| **First Author, Year****Trial Name** | **G1 (N)****G2 (N)** | **Mortality, N (%)** | **Quality of Life** | **Cognitive Impairment** | **MVAs, N (%)** | **CV Events, N (%)** | **CBV Events, N (%)** | **Heart Failure, N (%)** | **Headache, N (%)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Arias, 2005128 | Total (37)nCPAP first (14)Sham nCPAP first (13) | 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | NR | NR |
| Ballester, 1999170 | CPAP (68)Usual Care (37) | 0 (0.0)0 (0.0) | NHP domains: Emotional Reaction, mean (SE)BaselineCPAP: 28.4 (3.3)UC: 29.4 (5.0)12 wksCPAP: 17.0 (3.0)UC: 26.4 (4.5)Between groups p=0.080Sleep, mean (SE)BaselineCPAP: 30.1 (3.3)UC: 23.1 (3.8)12 wksCPAP: 18.1 (3.0)UC: 16.0 (4.0)Between groups p=0.183Physical, mean (SE)BaselineCPAP: 24.2 (2.6)UC: 25.0 (3.6)12 wksCPAP: 15.1 (2.1)UC: 21.1 (3.2)Between groups p=0.090Continued from above rowSocial isolation, mean (SE)BaselineCPAP: 14.2 (2.3)UC: 13.2 (3.0)12 wksCPAP: 8.5 (1.8)UC: 11.2 (3.4)Between groups p=0.030NHP Domains: Pain, mean (SE)BaselineCPAP: 20.5 (3.3)UC: 20.6 (4.0)12 wksCPAP: 14.8 (3.1)UC: 15.1 (3.9)Between groups p=0.940Energy, mean (SE)BaselineCPAP: 34.3 (4.7)UC: 23.2 (4.6)12 wksCPAP: 12.7 (3.3)UC: 22.2 (5.0)Between groups p<0.005 | Daytime function, mean (SE)BaselineCPAP: 33.9 (1.3)UC: 32.3 (1.7)12 wksCPAP: 24.2 (1.2)UC: 29.7 (2.0)Between groups p<0.005 | NR | NR | NR | NR | NR |
| Barbe, 2001130 | Total (55)CPAP (29)Sham CPAP (26) | 0 (0.0)0 (0.0) | FOSQ, mean (SE)BaselineCPAP: 102 (3)Sham: 107 (3)6 wksCPAP 108 (2)Sham: 110 (2)Change from BLCPAP: 7 (2)Sham: 3 (3)Between group: p>0.2SF-36 PCS, mean (SE) BaselineCPAP: 49 (1)Sham: 48 (1)6 wksCPAP: 51 (1)Sham: 50 (1)Change from BLCPAP: 2 (1)Sham: 1 (1)Between group: p>0.2SF-36 MCS, mean (SE)BaselineCPAP: 51 (2)Sham: 50 (2)6 wksCPAP: 51 (2)Sham: 52 (2) Change from BLCPAP Change: -1 (2)Sham Change: 1 (2)Between group: p>0.2 | Hits on Steer Clear test, mean (SE) %BaselineCPAP: 5 (1)Sham: 6 (2)6 wksCPAP: 4 (1)Sham: 5 (2)Change from BLCPAP: -1 (1)Sham:-1 (1)Between group p>0.2Also reported: WAIS digit symbols, block design, digit span, PASAT 1-4, Trail making test A & B, Wechsler memory scale  | NR | NR | NR | NR | NR |
| Barbe, 2012172 | CPAP (357) Control (366) | All-cause:\* 8 (2.2)3 (0.8)CVD-specific: 1 (0.3)0 (0.0) | NR | NR | NR | Total: 19 (5.3)19 (5.2)CV† Hospitalizations: 17 (4.8)11 (3.0)Nonfatal myocardial infarction:2 (0.6)8 (2.2) | TIA: 2 (0.6)5 (1.4)Non-fatal stroke: 3 (0.8)2 (0.5) | 3 (0.8)5 (1.4) | NR |
| Barnes, 2004173 | CPAP (97)Placebo (98) | 0 (0.0)0 (0.0) | FOSQ mean score, mean (SE):Baseline: 3.1 (0.1)3.3 (0.1), p < 0.0013.3 (0.1), p < 0.01CPAP vs. Placebo p < 0.05  | Reported: Word Pair Memory Recall; Logical Memory Test; Digit Span Backwards; Trailmaking B; Digit Symbol Substitution Task; COWAT; PVT; Stroop Color Association Test | NR | NR | NR | NR | NR |
