perspective
Participants	Data from 99 patients with moderate to severe OSAHS were used to establish the proportion of patients in each sex/age group	Based on a cohort of 5000 patients with moderate to severe OSAS to establish the proportion of patients in each sex/age group
Setting, country of study	US	Spain
Intervention group	CPAP	nCPAP
Control group	No CPAP	No CPAP
Resources used	Health care; costs of diagnosis and treatment of OSAHS, costs attributable to motor vehicle accidents and maintenance costs of the devices and costs of medical follow-up	Health care; costs of investigation, diagnosis and treatment of OSAS, costs attributable to CVE morbidity and maintenance costs of the devices and costs of medical follow-up
Source of effectiveness data	Base case used single study (Chakravorty *et al.*, 2002[97]). For patients who had an RTA, utility estimates were adjusted using the FCI	Survey of OSAS patients before the initiation of CPAP and 3 months post CPAP
Length of follow-up	5 years	Results were extrapolated to 5 years and over the lifespan of the patient
Source of resource use data	A primary referral centre and national data. Not all sources of resource use data were reported	Single sleep centre located in a hospital
Source of unit cost data	The cost of CPAP was obtained from Medicare fee schedules. Costs of RTAs were obtained from the National Highway Traffic Safety Administration	The device cost was the price of the CPAP S VI Plus model. Regional hospital costs were used for the health-care costs
Link between cost and effectiveness data	Cost and effectiveness data were not linked directly	Cost and effectiveness data were not linked directly
Clinical outcomes measured and methods of valuation used	The base case used a single study (Chakravorty *et al.*, 2002[97]) to obtain the relative treatment effect of CPAP vs do nothing. The utilities were elicited using patient preferences and were valued using the standard gamble. For the secondary analysis, EQ-5D estimates were used based on societal preferences (Jenkinson *et al.*, 1998[349] and Mar *et al.*, 2003[123]). For patients who had an RTA, utility estimates were adjusted using rating scale preference weights obtained from the FCI (Graham *et al.*, 1997[143])	Utility values were obtained using the EQ-5D. The health states for 46 patients were elicited and societal preferences were applied using the time trade-off technique No data were available on quality of life in OSAS patients with stroke and CHD; therefore this was modelled by assigning quality adjustment factors of 0.8 and 0.9 respectively to these health states, based on an estimate in the published literature

ResMed, 2007[120]	**Chilcott *et al.*, 2000**[44]
Cost–utility analysis and cost-effectiveness analysis	Cost–utility analysis
£ sterling, 2005	£ sterling, no report of financial year of costs
Markov model using effectiveness estimates from a before and after study	Review synthesis. Effectiveness estimates based on results from two studies. Estimates based on before and after data
Health-care perspective	Health-care perspective
Based on a simulated cohort of 2000 patients with moderate to severe OSAHS	Patients referred to a sleep clinic. Typically middle-age group (45+ years old)
UK	UK
CPAP (fixed)	nCPAP
CPAP (auto); no CPAP	Dental devices; no CPAP
Health care; costs of investigation, titration, diagnosis and treatment of OSAHS, costs attributable to CVE and RTA morbidity and maintenance costs of the devices and costs of medical follow-up	Health care; costs of investigation, diagnosis and treatment of OSAHS and maintenance costs of the devices and costs of medical follow-up
Base case used Mar *et al.*, 2003[123] results	Three studies (Waterhouse *et al.*, 2000[150,151] and Jenkinson *et al.*, 1999[77]) using before and after (up to 4 weeks) initiation of CPAP Jenkinson, 1999[77]
14 years. Used results of Marin *et al.*, 2005[130] and Mar *et al.*, 2003[123] to calculate annual incidence of fatal and non-fatal CVE and cerebrovascular events in CPAP-treated and untreated patients with severe OSAHS (AHI $\geq$30) to 12 years and extrapolated these results over another 2 years. Used the Mar *et al.*, 2003[123] results to estimate the ratio of CHD and stroke in patients with untreated severe OSAHS as 1.185 and 1.353 respectively. Estimated the ratio of developing CHD to stroke as 1 : 1.13. Estimated ratio of CHD to stroke in treated patients as 1 : 1. Using these estimates, ResMed calculated the annual risk of CVE and stroke	5 years
19 clinicians	Published literature, administrative database and clinical opinion
List prices, published literature, government statistics	Published literature, administrative database and clinical opinion
Cost and effectiveness data were not linked directly	Cost and effectiveness data were not linked directly
Utility values were obtained from the EQ-5D using the Mar *et al.*, 2003[123] results. The health states for 46 patients were elicited and societal preferences were applied using the time trade-off technique	Utility values generated via SF-36 survey, using the Brazier *et al.*, 1998[148] algorithm. Societal preferences were applied using the TTO and/or standard gamble
No data were available on quality of life in OSAHS patients with stroke and CHD; therefore this was modelled by assigning quality adjustment factors of 0.8 and 0.9 respectively to these health states, based on an estimate in the published literature. To estimate utility associated with a non-fatal RTA, ResMed took the average utility for OSAHS and a non-fatal CVE in treated and untreated patients	

