

Supplementary Online Content

Yu J, Zhou Z, McEvoy D, et al. Association of positive airway pressure with cardiovascular events and death in adults with sleep apnea: a systematic review and meta-analysis. *JAMA*. doi:10.1001/jama.2017.7967

eAppendix. Search Strategy

eFigure 1. Assessment of Risk of Bias Using Cochrane Collaboration Tool

eFigure 2. Random-Effects Meta-Regression of Selected Trial Characteristics on Risk Ratio of Major Adverse Cardiovascular Events Plus Hospitalization for Unstable Angina

eFigure 3. Random-Effects Meta-Regression of Selected Trial Characteristics on Risk Ratio of Cardiovascular Death

eFigure 4. Association of Positive Airway Pressure With Major Adverse Cardiovascular Events (MACE) and MACE Plus Hospitalization for Unstable Angina After Exclusion of Outlying Study Using Random-Effects Meta-Analysis

eFigure 5. Assessment of Publication Bias on Vascular Outcomes and Death

eTable 1. Individual Trial Data and Pooled Outcomes Using Random-Effects Model

eTable 2. Individual Trial Data and Pooled Outcomes in Subgroups Using Random-Effects Meta-Analysis

eReferences.

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Search Strategy

Medline and Cochran Central Register of Controlled Trials (Central) both searched via Ovid

1. randomized controlled trial.pt
2. controlled clinical trial.pt
3. randomized.tw
4. clinical trial/
5. randomly.ab
6. trial.ti
7. control.tw
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. exp sleep apnea syndromes/
10. exp sleep disorders/ and exp respiration/
11. (sleep* adj5 (apnea or apnoea or hypopnea or hypopnoea)).tw.
12. (sleep adj5 (cessation or cease* or periodic) adj5 (respiration or ventilation or air flow)).tw.
13. (SDB or OSAS or CSAS or OSA or SAHS or SAS).tw.
14. snoring.mp. or exp Snoring/
15. upper airway resistance syndrome.mp
16. exp sleep/ and exp breathing/
17. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18. exp positive-pressure respiration/
19. continuous positive airway*.tw.
20. airway pressure release ventilation.tw.
21. (positive pressure or positive-pressure).mp.
22. (CPAP or nCPAP or APRV or biPAP or apap or auto-cpap).mp

eAppendix. Search Strategy (*continued*)

23. 18 or 19 or 20 or 21 or 22

24. 8 and 17 and 23

EMBASE

1. 'randomized controlled trial'/exp or 'randomized controlled trial'.mp.
2. sleep apnea syndromes.mp. or sleep disordered breathing/
3. sleep disorder/ or sleep wake disorder.mp. or sleep/
4. 'sleep respiration'/exp OR 'sleep respiration'.mp.
5. central sleep apnea syndrome/ or sleep disorder/ or sleep apnea syndrome/ or sleep/ or sleep disordered breathing/ or sleep respiration.mp. or breathing/ or Cheyne Stokes breathing/
6. 'sleep apnoea'
7. 'sleep hypopnea'/exp OR 'sleep hypopnea'
8. 'sleep hypopnoea'/exp OR 'sleep hypopnoea'
9. 'sleep cessation'/exp OR 'sleep cessation' OR 'cease' OR 'periodic' OR 'respiration' OR 'ventilation' OR 'air flow'
10. 'SDB'/exp OR 'SDB'
11. 'OSAS'/exp OR 'OSAS'
12. 'CSAS'/exp OR 'CSAS'
13. 'OSA'/exp OR 'OSA'
14. 'SAHS'/exp OR 'SAHS'
15. 'SAS '/exp OR ' SAS '
16. 'snoring'/exp OR 'snoring'
17. 'Snoring'/exp OR 'Snoring'

eAppendix. Search Strategy (*continued*)