| Craig, 2012174 | CPAP (195) Standard Care (196) | 1 (0.5)0 (0.0) | MCS, Mean (SD) Baseline:48.2 (10.4)46.6 (11.3)24 weeks:52.0 (9.8)48.5 (11.0)Between group difference:2.6 (95% CI, 0.9 to 4.2; p=0.003) EQ-5D score, Mean (SD)ǂBaseline: 0.80 (0.17)0.75 (0.24)24 weeks:0.83 (0.19)0.80 (0.22)Between group difference:+0.20 (95% CI, -0.03 to 0.06; p=0.43)SAQLI, mean (SD) Baseline: 4.9 (1.1)4.8 (1.2)24 weeks: 5.6 (1.0)5.0 (1.3)Mean change (SE)0.7 (0.1)0.2 (0.1)Between group difference: p<0.0001 | NR | NR | Angina: 1 (0.6)3 (1.7)MI:0 (0.0)0 (0.0)PVD:2 (1.2)1 (0.6)AF:6 (3.5)7 (4.1) | TIA: 1 (0.6)0 (0.0)Stroke:0 (0.0)0 (0.0) | NR | NR |
| Durán-Cantolla, 2010137 | CPAP (169)Sham (171) | 0 (0.0)0 (0.0) | EuroQol, mean (SD) at baseline, 6 wks, 12 wlsCPAP 69 (15), 74 (14),§ 76 (16)‖Sham CPAP 72 (17), 72 (16), 73 (15) | NR | NR | NR | NR | NR | NR |
| Egea, 2008138 | CPAP¶ (35)Sham CPAP (38) | 0 (0.0)1 (2.6) | OSA Only SF-36 – PCS, Mean (SE)Baseline:41.4 (2.0)42.0 (2.1)12 weeks44.9 (1.8), p = 0.1040.7 (2.1), p = 0.41Between group p=NSSF-36 – MCS, Mean (SE)Baseline:46.4 (3.0)45.8 (2.7)12 weeks48.8 (2.3), p = 0.4048.7 (2.2), p = 0.27Between group p=NS | NR | NR | Angina0 (0.0)1 (2.6) | NR | NR | NR |
| Engleman, 1994216 | CPAP first (17)Oral placebo first (15) | 0 (0.0)0 (0.0) | NHP-2,4 wks:4.9 (SE 0.9)7.9 (SE 0.9)Between groups p=0.002CPAP > placebo (p<0.05) for social life, sex life, and ability to carry out domestic chores | Mental Flexibility (Trailmaking B)66 (SE 5)75 (SE 5)Between groups P= 0.02Coding efficiency (Digit symbol substitution)52 (SE 2)51 (SE 2)Between groups P= 0.05Vigilance (Steer Clear, N objects hit)76 (SE 5)81 (SE 6)Between groups P= 0.01IQ decrement score4.0 (SE 2.1)7.2 (SE 2.0)Between groups P= 0.04Concentration (PASAT 2)Between groups P= 0.02 but after adjustment for order effect, P=0.11 | NR | NR | NR | NR | NR |
| Engleman, 1997217 | CPAP first (8)Oral placebo first (8) | 0 (0.0)0 (0.0) | Nottingham Health Profile Part 2, total score4 wks3.8 (SE 1.1)5.8 (SE 1.4)Betw groups p=NSBetter compliers (mean 5 hrs/night), NHP Part 2 total score4 wks2.4 (SE 1.5)6.8 (SE 2.5)Betw groups p=0.03 | Reports IQ decrement, Trailmaking, SteerClear, PASAT2, RVIPT, reaction time, verbal fluency, BVRT.Only significant changes on TrailMaking B no changes on other various cognitive functioning measures | NR | NR | NR | NR | NR |
| Engleman, 1998175 | CPAP first (10)Placebo (13) | 0 (0.0)0 (0.0) | NHP-2Baseline, mean (SD)8.0 (5.0)4 wks, mean (SD)5.8 (5.4)6.3 (5.7)Between group change: -0.5 (95% CI, -2.5 to 1.5; p=NS) | No significant difference between groups on changes in the following: 30 min. SteerClear;TrailMaking B; WAIS-R performance IQ (Block Design and Digit Symbol Substitution);NART; RVIP;# 8-choice reaction time; PASAT;\*\* Verbal fluency; BVRT††  | NR | NR | NR | NR | NR |