continued

	Ayas *et al.*, 2006[122]	Mar *et al.*, 2003[123]
Outcome results/adverse events	CPAP utility = 0.55, no CPAP utility = 0.32. Treatment with CPAP reduced the rate of RTAs sevenfold (OR of RTA with CPAP vs no CPAP = 0.15, 95% CI 0.10–0.22. No consideration was given to the effect of adverse events due to CPAP The incremental QALY for CPAP was 0.75 QALYs, i.e. 2.22 QALYs (95% CI 0.86–3.89) vs 1.47 QALYs (95% CI 0.28–3.08)	Among the patients who were diagnosed with moderate to severe OSAS, there was a 10% dropout rate from treatment in the first year. In the analysis this impacted on costs but was not included in terms of outcomes The mean EQ-5D score was 0.738 (0.646–0.829) before beginning nCPAP. The mean gain 3 months later was 0.073 (0.015–0.131) QALYs were 3.73 at 5 years and 14.38 over the lifespan in the nCPAP arm, and 3.39 at 5 years and 12.90 over the lifespan in the no CPAP arm
Cost data handled appropriately	Some unit costs and resource use were reported separately	Unit costs and resource use were reported separately
Cost results	From the third-party payer perspective, the incremental cost for CPAP was $2519, i.e. $4177 (95% CI $2804–$6057) vs $1659 (95% CI $283–$3936) From the societal perspective, CPAP was more costly, i.e. $7123 (95% CI $4324–$11,906) vs $6887 (95% CI $313–$14,843)	Costs were €2719 at 5 years and €7902 over the lifespan in the nCPAP arm, and €55 at 5 years and €591 over the lifespan in the no CPAP arm
Subgroup analysis	Not undertaken	Not undertaken
Modelling summary	Third-party payer perspective: CPAP more costly and more effective than no CPAP. ICER = $3354 per QALY (95% CI $1062–$9715) Societal perspective: CPAP more costly and more effective. ICER = $314 (95% CI cost saving to $6114) From the third-party payer perspective and the societal perspective, 100% of simulations favoured the cost-effectiveness of CPAP, assuming the threshold value is $50,000 per QALY	nCPAP was estimated to be more costly and more effective than no CPAP. The ICER for CPAP was €7861 per QALY over a 5-year time horizon and €4938 per QALY for the lifetime horizon
Direction of result with appropriate quadrant location	North-east quadrant	North-east quadrant
Statistical analysis for patient-level stochastic data	Not undertaken	Not undertaken
Appropriateness of statistical analysis	Not undertaken	Not undertaken
Uncertainty around cost-effectiveness expressed and appropriateness of method of dealing with uncertainty around this	Yes	No