18. 'upper airway resistance syndrome'/exp OR 'upper airway resistance syndrome'
19. 'sleep'/exp OR 'sleep'
20. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 'positive-pressure respiration'/exp OR 'positive-pressure respiration'
22. 'continuous positive airway'/exp OR 'continuous positive airway'
23. 'airway pressure release ventilation'/exp OR 'airway pressure release ventilation'
24. 'positive pressure'/exp OR 'positive pressure'
25. 'positive-pressure'/exp OR 'positive-pressure'
26. 'CPAP'/exp OR 'CPAP'
27. 'nCPAP'/exp OR 'nCPAP'
28. 'APRV'/exp OR 'APRV'
29. 'biPAP'/exp OR 'biPAP'
30. 'apap'/exp OR 'apap '
31. 'auto-cpap'/exp OR 'auto-cpap'
32. 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33. 1 and 20 and 32

clinicaltrials.gov

1. sleep apnea syndromes.tw
2. sleep disorders.tw
3. (sleep* adj5 (apnea or apnoea or hypopnea or hypopnoea)).tw.
4. (sleep adj5 (cessation or cease* or periodic) adj5 (respiration or ventilation or air flow)).tw.
5. (SDB or OSAS or CSAS or OSA or SAHS or SAS).tw.

eAppendix. Search Strategy (*continued*)

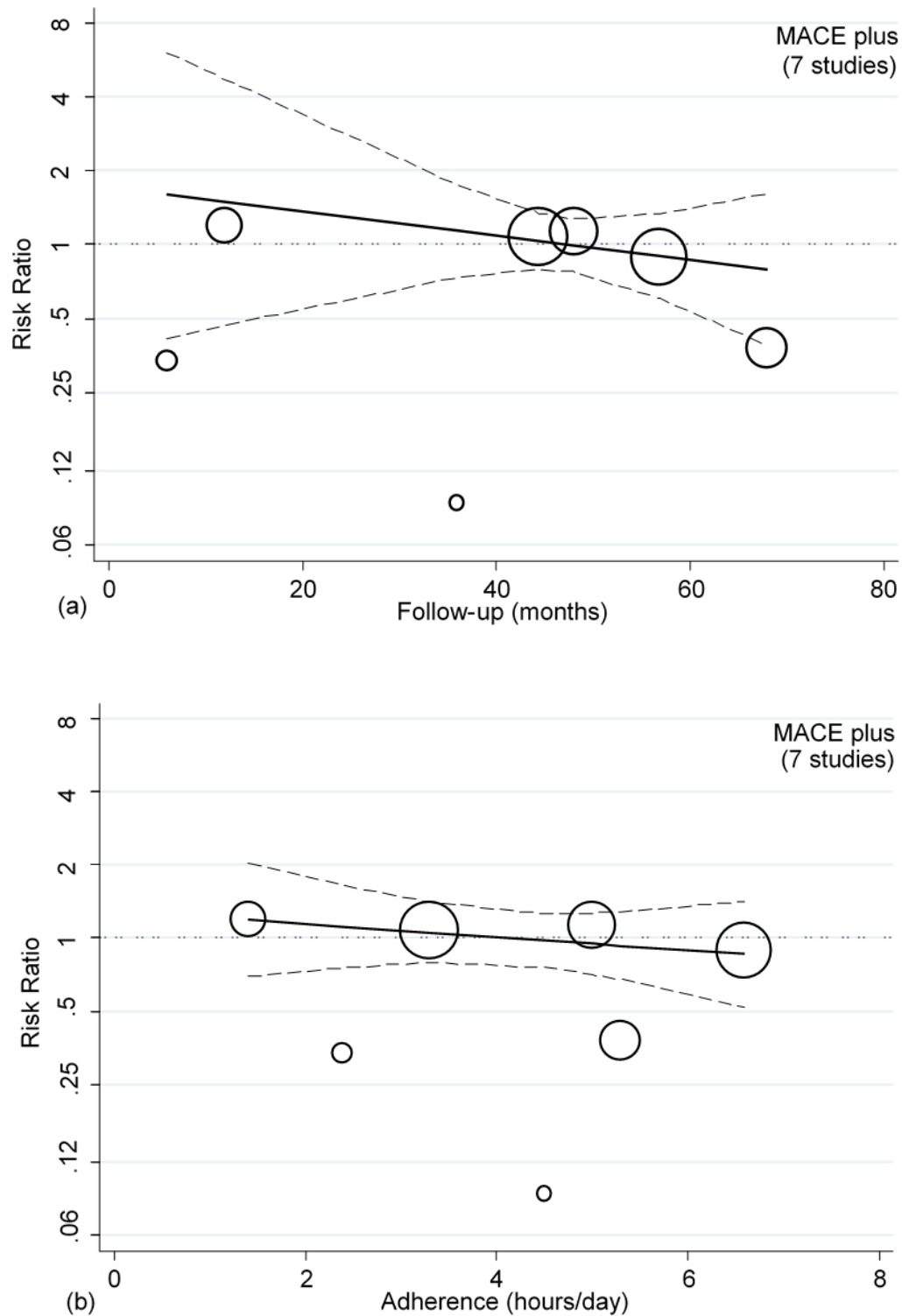
6. snoring.mp. or exp Snoring/
7. upper airway resistance syndrome.mp
8. positive-pressure respiration.tw
9. continuous positive airway*.tw.
10. airway pressure release ventilation.tw.
11. (positive pressure or positive-pressure).mp.
12. (CPAP or nCPAP or APRV or biPAP or apap or auto-cpap).mp

