**Effect of continuous positive airway pressure on blood pressure in patients with minimally symptomatic obstructive sleep apnoea: a meta-analysis using individual patient data from four randomised controlled trials – Online supplement**

**Contents**

**1.  Search Strategy for MEDLINE**
1       randomized controlled trial.pt
2       controlled clinical trial.pt
3       randomized.ab
4       placebo.ab
5       clinical trials as topic.sh
6       randomly.ab
7       trial.ti
8       1 or 2 or 3 or 4 or 5 or 6 or 7
9       apn$ea.af
10      OSA$.af
11      hypopn$ea.af
12      SAHS.af
13      obstructive sleep apn$ea.af
14      9 or 10 or 11 or 12 or 13
15      CPAP.af
16      continuous positive airway pressure.af
17      15 or 16
18      Blood pressure.af
19      Minimally symptomatic.af
20      Non$sleepy.af
21      Non$symptomatic.af
22      Aymptomatic.af
23      19 or 20 or 21 or 22
24      8 and 14 and 17 and 18 and 23

2. **Summary of CPAP adherence**

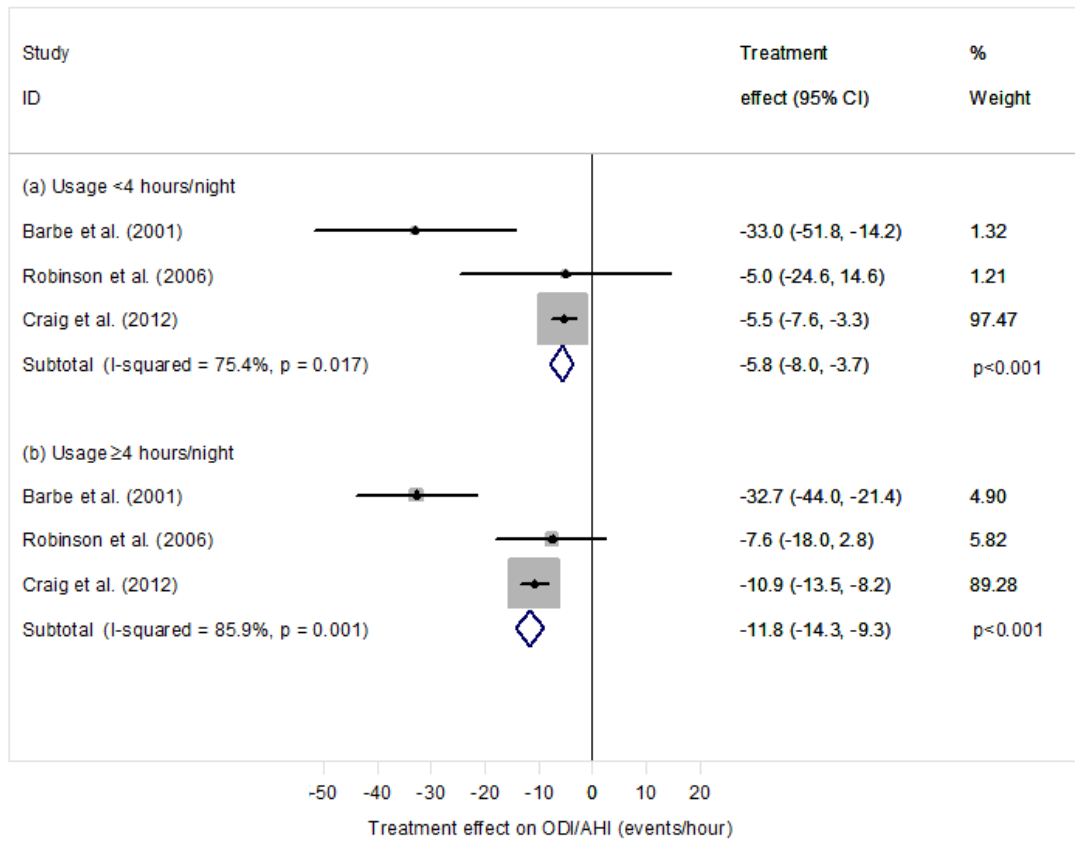| Trial | No. allocated to CPAP | Median usage (25$^{th}$, 75$^{th}$ percentiles) (hours/night) | No. (%) using ≥4 hours/night |
|---|---|---|---|
| Barbé (2001) | 29 | 5.1 (4.0, 6.5) | 22 (76%) |
| Robinson (2006) | 17 | 5.5 (4.4, 7.0) | 14 (82%) |
| Barbé (2012) | 358 | 5.0 (3.0, 6.3) | 219 (61%) |
| Craig (2012) | 195 | 2.5 (0.5, 4.9) | 66 (34%) |
| Total | 599 | 4.7 (2.1, 6.0) | 321 (54%) |

**eTable 2.1 - Summary of adherence to CPAP**

Summary of average adherence to CPAP (hours/night) and the proportion of participants using CPAP ≥4 hours/night in each study and overall. Average adherence for each patient is calculated as the total number of hours used divided by total number of days used over follow-up.