ResMed, 2007[120]	**Chilcott *et al.*, 2000**[44]
The utility associated with untreated OSAHS is 0.738 and with treated OSAHS is 0.811. The utility of non-fatal stroke in untreated OSAHS patients was 0.590 and in treated patients was 0.649. The utility of non-fatal CVE in untreated OSAHS patients was 0.664 and in treated patients was 0.730. The utility of non-fatal RTA in untreated OSAHS patients was 0.701 and was 0.771 in treated patients At 14 years the estimated QALY gains were 7.22 (6.85–7.62) for no treatment, 8.19 (7.79–8.69) for CPAP (fixed) and 8.32 (7.97–8.81) for CPAP (auto) It was estimated that 79% of patients would continue to use CPAP (fixed) and 84% CPAP (auto) after the first year of treatment and that following this there would be no further loss to compliance	The gain in HRQoL as measured by the SF-36 single index was 0.12 QALYs (95% CI 0.09–0.16) over 1 year
Unit costs and resource use were reported separately	Unit costs and resource use were reported separately
Costs were estimated over 14 years. From the NHS perspective the cost of no treatment was £10,645 (95% CI £7912–£14,177), and £9086 (95% CI £6851–£11,117) for CPAP (fixed) and £8622 (95% CI £6712–£10,947) for CPAP (auto)	Total recurring annual cost of £250 per patient on long-term CPAP therapy
Not undertaken	Not undertaken
CPAP was estimated to be more costly and more effective than no CPAP	Authors undertook a review of the evidence. nCPAP was estimated to be more costly and more effective than no CPAP. The ICER for CPAP was £8300 at 1 year and £3200 at year 5. Small differences in clinical effectiveness and cost were found when comparing nCPAP with dental devices but these were not explicitly quantified
South-east quadrant	North-east quadrant
Not undertaken	Not undertaken
Yes	Not undertaken
Yes	No

continued

	Ayas *et al.*, 2006[122]	Mar *et al.*, 2003[123]
Sensitivity analysis and appropriateness	Sensitivity analysis was undertaken on utility values, discount rate, compliance rate, time horizon, scaling factor for converting lifetime costs to the 5-year model time frame and reduction in rates of RTAs according to the 95% confidence limits determined in the meta-analysis. Probabilistic sensitivity analysis was also undertaken. The analyses were appropriate	A series of univariate and multivariate sensitivity analyses were conducted by age, sex, relative risk of stroke (untreated), different utility estimates, benefit of nCPAP on blood pressure, dropout rate, cost of nCPAP and discount rate/s It was found that the estimation of the ICER was sensitive to the time horizon
Modelling inputs and appropriate techniques	Markov model using second-order Monte Carlo simulations to generate 1000 incremental cost and effectiveness pairs was appropriate	Yes
Authors' conclusions	Treatment for OSAHS with CPAP has a cost-effectiveness in line with that of other commonly funded treatments such as antihypertensive drugs	Treatment for OSAS with nCPAP has a cost-effectiveness in line with that of other commonly funded treatments such antihypertensive drugs. The key clinical benefit of nCPAP is improvement in the quality of life of patients with OSAS

AHI, apnoea–hypopnoea index; CHD, coronary heart disease; CI, confidence interval; CVE, cardiovascular event; EQ-5D, EuroQol-5 Dimensions; FCI, Functional Capacity Index; HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio; nCPAP, nasal continuous positive airway pressure; OSAHS, obstructive sleep apnoea–hypopnoea syndrome; OSAS, obstructive sleep apnoea syndrome; QALY, quality-adjusted life-year; RTA, road traffic accident; SF-36, Medical Outcomes Survey Short Form; TTO, time trade-off.