eFigure 1. Assessment of Risk of Bias Using Cochrane Collaboration Tool

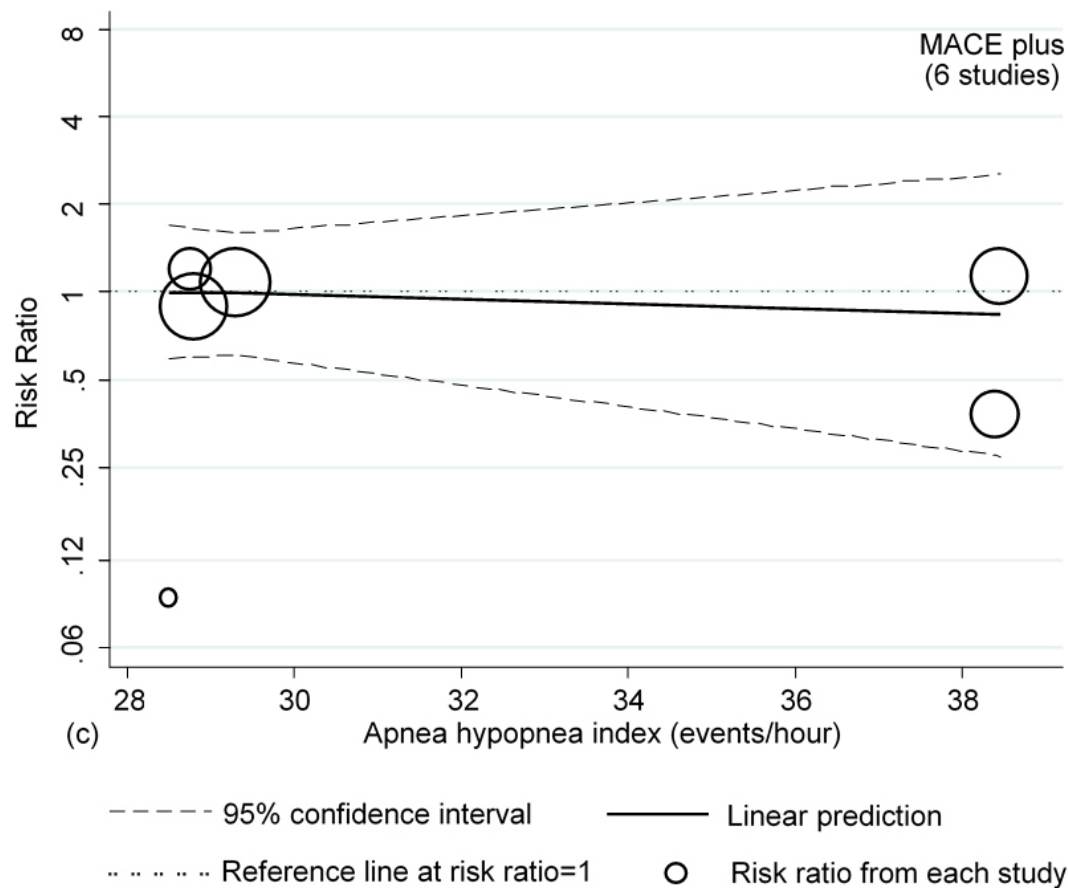
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bradley 2005 [1]	+	+	-	+	+	+	+
Barbe 2012 [2]	+	+	-	+	+	+	+
Craig 2012 [3]	+	+	-	+	+	+	+
Kushida 2012 [4]	+	+	+	+	+	+	+
McMillan 2014 [5]	+	+	-	+	+	+	+
Cowie 2015 [6]	+	+	-	+	+	+	+
Huang 2015 [7]	+	+	-	+	+	+	+
Parra 2015 [8]	+	+	-	?	+	+	+
McEvoy 2016 [9]	+	?	-	+	+	+	+
Peker 2016[10]	+	+	-	+	+	+	+