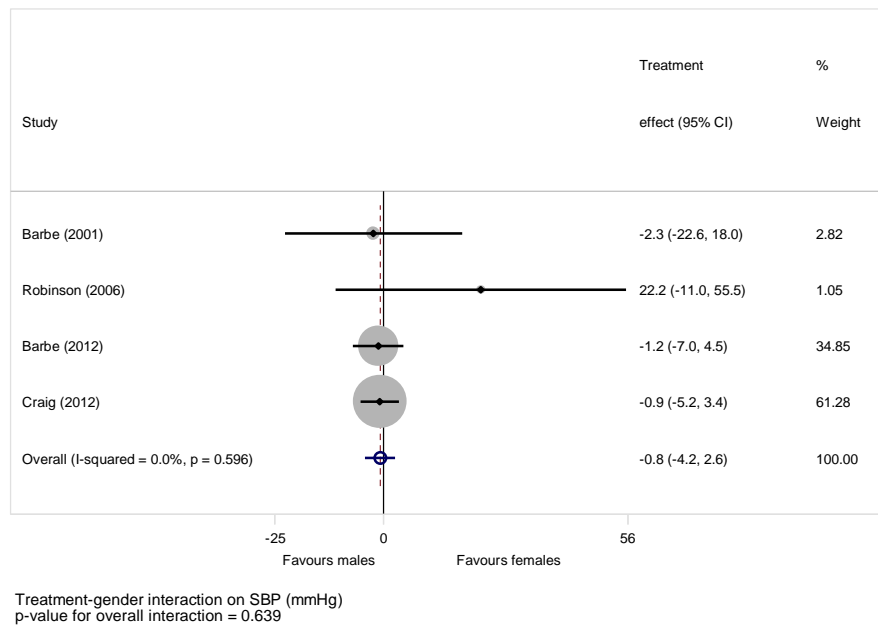## 3. Effect of CPAP usage on secondary outcomes
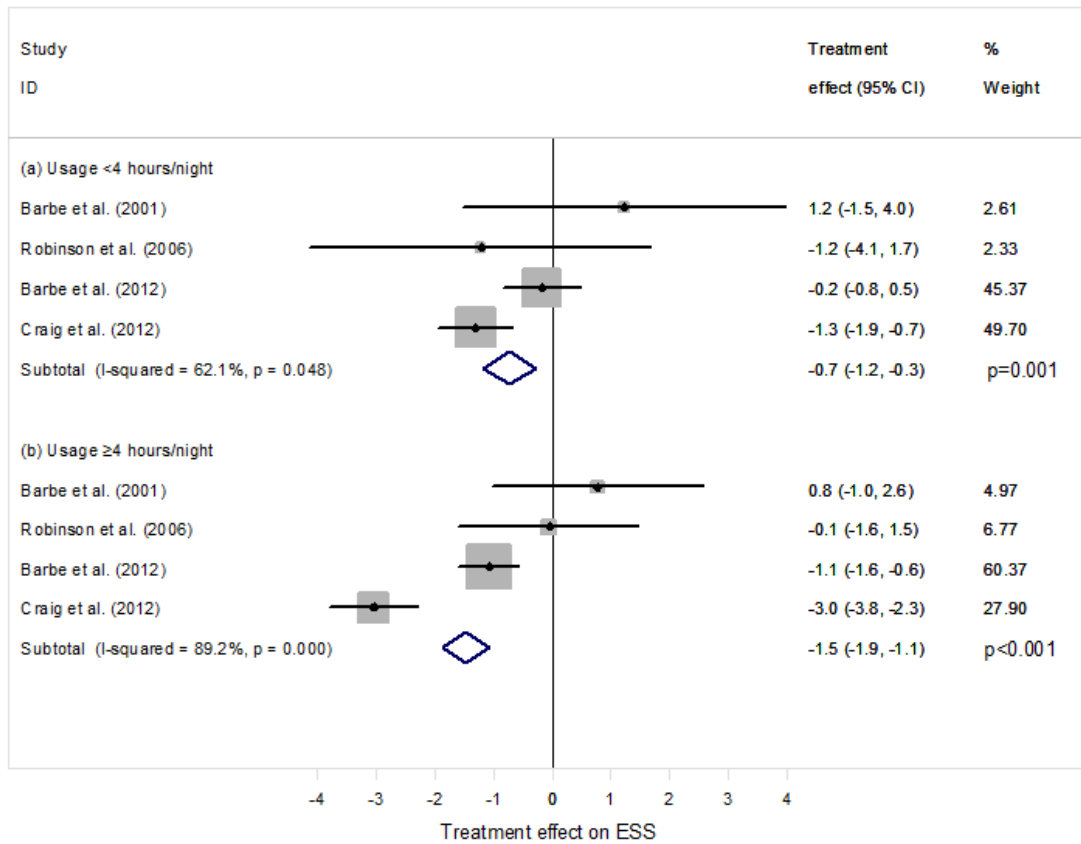