ResMed, 2007[120]	**Chilcott *et al.*, 2000**[44]
A series of univariate and multivariate sensitivity analyses were conducted as reported in *Table 20*	A series of univariate sensitivity analyses were conducted on impact of analytical time horizon, costs of investigation for nCPAP, long-term costs of maintenance, follow-up and other health-care resource usage, long-term impact of gross annual health-care costs, potential impact of improved mortality from use of nCPAP treatment, impact of uncertainty in morbidity benefits from nCPAP therapy and discount rate
Yes	Not undertaken
CPAP (fixed) dominates no treatment and CPAP (auto) dominates no treatment after a minimum of 2 years' treatment. Based on current evidence, use of CPAP (auto) is associated with marginally better outcomes and no additional cost compared with CPAP (fixed)	Treatment for OSAHS with CPAP has a cost-effectiveness in line with that of other commonly funded treatments. The incremental cost-effectiveness of nCPAP over dental devices was likely to be highly uncertain

Appendix 7
Review of utility data

The approach recommended by the National Institute for Health and Clinical Excellence (NICE) and other bodies, when undertaking cost-effectiveness analyses, is to measure the incremental cost per quality-adjusted life-year (QALY) gained of the intervention under study versus an appropriate comparator. QALYs are calculated by multiplying the amount of time spent in a health outcome by the preference value or utility attached to that outcome. This latter quality adjustment is based on a set of values or weights for each possible health state that reflect the relative desirability of that health state as judged by individuals or society. In the case of cost-effectiveness studies of CPAP, utility values are required that quantify the impact on HRQoL of experiencing sleep apnoea and also the influence of receiving CPAP therapy on HRQoL. This report reviews the clinical and cost-effectiveness literature on CPAP and sleep apnoea in order to identify possible utility values for the economic analysis.

A search was undertaken of the MEDLINE database in order to identify relevant literature. The search strategy identified 160 abstracts. Abstracts were screened by one reviewer (SvH) and copies of those that were considered relevant were obtained. Four papers were identified as containing potentially relevant HRQoL/utility data. These are appraised below with respect to their utility data.

Tousignant *et al.*, 1994[124]

This study assessed the impact of nCPAP therapy on the quality of life of 19 patients with sleep apnoea.

Patients attending a hospital sleep clinic (mean age 57 years, SD 10), who had been receiving nCPAP treatment for an average of 9 months, completed a standard gamble exercise. The health states valued were receiving treatment for nCPAP, pre-treatment, full health and immediate death. To assess the reliability of the results patients completed the exercise on two occasions 2–3 weeks apart. The mean utility score for the pre-treatment health state was 0.63 (0.29) and the mean utility score for the nCPAP treatment health state was 0.87 (0.17). The intraclass correlation coefficients for the retest data were above 0.7 for both the treatment health state and the pre-treatment health state.

Comments
As all the patients were currently receiving nCPAP therapy, the valuation of their pre-treatment health state was done retrospectively. Given this, it is difficult to ascertain the extent to which the difference in pre-treatment and treatment utility scores is a real difference, reflecting the impact of nCPAP treatment and the extent to which it demonstrates some sort of measurement error due to bias in recall.

Jenkinson *et al.*, 1997[152]

This study compared the performance of three commonly used quality of life measures [SF-36, EQ-5D and the Functional Limitations Profile (FLP)] in patients with sleep apnoea before and after nCPAP therapy and compared the data with those for a normal population.

One hundred and eight male patients (mean age 50 years, SD 10) with a mean baseline ESS of 14 (SD 5) attending a sleep clinic for a therapeutic assessment of nCPAP therapy completed the three HRQoL measures before and 5 weeks after commencing treatment.

At baseline the mean EQ-5D index score was 0.79 (0.21) and after treatment the score had increased to 0.84 (0.25), which was not statistically significant and indicates only minor benefits from nCPAP therapy. In contrast, both SF-36 and the FLP showed statistically significant improvements in scores on the majority of their dimensions. The authors suggest that the failure of EQ-5D to show a similar magnitude of change to the other measures may be because it does not contain questions that specifically address areas of health thought to be affected by sleep apnoea such as sleep, tiredness, energy and social functioning. With this in mind, they caution the use of measures such as EQ-5D when evaluating therapy in this area.