Legend:  Low risk of bias  High risk of bias  Unclear risk of bias

eFigure 2. Random-Effects Meta-Regression of Selected Trial Characteristics on Risk Ratio of Major Adverse Cardiovascular Events Plus Hospitalization for Unstable Angina



eFigure 2. (continued)



Legend: (a) Meta regression on risk ratio of MACE plus in 7 included studies^{2,3,5,7-10} according to length of follow-up with regression coefficient of -0.01 [95% confidence interval, -0.04 to 0.02] and p value =0.37.

(b) Meta regression on risk ratio of MACE plus according to adherence to positive airway pressure in 7 included studies^{2,3,5,7-10} with regression coefficient of -0.06 [-0.22 to 0.10] and p value =0.36.

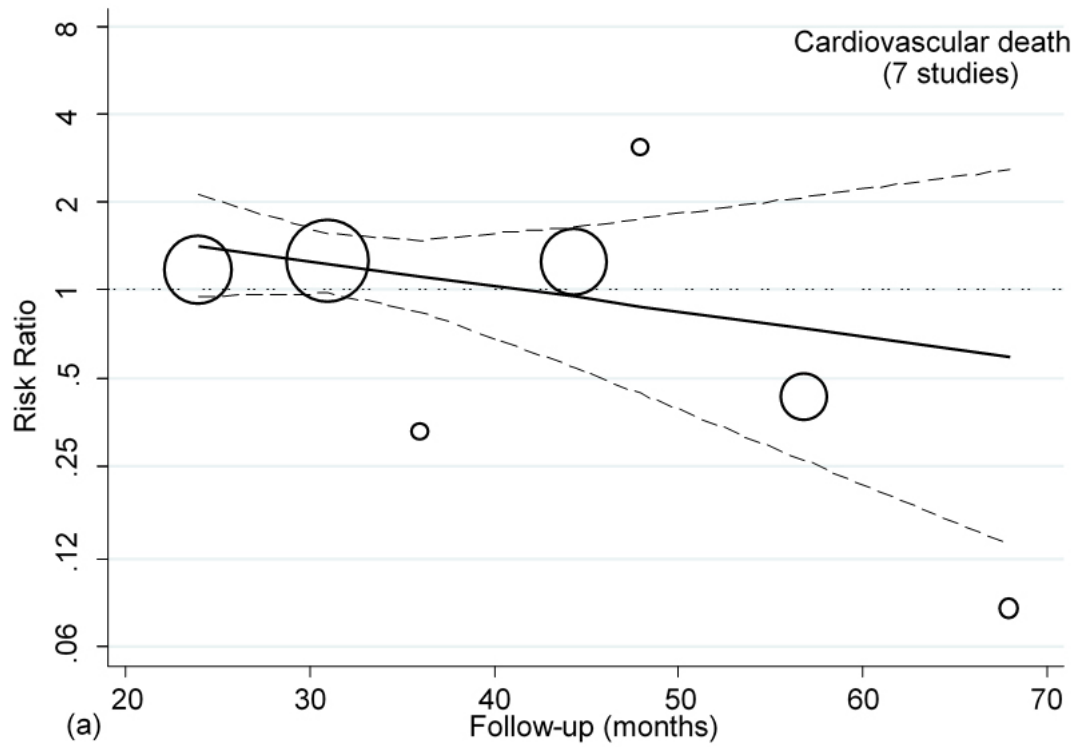
(c) Meta regression on risk ratio of MACE plus according to apnea hypopnea index at baseline in 6 included studies^{2,5,7-10} with regression coefficient of -0.02 [-0.13 to 0.09] and p value =0.68.