| Engleman, 1999176 | Total (37)CPAP first (NR)Oral Placebo first (NR) | 0 (0.0)0 (0.0) | NHP- 2 score, mean (SD)Baseline: 10.5 (4.8)4 wks CPAP: 6.1 (4.7)4 wks placebo: 7.3 (5.2)Between groups p = NSSF-36 Domains only: Physical FunctionBaseline: 75 (27)4 wks CPAP: 84 (22)4 wks placebo: 83 (23)Between groups p=NSMental healthBaseline: 64 (19)4 wks CPAP: 79 (16)4 wks Placebo: 75 (15)Between groups p=NSGeneral HealthBaseline: 68 (21)4 wks CPAP: 76 (19)4 wks placebo: 74 (20)Between groups p=NS | SteerClear (obstacles hit), mean (SD)Baseline: 295 (183)4 wks CPAP: 189 (156)4 wks placebo: 195 (158)Between groups p=NSAlso reportedTrailMaking A, Trailmaking B, Digit Symbol, Block Design, performance IQ, PASAT  | NR | NR | NR | NR | 0 (0.0)3 (8.8) |
| Faccenda, 2001177 | Total (71)CPAP first (35)Pbo capsule first (36) | 0 (0.0)0 (0.0) | FOSQ total, mean change from baseline (SE):12.4 (0.5)11.6 (0.7)P=0.010 | NR | NR | NR | NR | NR | NR |
| Gottlieb, 2014178HeartBEAT | CPAP+ usual care (106)Usual care alone (106) | 0 (0.0)0 (0.0) | NR | NR | 0 (0.0)0 (0.0) | Unstable angina:0 (0.0)1 (0.9)MI:0 (0.0)1 (0.9)PCI for worsening angina:0 (0.0)1 (0.9AF:1 (0.9)0 (0.0)Arrhythmiaǂǂ0 (0.0)1 (0.9) | Stroke:0 (0.0)1 (0.9) | NR | NR |
| Haensel, 2007139 | CPAP (25)Sham CPAP (25) | 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | NR | NR |
| Hoyos, 2012140 | CPAP (34)Sham CPAP (31) | All-cause: 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | NR | NR |
| Jenkinson, 1999142Hack, 2000143 | CPAP (54)Subtherapeutic CPAP (53) | 0 (0.0)0 (0.0) | SF-36 MCS, mean (SD)Baseline:44.8 (10.4)43.5 (10.7)4 wks: 55.4 (7.0)47.8 (10.1)Between group change: p=0.002SF36 PCS, mean (SD):Baseline: 43.7 (11.6)42.6 (10.1)4 wks: 49.4 (10.1)45.5 (10.4)5.7 (NR); p<0.0012.9 (NR); p=0.007Between group change: p=0.080 | Measures of driving simulation | NR | NR | NR | NR | NR |
| Kushida, 2012145 Batool-Anwar, 2016288APPLES | CPAP (558)Sham (547) | 2 (0.4)2 (0.4) | SAQLI, mean (SD)Compliance < 4 hoursBaseline:4.7 (0.8)4.6 (0.8)6 months:4.7 (0.8)4.6 (1.0)Between-group change: p≥0.05Compliance > 4 hoursBaseline:4.7 (0.8)4.8 (0.8)6 months:5.0 (0.7)4.9 (0.7)Between-group change: p<0.05 | No difference between groups on multiple measures of neurocognitive function (Pathfinder NumberTest, Buschke Selective Reminding Test,Sustained Working Memory Test)  | 10 (1.8)11 (2.0) | CV events reported as “adverse events” but not defined: 31 (5.6)29 (5.3) | NR§§ | NR | NR |