Comments
Unlike the SF-36 and FLP, EQ-5D does not contain dimensions relating to sleep and/or vitality,

which undoubtedly are of importance in this area; however, its usual activities dimension does arguably measure aspects of social functioning. If the intention were to measure change in sleepiness or tiredness then EQ-5D would not be the first choice. However, if the intention is to measure change in overall HRQoL then EQ-5D is a well-validated, globally used measure that, unlike the other two measures, generates a score that is weighted by the values of the general population. The EQ-5D index score is the main output of interest to those who require a score for use in decisions relating to resource allocation. However, within the context of this paper, it is not clear why the authors restrict their assessment of the performance of EQ-5D to the performance of the EQ-5D index score alone and appear to disregard the EQ-5D visual analogue scale score or, indeed, the score on the five dimension questions separately.

Chakravorty *et al.*, 2002[97]

This study compared the effectiveness of CPAP therapy with a conservative lifestyle management as assessed using two different methods for eliciting health utilities (EQ-5D and a standard gamble task).

Seventy-one patients referred to a hospital sleep clinic with a history of snoring and excessive daytime sleepiness were recruited to the study and randomised to receive either CPAP therapy or lifestyle management. Each treatment phase lasted for 3 months. Prior to randomisation and at the end of treatment patients completed EQ-5D and a standard gamble task in which they were asked whether they would choose to stay in their current state of health or receive treatment leading to one of two outcomes: either complete cure or failure leading to a worst health state/death.

Standard gamble scores showed a mean gain of 0.23 (from 0.32 to 0.55) for the CPAP group compared with a gain of 0.04 (from 0.31 to 0.35) for the lifestyle group. In comparison, EQ-5D index scores showed a much smaller mean gain of 0.04 (from 0.73 to 0.77) for the CPAP group and no change for the lifestyle group. Both groups showed significant improvements in their ESS score, and the CPAP group but not the lifestyle group also showed significant improvement in their AHI score.

The authors suggest that the results indicate that EQ-5D may not be an appropriate instrument to use among patients with sleep apnoea because it only showed a mild change in patients with an effective positive treatment response to CPAP, and failed to record the small improvement seen in the lifestyle group (as measured using standard gamble). However, it should be noted that the lifestyle group did not show significant improvement in terms of the objective polysomnographic measures reported in the study.

Comments

EQ-5D scores were relatively high at baseline and were similar to those reported in other studies for this patient group.

It is not surprising that the utility values obtained using the two methods are different as they were elicited by means of completely different questions. Given this, the authors' conclusions about EQ-5D appear to be somewhat unwarranted.

Comparing utility values elicited using two different methods is problematic; the authors appear to treat the utilities elicited using the standard gamble approach as the 'gold standard' but their justifications for doing so in this context, other than describing the standard gamble approach as the 'classical approach to calculating utilities', are unclear.

Mar *et al.*, 2003[123]

This paper aimed to analyse the long-term cost-effectiveness of nCPAP treatment in patients with moderate to severe obstructive sleep apnoea in comparison with conventional treatment.

The authors undertook a survey to obtain EQ-5D utility values for patients with sleep apnoea. Forty-six patients referred to a hospital sleep unit were recruited and interviewed twice, once before commencing treatment and again after using nCPAP for 3 months. The mean age of the sample was 53 years (SD 12), 87% were male and their mean ESS was 13.8 (SD 5.8). Before starting nCPAP the mean EQ-5D index score for the sample was 0.738 (0.646–0.829); 3 months later the mean gain was 0.073 (0.015–0.131). Utilities for non-fatal stroke and non-fatal CHD also included in the model were obtained from the literature but were not specific to patients with sleep apnoea.

Comments

EQ-5D utility values were chosen as the study was designed to consider CPAP within the context of resource allocation; in addition EQ-5D has been

validated in a Spanish population.[124] Improvement was similar to that reported in the study by Jenkinson *et al*., 1997[152] (see above) which used EQ-5D in a similar population.However, the authors point out that the lack of a control group is a limitation of most studies that measure utility values in patients with sleep apnoea, and warn that the improvement in HRQoL observed may be an overestimation due to the placebo effect.