The size of the circles represents the weight given to each study. The circles are centred on the intersection of the relative risk for MACE on the vertical axis and the mean trial value of the metric of interest on the x-axis.

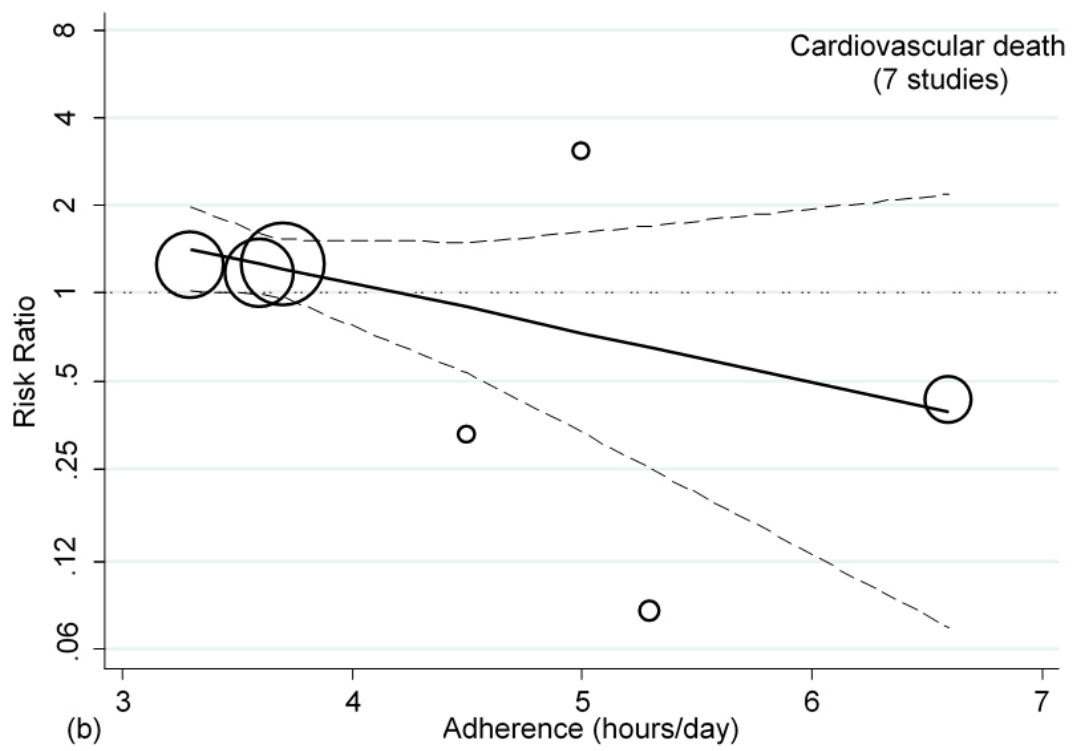
eFigure 2. *(continued)*

Abbreviations: MACE plus, major adverse cardiovascular events (consists of cardiovascular death, non-fatal acute coronary syndrome and non-fatal stroke) and hospitalization for unstable angina.