| Lam, 2007180 | CPAP (34)Usual care (33) | 0 (0.0)0 (0.0) | SAQLI total score, mean (SE) Baseline: 5.0 (0.1)5.1 (0.1)10 weeks: 5.5 (0.1)5.0 (0.1)Between group difference: 0.77 (-1.5 to 0.4); p=0.04SF36, mean (SEM); p-val of within group change from BL; between group change from BL vs. usual carePhysical function domain, Baseline84.7 (2.2)82.3 (2.6)10 weeks88.2 (1.7); p<0.05; p<0.0578.9 (3.6)General health domain,Baseline48.3 (3.1) 51.2 (3.3)10 weeks58.9 (3.3); p<0.05; p=NS 54.8 (3)Mental health domain,Baseline66.8 (2.5) 65.6 (2.5)10 weeks71.8 (2.8); p=NS; p=NS 68.0 (2.5) | NR | NR | NR | NR | NR | NR |
| Lee, 2011147 | Total (38)CPAP (17)Sham CPAP (21) | 0 (0.0)0 (0.0) | NR | Measured:WAIS-III; Digit Symbol; Digit Span; Letter-Number Sequencing; Symbol Search; Brief Visuospatial Memory Test-Rev; Hopkins Verbal Learning Test-Rev; Trail Making A/B; Digit Vigilance; Stroop Color-Word; Word Fluency  | NR | NR | NR | NR | NR |
| Lim, 2007215 | Total (46)nCPAP (17)Sham CPAP (14) | NR | NR | Reports multiple cognitive function outcomes | NR | NR | NR | NR | NR |
| Malow, 2008150 | Total (35)CPAP (22)Sham CPAP (13) | 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | NR | NR |
| Marshall, 2005151 | Total (31)CPAP first (15)Sham first (16) | 0 (0.0)0 (0.0) | FOSQ total, mean (SE):Baseline: 12.6 (0.3)13.6 (0.3), p < 0.0113.3 (0.3), p=nsBtwn groups diff= 0.3 (-0.5 to 1.1)**SF36 domains**Mental healthBaseline: 75 (3)77 (2) p=NS80 (2) p <0.05Btwn groups diff=-3 (-10 to 3)Physical functioningBaseline: 82 (3)81 (2) p=NS80 (2) p=NSBtwn groups diff=1 (-3 to 6)General healthBaseline: 74 (3)76 (2) p=NS76 (2) p=NSBtwn groups diff=0 (-6 to 7) | Psychomotor vigilance task:Mean (SE) reaction time (ms):Baseline: 264 (5)266 (5) p=NS259 (5) p=NSBetw groups diff=7 (-7 to 20)Mean (SE) lapses (>500 ms reaction time):Baseline: 1.3 (0.3)3.2 (0.7) p=NS3.3 (0.7) p=NSBetw groups diff=0.4 (-0.7 to 1.4)Errors, mean (SE):Baseline: 2.8 (0.5)3.2 (0.7) p=NS3.3 (0.7) p=NSBetw groups diff=-0.1 (-2.0 to 1.9) | NR | Non-fatal MI: 0 (0.0)1 (3.2)  | NR | NR | NR |
| McMillan, 2014182 | Total (278)CPAP + BSC (140)BSC only (138) | NR | SAQL, baseline, mean (SD)4.8 (1.2)4.7 (1.2)12 weeks, mean (SD)5.3 (1.1)5.0 (1.1)between groups p=0.00552 weeks, mean (SD)5.5 (1.1)5.1 (1.1)between groups p=0.001SF-36 reported in Figure only; authors report improvement on the energy and vitality subscales | No difference between groups in cognitive function measures: Digit symbol substitutionTrail Making B Simple reaction time | 52 weeks: 2 (3.0)1 (1.0) | 52 weeks: MI 3 (2.1)0 (0.0)New Angina2 (1.4)3 (2,2)New A-fib6 (4.3)12 (8.7)New PVD1 (0.3)0 (0.0)All12 (4.3)15 (10.1)betw groups for all CV events p=0.72 | 52 weeks:Stroke 0 (0.0)0 (0.0)“Mini-stroke”1 (0.3)2 (1.4)between groups for al adverse CV events p=0.72 | NR |  |
| Montserrat, 2001154 | CPAP (24)Placebo CPAP (24) | 0 (0.0)0 (0.0) | FOSQ total, mean change from baseline (SD):25.0 (NR); P<0.00114.5 (NR); P=0.008Between groups P=0.12SF36 MCS, mean change from baseline (SD):1.32 (NR); P=0.614.92 (NR); P=0.006Between groups P=0.52SF36 PCS, mean change from baseline (SD):4.18 (NR); P=0.0021.62 (NR); P=0.36Between groups P=0.23 | NR | NR | NR | NR | NR | NR |