**eFigure 3.1: Forest plots showing the effect of less than and more than 4 hours/night CPAP usage on Epworth Sleepiness Score (ESS) compared to control in each study and overall**
Difference between pooled treatment effects: p<0.001

| Study ID | | Treatment effect (95% CI) | % Weight |
|---|---|---|---|
| **(a) Usage <4 hours/night** | | | |
| Barbe et al. (2001) | | -33.0 (-51.8, -14.2) | 1.32 |
| Robinson et al. (2006) | | -5.0 (-24.6, 14.6) | 1.21 |
| Craig et al. (2012) | | -5.5 (-7.6, -3.3) | 97.47 |
| Subtotal (I-squared = 75.4%, p = 0.017) | | -5.8 (-8.0, -3.7) | p<0.001 |
| **(b) Usage ≥4 hours/night** | | | |
| Barbe et al. (2001) | | -32.7 (-44.0, -21.4) | 4.90 |
| Robinson et al. (2006) | | -7.6 (-18.0, 2.8) | 5.82 |
| Craig et al. (2012) | | -10.9 (-13.5, -8.2) | 89.28 |
| Subtotal (I-squared = 85.9%, p = 0.001) | | -11.8 (-14.3, -9.3) | p<0.001 |

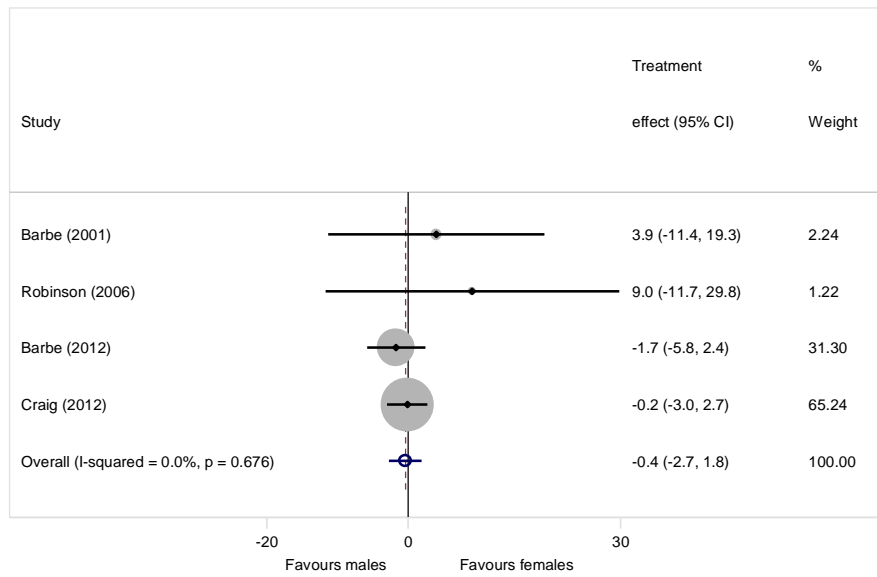Treatment effect on ODI/AHI (events/hour)

**eFigure 3.2: Forest plots showing the effect of less than and more than 4 hours/night CPAP usage on sleep apnoea severity (ODI/AHI, events/hour) in each study and overall**
Difference between pooled treatment effects: p<0.001

## 4. Treatment interactions with binary baseline covariates



| Study | Treatment effect (95% CI) | % Weight |
|---|---|---|
| Barbe (2001) | -2.3 (-22.6, 18.0) | 2.82 |
| Robinson (2006) | 22.2 (-11.0, 55.5) | 1.05 |
| Barbe (2012) | -1.2 (-7.0, 4.5) | 34.85 |
| Craig (2012) | -0.9 (-5.2, 3.4) | 61.28 |
| Overall (I-squared = 0.0%, p = 0.596) | -0.8 (-4.2, 2.6) | 100.00 |

Favours males          Favours females

Treatment-gender interaction on SBP (mmHg)
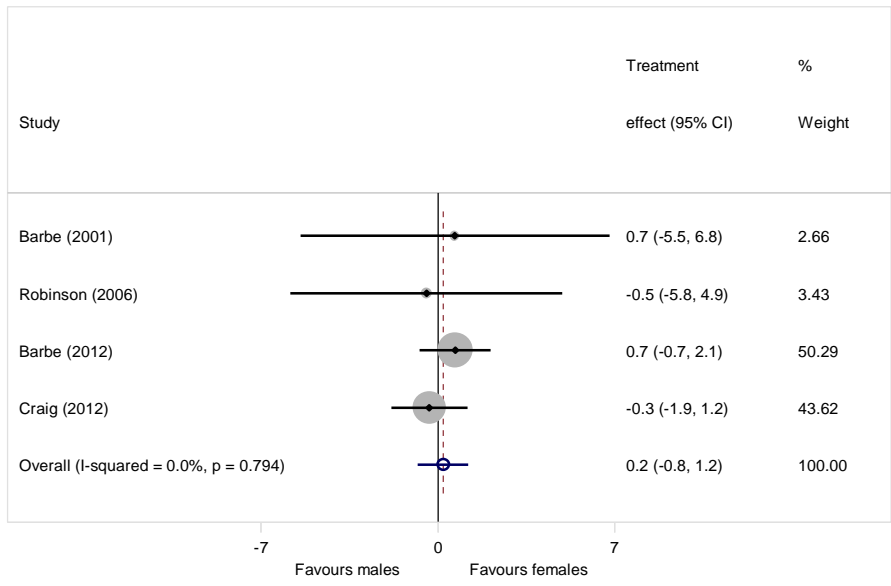p-value for overall interaction = 0.639