Appendix 8

Bivariate random-effects meta-analysis in WinBUGS

The randomised controlled trials identified in the systematic review reported a range of outcomes that were potentially relevant to the appraisal of CPAP for the treatment of OSAHS. In Chapter 3 a separate univariate meta-analysis was performed for each outcome of interest (where there were sufficient data from comparable studies). An alternative approach would be to perform a multivariate meta-analysis to jointly calculate pooled estimates for each outcome. By performing a multivariate meta-analysis the correlation between outcomes can be estimated and incorporated. Under a univariate approach, outcomes that are not reported are assumed to be missing completely at random (MCAR) and the between-study correlation between treatment effects on different outcomes is assumed to be zero. Using the multivariate approach, outcomes that are not reported are assumed to be missing at random (MAR), with the mechanism for missingness informed by the between-study correlation and the treatment effects for those outcomes that are reported.

Two outcomes identified in the systematic review were selected to inform the York economic model: mean difference in ESS score and mean difference in SBP. A random-effects analysis was performed in both the univariate and bivariate meta-analysis approaches, where each study's summary statistics [ess_i ($essVar_i$), bp_i ($bpVar_i$)] were assumed to represent an estimate of different underlying true values ($essMu_i$, $bpMu_i$), and these underlying true values were assumed to be drawn from a distribution with a particular mean (essReMu, bpReMu) and variance (essReVar, bpReVar). The framework for the bivariate approach is as follows:

$$\begin{pmatrix} ess_i \\ bp_i \end{pmatrix} \sim N\left(\begin{pmatrix} essMu_i \\ bpMu_i \end{pmatrix}, \delta_i\right), \delta_i = \begin{pmatrix} essVar_i & \frac{essVar_i}{\varphi_i essVar_i} \\ bpVar_i & bpVar_i \end{pmatrix}$$

$$\begin{pmatrix} essMu_i \\ bpMu_i \end{pmatrix} \sim N\left(\begin{pmatrix} essReMu \\ bpReMu \end{pmatrix}, \Omega_i\right), \Omega_i = \begin{pmatrix} essReVar_i & \frac{\Phi essReVar}{\Phi essReVar_i} \\ \Phi essReVar_i & bpReVar \end{pmatrix}$$

where $\phi_i essVar_i$ is the within-study covariance and $\Phi essReVar$ is the between-study covariance. None of the trials reported within-study covariance between mean difference in ESS and mean difference in SBP, and so a set of patient-level data containing both outcomes was obtained from which an informative prior could be specified. In addition, owing to the small number of studies reporting both outcomes when incorporating only SBP measured by ABPM, an informative prior was specified for the variance ($essVar_i$, $bpVar_i$) to be used where studies did not report one of the outcomes of interest. This prior was specified by multiplying the variance by the sample size, with a crude adjustment for the study design (i.e. doubling the sample size for crossover studies).

A product-normal approach was used to specify the model to estimate the effect of CPAP compared with conservative management on ESS score and SBP. The WinBUGS code for the model and the data sets used in the analyses are presented below. The output from 10,000 iterations was used to inform the York economic model after discarding the first 50,000 iterations.

WinBUGS code for bivariate random-effects meta-analysis

```
model{
          bpReMu ~ dnorm(0,1.0E-6)
          essReMu ~ dnorm(0,1.0E-6)

          essReTau <- 1/pow(essReSe,2)
          zReTau <- 1/(bpReVar - pow(bBeta,2)*essReVar)

          bpReVar <- pow(bpReSe,2)
          essReVar <- pow(essReSe,2)

          bpReSe ~ dunif(0,10)
          essReSe ~ dunif(0,10)

          bPsi ~ dunif(-0.99,0.99)
          bBeta <- (pow(bpReVar,0.5)/pow(essReVar,0.5))*bPsi

          essVarPA ~ dgamma(0.001,0.001)
          essVarPB ~ dgamma(0.001,0.001)

          bpVarPA ~ dgamma(0.001,0.001)
          bpVarPB ~ dgamma(0.001,0.001)

                    for (i in 1:nStudies) {
                              essMu[i] ~ dnorm(essReMu,essReTau)

                              bpMu[i] ~ dnorm(bpReMuD[i],zReTau)

                              bpReMuD[i] <- bpReMu - bBeta*(essReMu-essMu[i])

                              ess[i] ~ dnorm(essMu[i],essTau[i])

                              essTau[i] <- 1/essVar[i]
                              essVar[i] <- essPopVar[i]/(n[i]*typ[i])
                              essPopVar[i] ~ dgamma(essVarPA,essVarPB)

                              bpVar[i] <- bpPopVar[i]/(n[i]*typ[i])
                              bpPopVar[i] ~ dgamma(bpVarPA,bpVarPB)

                              bp[i] ~ dnorm(bpMuD[i],zTau[i])
                              bpMuD[i] <- bpMu[i] - wBeta[i]*(essMu[i]-ess[i])

                              zTau[i] <- 1/(bpVar[i] -
                              pow(wBeta[i],2)*essVar[i])

                              wBeta[i] <- pow(bpVar[i],0.5)/
                              pow(essVar[i],0.5)*wPsiD[i]
                              wPsiD[i] ~ dnorm(wPsi,t)I(-1,1)
                    }
          wPsi <- 0.2852149
          t <- 1/pow(.0739224,2)
}
```