| Neikrug, 2014155 | CPAP (19)Sham CPAP (19) | 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | NR | NR |
| Nguyen, 2010157 | nCPAP (10), sham CPAP (10) | 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | NR | NR |
| Phillips, 2011161 | Total (38)CPAP first (18)Sham CPAP first (19) | NR | FOSQ total, mean (SD):Baseline:15.2 (3.1)8 week, mean (SE):16.0 (0.53)16.7 (0.52)Between groups P=0.056 | NR | NR | NR | NR | NR | NR |
| Redline, 1998183 | Total (111)nCPAP (59)Conservative therapy (52) | 0 (0.0)0 (0.0) | SF-36 Energy/fatigue subscore, mean (SD) Baseline:51.7 (19.8)58.3 (19.0)Change from BL to 8-12 wks10.3 (17.8)2.3 (16.8)Between groups p<0.05 | NR | NR | NR | NR | NR | NR |
| Robinson, 2006162  | Total (35)CPAP first (18)Sham first (17) | 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | NR | NR |
| Ruttanaumpawan, 2008184 | CPAP (12)No treatment (12) | 0 (0.0)0 (0.0) | NR | NR | NR | NR | NR | (All pts had HF) | NR |
| Siccoli, 2008164 | CPAP (51)Sham CPAP (51) | 0 (0.0)0 (0.0) | SF-36 PCS,‖‖ Mean (SD)Baseline62.0 (20.0)69.4 (21.5)4 weeks70.8 (18.5) P<0.000170.0 (18.8) P=0.68Between groups P=0.010SF-36 MCS, Mean (SD)Baseline62.2 (20.2)64.8 (21.2)4 weeks76.8 (16.2) P<0.000168.6 (22.7) P=0.17Between groups P=0.002SAQLI , Mean (SD)Baseline3.5 (1.0)3.8 (1.1)4 weeks4.4 (1.1) P<0.00013.8 (1.6) P=0.65Between groups P=0.001 | NR | NR | NR | NR | NR | NR |
| Smith, 2007163 | Total (26)CPAP first (11)Sham first (13) | 0 (0.0)0 (0.0) | MLHFBaseline: 38 (27)G1: 36 (29)G2: 34 (28)Between groups difference 1.0 (-4.3 to 6.4) P=0.70SF36 PCSBaseline: 34 (16)G1: 34 (14)G2: 35 (14)Between groups difference -1.0 (-3.6 to 1.6) P=0.43SF36 MCSBaseline: 51 (10)G1: 49 (12)G2: 50 (11)Between groups difference -0.5 (-4.2 to 3.2) P=0.79 | NR | NR | NR | NR | NR | NR |
| Weaver, 2012166 | Total (281)CPAP (141)Sham CPAP (140) | 0 (0.0)0 (0.0) | FOSQ total, unadj mean change from BL (SD):0.98 (2.89) p=0.0005-0.14 (2.61) p=0.57Adj mean change from BL (SD):0.89 (NR)-0.06 (NR)Adj diff in mean change (SE);0.95 (0.34)Between groups p=0.006SF-36, PCSAdj mean change from BL: 3.890.04Adj between group difference in mean change from BL (SE):3.85 (1.17)95% CI, 1.53-6.17p=0.001SF-36, MCS Adj mean change from BL: 3.072.21Adj between group difference in mean change from BL (SE): 0.86 (1.42)95% CI, -1.95 -3.67p=0.546 | NR | NR | NR | NR | NR | NR |
| West, 2007168 | CPAP (20)Sham CPAP (22) | NR | SAQLI, mean (SD)Baseline4.3 (1.1)4.4 (0.9)Change from BL at 12 wks:+0.8 (1.0)+0.03 (1.2)Between-group difference (95% CI):0.77 (-1.5 to 0.04); p=0.04 | NR | NR | 1 CPAP patient (5%) had emergency cardiac surgery | NR | NR | NR |