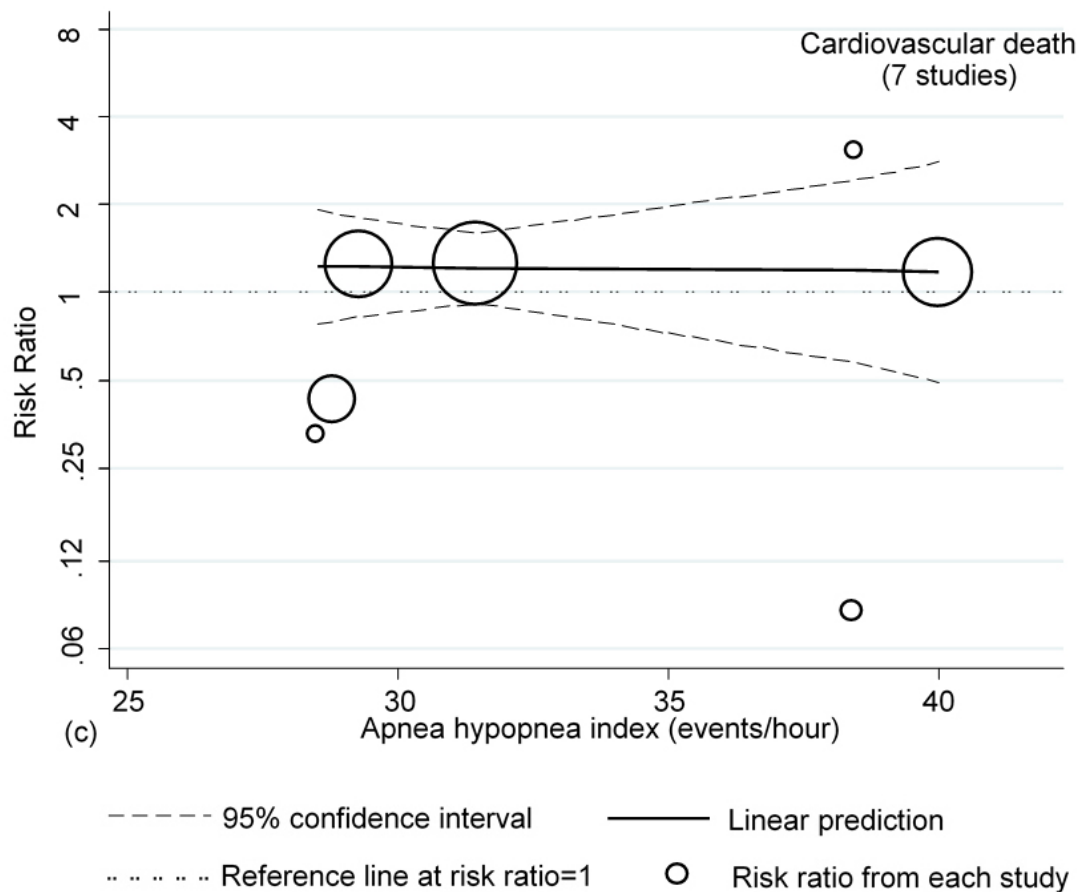
eFigure 3. Random-Effects Meta-Regression of Selected Trial Characteristics on Risk Ratio of Cardiovascular Death



eFigure 3. (continued)



eFigure 3. (continued)



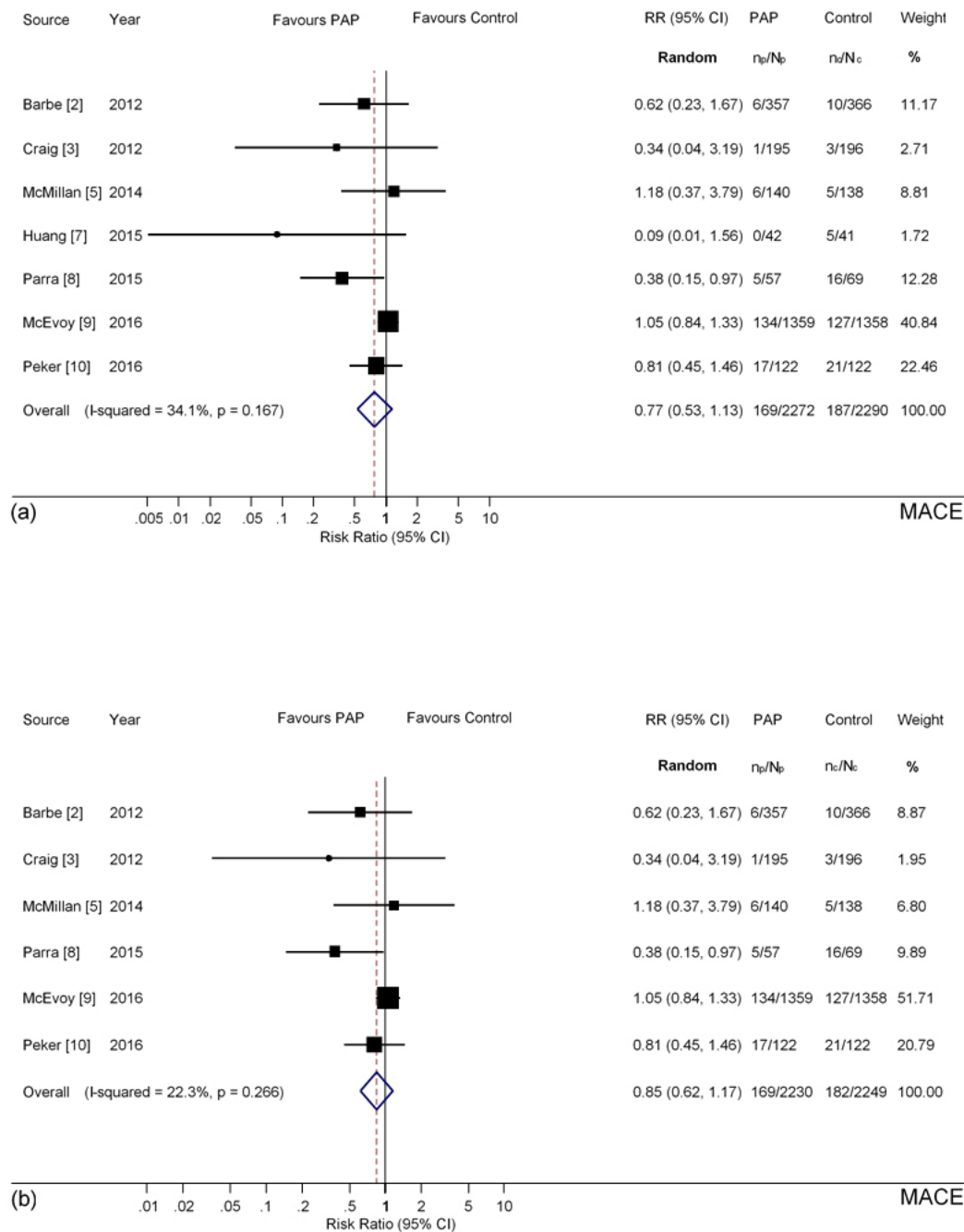
Legend: (a) Meta regression on risk ratio of cardiovascular death in 7 included studies^{1,2,6-10} according to length of follow-up with regression coefficient of -0.02 [95% confidence interval, -0.06 to 0.02] and p value =0.23.