**eFigure 4.1: Forest plot showing the difference in treatment effects on systolic blood pressure (SBP, mmHg) between males and females in each study and overall**
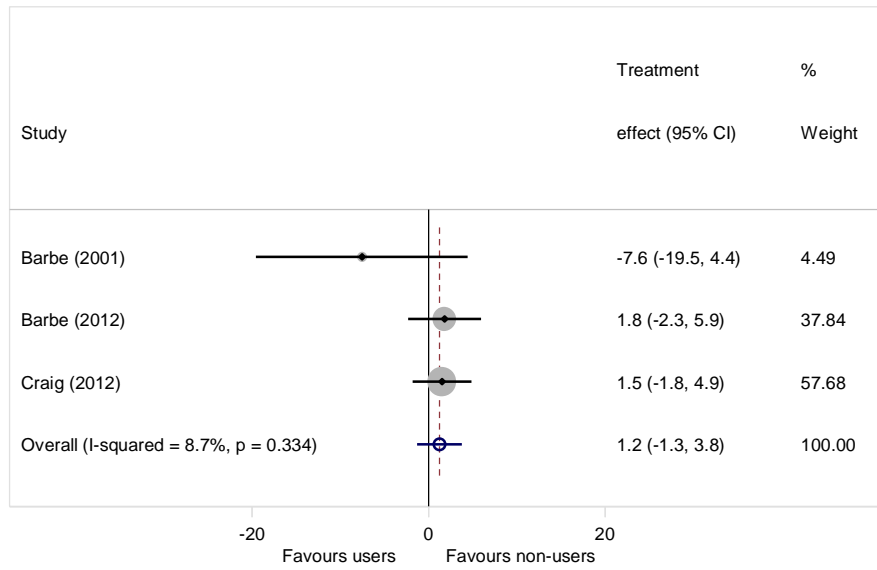
| Study | Treatment effect (95% CI) | % Weight |
|---|---|---|
| Barbe (2001) | 3.9 (-11.4, 19.3) | 2.24 |
| Robinson (2006) | 9.0 (-11.7, 29.8) | 1.22 |
| Barbe (2012) | -1.7 (-5.8, 2.4) | 31.30 |
| Craig (2012) | -0.2 (-3.0, 2.7) | 65.24 |
| Overall (I-squared = 0.0%, p = 0.676) | -0.4 (-2.7, 1.8) | 100.00 |

-20    0    30

Favours males    Favours females

Treatment-gender interaction on DBP
p-value for overall interaction = 0.703

**eFigure 4.2: Forest plot showing the difference in treatment effects on diastolic blood pressure (DBP, mmHg) between males and females in each study and overall**
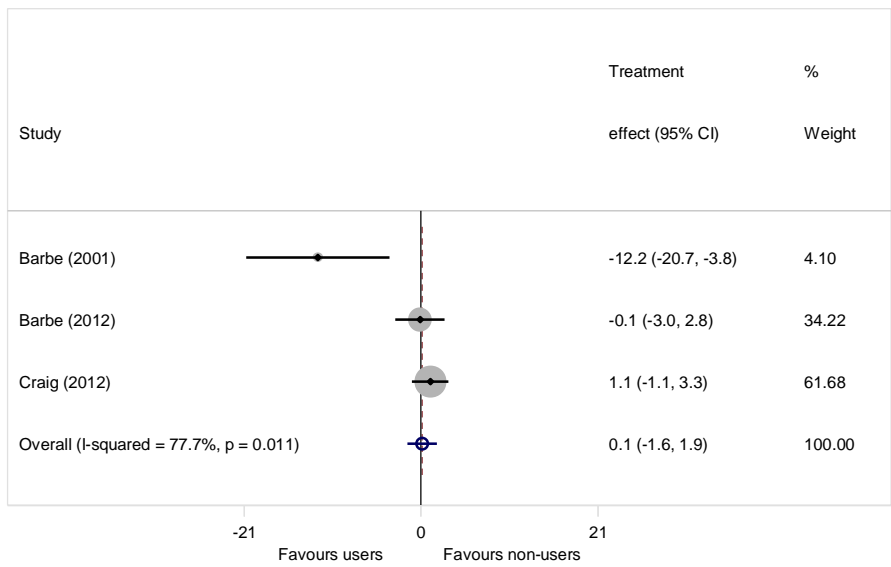
| Study | Treatment effect (95% CI) | % Weight |
|-------|---------------------------|----------|
| Barbe (2001) | 0.7 (-5.5, 6.8) | 2.66 |
| Robinson (2006) | -0.5 (-5.8, 4.9) | 3.43 |
| Barbe (2012) | 0.7 (-0.7, 2.1) | 50.29 |
| Craig (2012) | -0.3 (-1.9, 1.2) | 43.62 |
| Overall (I-squared = 0.0%, p = 0.794) | 0.2 (-0.8, 1.2) | 100.00 |