Data for evidence synthesis with daytime SBP based on ABPM

Data

typ	ess	essVar	bp	bpVar	n
1	0	1.36515856	3	13.01117041	54
2	−1.2	0.16654561	NA	NA	35
1	−5	1.24835929	NA	NA	105
2	0.1	1.401856	NA	NA	18
2	−6	2.3409	NA	NA	23
1	−1.09	0.5184	NA	NA	111
2	−3	1.138489	NA	NA	37
2	−2.4	0.5041	NA	NA	71
1	−2.2	0.92006464	NA	NA	142
2	−0.6	1.7689	−2.9	29.16	42
1	−3.8	2.46929796	−10.3	27.88473636	60
2	−1	0.32069569	NA	NA	114
2	−2.4	0.84327489	NA	NA	31
1	−1	0.5625	NA	NA	72
1	−1.1	1.99741689	−2.5	8.4681	56
1	−3	1.99741689	NA	NA	101
2	−3.1	0.5041	NA	NA	35
1	−4	2.1904	NA	NA	42
1	−4.8	0.806404	NA	NA	107
1	−4	4.37562724	NA	NA	45
1	−7.94	1.62690025	NA	NA	48
1	−3	2.46929796	NA	NA	71
1	−4.5	1.03083409	NA	NA	118
2	NA	NA	−1	5.6169	13
2	NA	NA	0	4.4521	25
1	NA	NA	−1	15.47399569	21

Data for evidence synthesis with daytime SBP based on ABPM and office measurements

typ	ess	essVar	bp	bpVar	n
1	0	1.36515856	3	13.01117041	54
2	−1.2	0.16654561	NA	NA	35
1	−5	1.24835929	NA	NA	105
2	0.1	1.401856	NA	NA	18
2	−6	2.3409	NA	NA	23
1	−1.09	0.5184	NA	NA	111
2	−3	1.138489	NA	NA	37
2	−2.4	0.5041	NA	NA	71
1	−2.2	0.92006464	−8	11.68545856	142
2	−0.6	1.7689	−2.9	29.16	42
1	−3.8	2.46929796	−10.3	27.88473636	60
2	−1	0.32069569	NA	NA	114
2	−2.4	0.84327489	NA	NA	31
1	−1	0.5625	NA	NA	72
1	−1.1	1.99741689	−2.5	8.4681	56
1	−3	1.99741689	−3.6	46.69463	101
2	−3.1	0.5041	−6.7	3.009162849	35
1	−4	2.1904	NA	NA	42
1	−4.8	0.806404	NA	NA	107
1	−4	4.37562724	NA	NA	45
1	−7.94	1.62690025	NA	NA	48
1	−3	2.46929796	NA	NA	71
1	−4.5	1.03083409	NA	NA	118
2	NA	NA	−1	5.6169	13
2	NA	NA	0	4.4521	25
1	NA	NA	−1	15.47399569	21

Feedback

The HTA Programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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