\* Footnote: For all-cause mortality, the authors also report an incidence density ratio: 2.6 (95% CI, 0.70-11.8; P=0.16)

† Hospitalizations were for unstable angina or arrhythmias.

ǂ Authors also report the EQ-5D Health Status (Visual Analogue Score); there were no differences between groups in the total score (p=0.095).

§ P<0.001 compared with baseline; effect size (SD units) 0.31

‖ P<0.001 compared with baseline; effect size (SD units) 0.38; EuroQol scores improved significantly only in the CPAP group

¶Sample size includes some patients who had central sleep apnea.

# Rapid visual information proecessing

\*\* 2 second presentation rate

†† Benton visual retention test

ǂǂ Per authors, one person in the control group developed “unspecified tachyarrhythmia requiring hospitalization.”

§§ Authors report counts for neurological “adverse events” but do not specify how these were measured or defined: CPAP 36 events (6.5%) versus Sham 32 events (5.9%)

‖‖ Authors also report a score for the PCS and MCS components of the SF-12; results are similar to those seen on the SF-36.

**Abbreviations:** adj=adjusted; AF=atrial fibrillation; APPLES=Apnea Positive Pressure Long-term Efficacy Study; BL=baseline; BSC=best supportive care; btwn=between; BVRT=Benton Visual Retention Test; CBV=cerebrovascular; CI=confidence interval; COWAT=Controlled Oral Word Association Test; CPAP=continuous positive airway pressure; CV=cardiovascular; CVD=cardiovascular disease; EQ=EuroQoL; FOSQ=Functional Outcomes of Sleep Questionnaire; G=group; HeartBEAT=Heart Biomarker Evaluation in Apnea Treatment; HF=heart failure; MCS=Mental Component Score of the SF-36; IQ=intelligence quotient; MI=myocardial infarction; MLHF=Minnesota Living with Heart Failure; ms=milliseconds; MVA=motor vehicle accident; N=sample size; NART=National Adult Reading Test**;** NHP=Nottingham Health Profile; nCPAP=nasal continuous positive airway pressure; NR=not reported; NS=not significant; PASAT=Paced Auditory Serial Addition Test; PCI=percutaneous coronary intervention; PCS=Physical Component Score of the SF-36; pts=patients; PVD=peripheral vascular disease; PVT=psychomotor vigilance test; RVIP=Rapid Visual Information Processing; SAQLI=Sleep Apnea Quality of Life Index; SE=standard error; SF-36=36-Item Short Form Health Survey; TIA=transient ischemic attack; UC=usual care; WAIS=Wechsler Adult Intelligence Scale; wks=weeks.