-7   0   7

Favours males    Favours females

Treatment-gender interaction on ESS
p-value for overall interaction = 0.695

**eFigure 4.3: Forest plot showing the difference in treatment effects on Epworth Sleepiness Score (ESS) between males and females in each study and overall**

| Study | Treatment effect (95% CI) | % Weight |
|---|---|---|
| Barbe (2001) | -7.6 (-19.5, 4.4) | 4.49 |
| Barbe (2012) | 1.8 (-2.3, 5.9) | 37.84 |
| Craig (2012) | 1.5 (-1.8, 4.9) | 57.68 |
| Overall (I-squared = 8.7%, p = 0.334) | 1.2 (-1.3, 3.8) | 100.00 |

Treatment-antihypertensive medication interaction on SBP
p-value for overall interaction = 0.339

**eFigure 4.4: Forest plot showing the difference in treatment effects on systolic blood pressure (SBP) between users and non-users of anti-hypertensive medication in each study and overall**

| Study | | Treatment effect (95% CI) | % Weight |
|---|---|---|---|
| Barbe (2001) | | -12.2 (-20.7, -3.8) | 4.10 |
| Barbe (2012) | | -0.1 (-3.0, 2.8) | 34.22 |
| Craig (2012) | | 1.1 (-1.1, 3.3) | 61.68 |
| Overall (I-squared = 77.7%, p = 0.011) | | 0.1 (-1.6, 1.9) | 100.00 |

-21        0        21

Favours users        Favours non-users

Treatment-antihypertensive medication interaction on DBP
p-value for overall interaction = 0.873

**eFigure 4.5: Forest plot showing the difference in treatment effects on diastolic blood pressure (DBP) between users and non-users of anti-hypertensive medication in each study and overall**

## 5. Treatment interactions with continuous baseline covariates



p-value for interaction p = 0.525
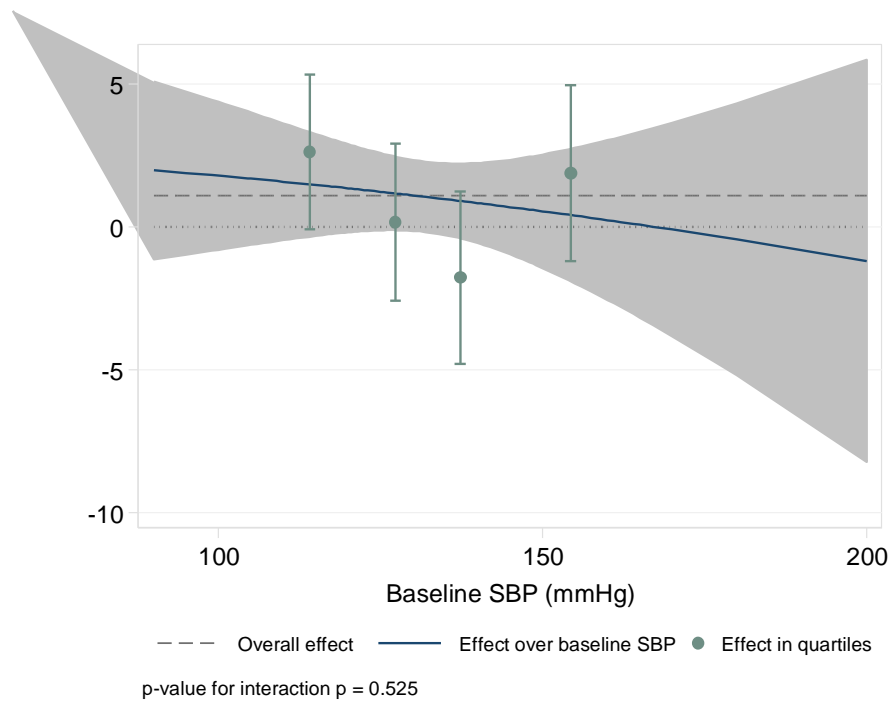
**eFigure 5.1: Effect of CPAP on change in systolic BP (SBP) compared to control over the full range and in quartiles of observed baseline systolic BP**
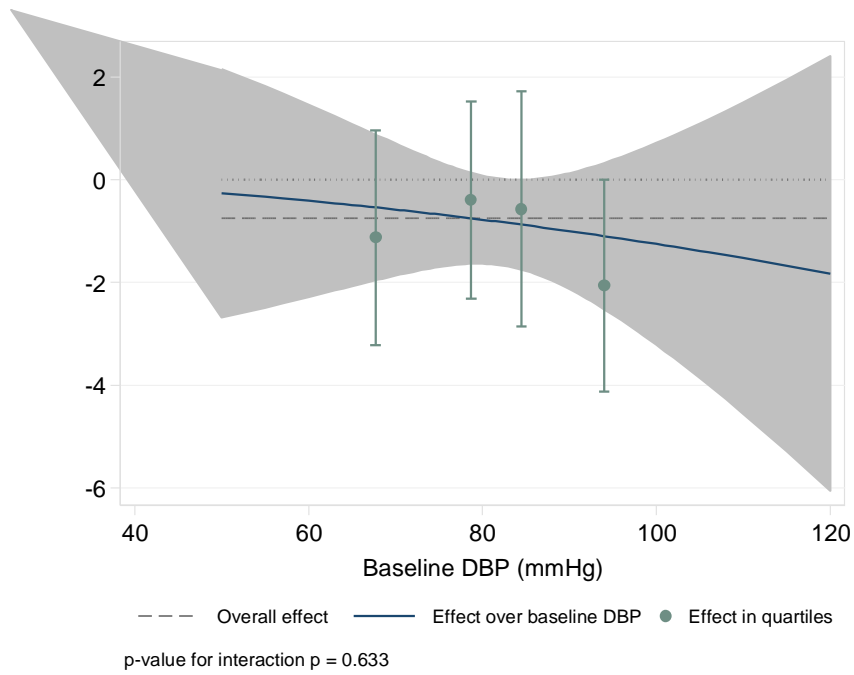


p-value for interaction p = 0.149
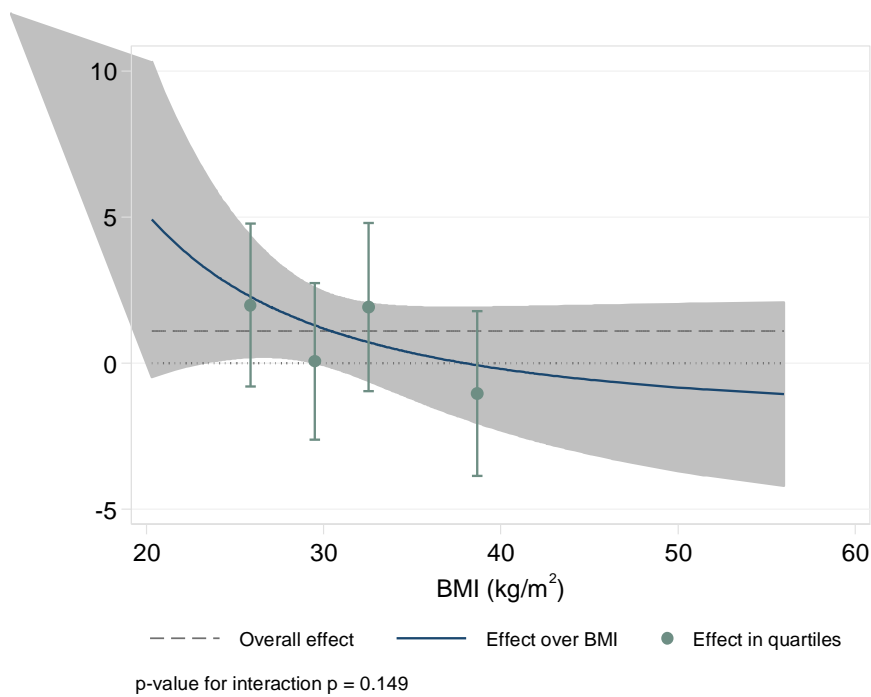
**eFigure 5.2: Effect of CPAP on change in systolic BP compared to control over the full range and in quartiles of observed body mass index (BMI)**
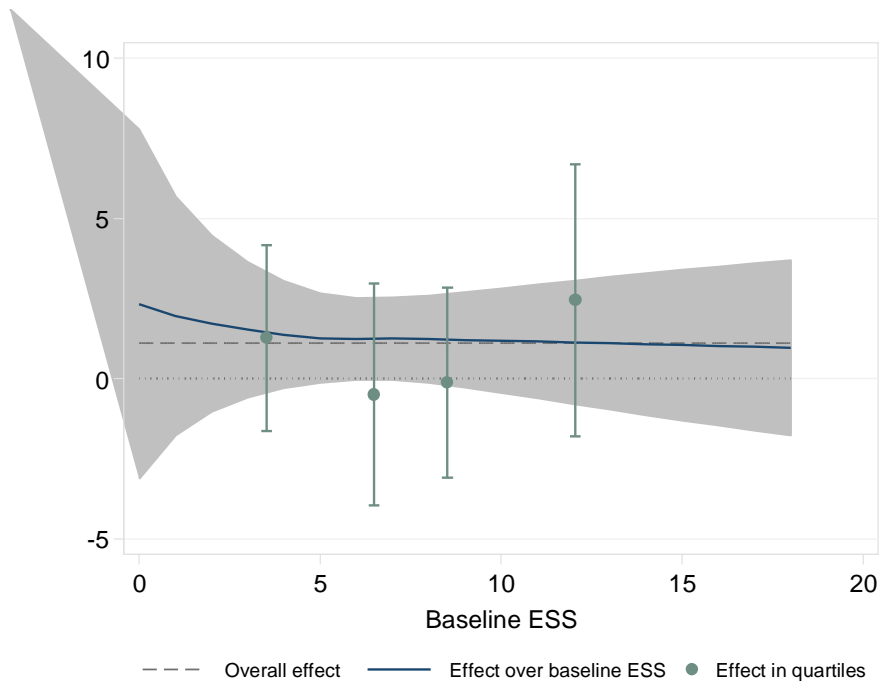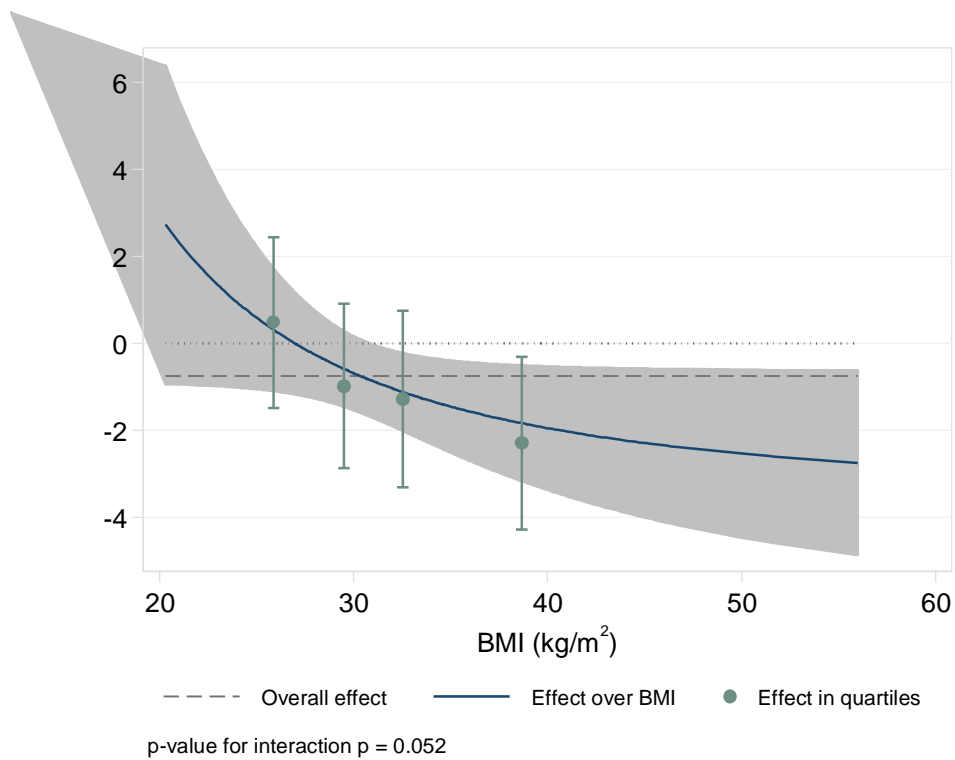
**eFigure 5.3: Effect of CPAP on change in systolic BP (SBP) compared to control over the full range and in quartiles of observed baseline Epworth Sleepiness Score (ESS)**



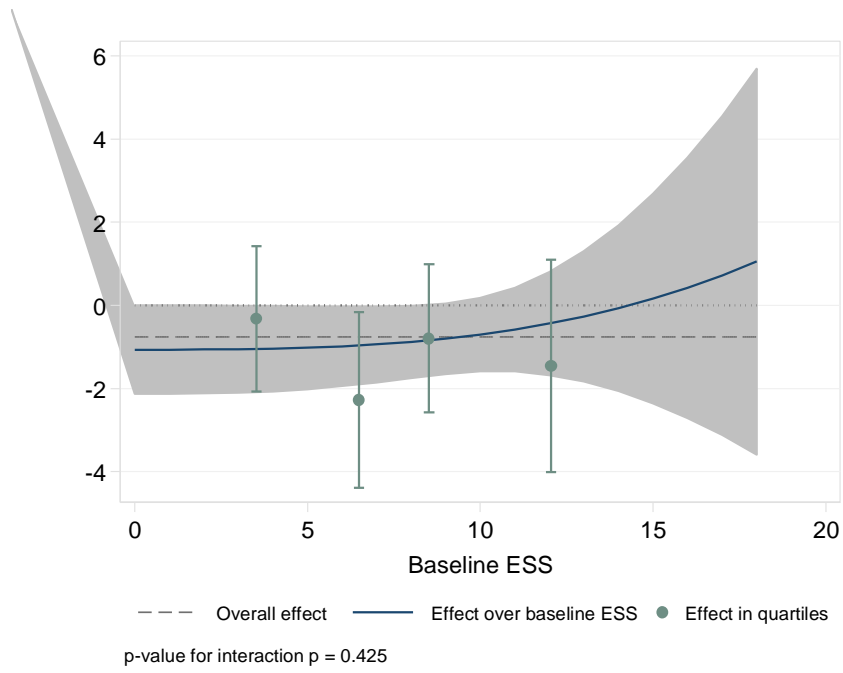p-value for interaction p = 0.098
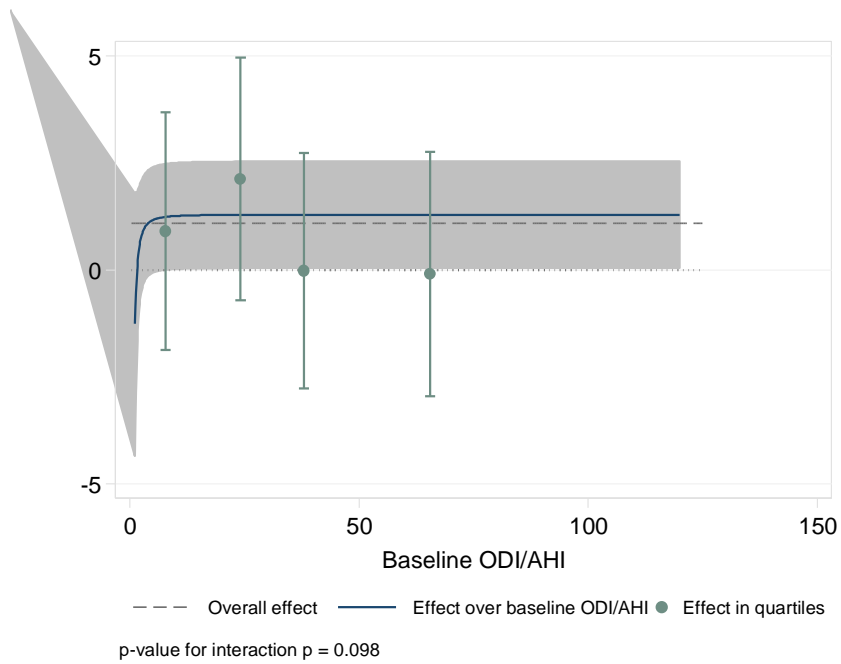
**eFigure 5.4: Effect of CPAP on change in systolic BP (SBP) compared to control over the full range and in quartiles of observed baseline ODI/AHI (events/hour)**
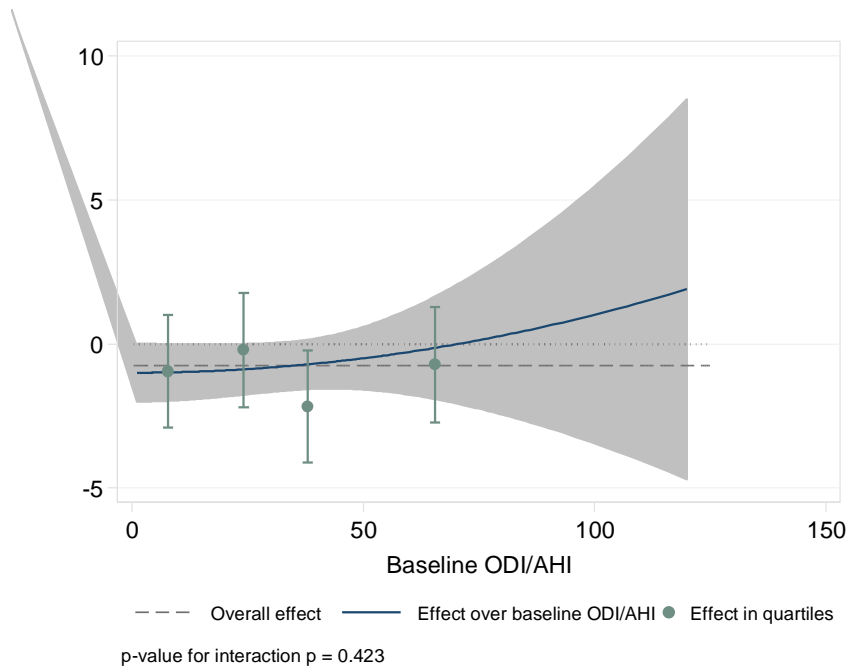
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**eFigure 5.5: effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed baseline DBP**
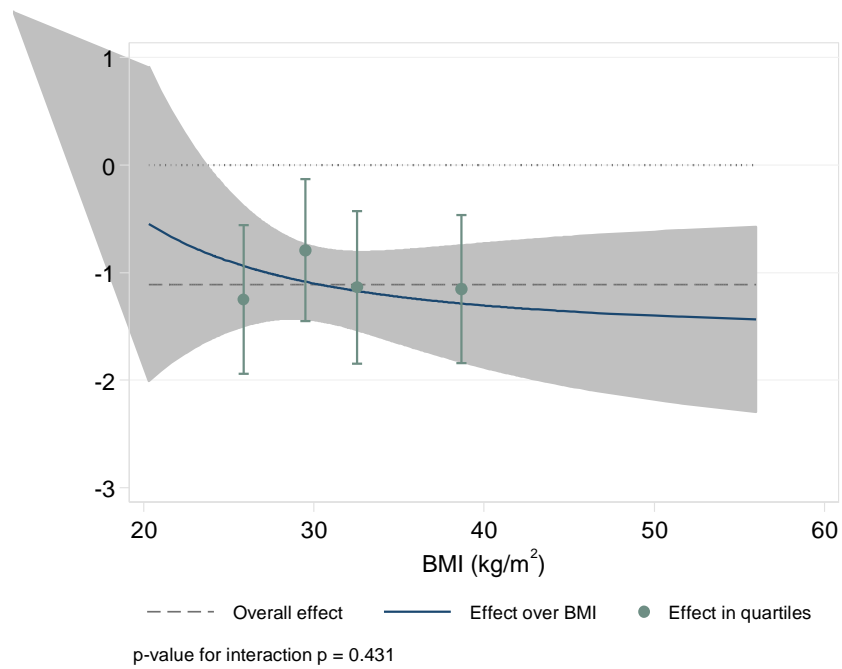


**eFigure 5.6: effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed BMI**

**eFigure 5.7: effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed baseline Epworth Sleepiness Score (ESS)**

**eFigure 5.8: Effect of CPAP on change in diastolic BP (DBP) compared to control over the full range and in quartiles of observed baseline ODI/AHI (events/hour)**



**eFigure 5.9: Effect of CPAP on change in Epworth Sleepiness Score (ESS) compared to control over the full range and in quartiles of observed body mass index (BMI)**