(b) Meta regression on risk ratio of cardiovascular death according to adherence to positive airway pressure in 7 included studies^{1,2,6-10} with regression coefficient of -0.39 [-0.93 to 0.16] and p value =0.13.

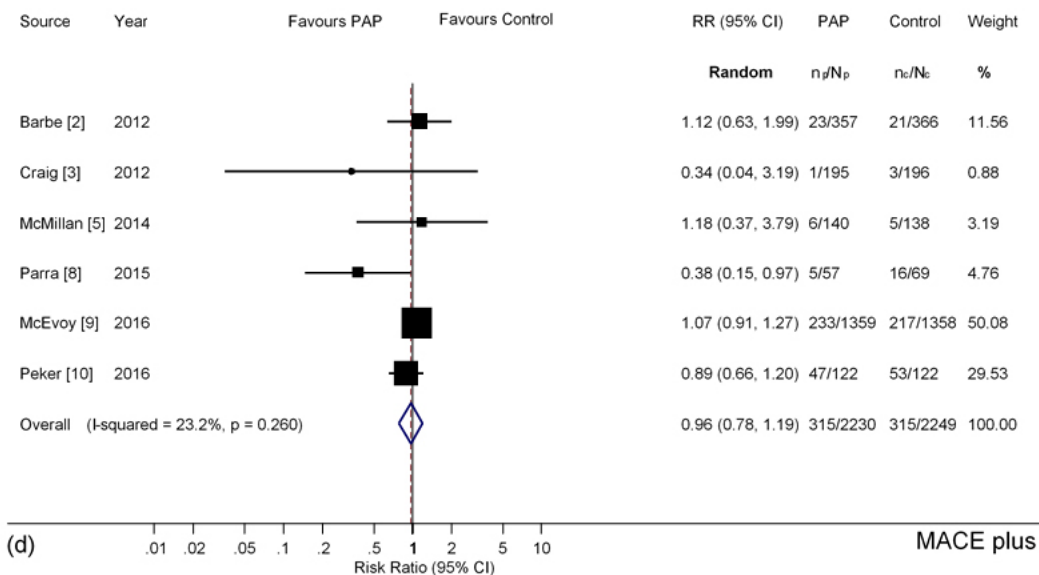
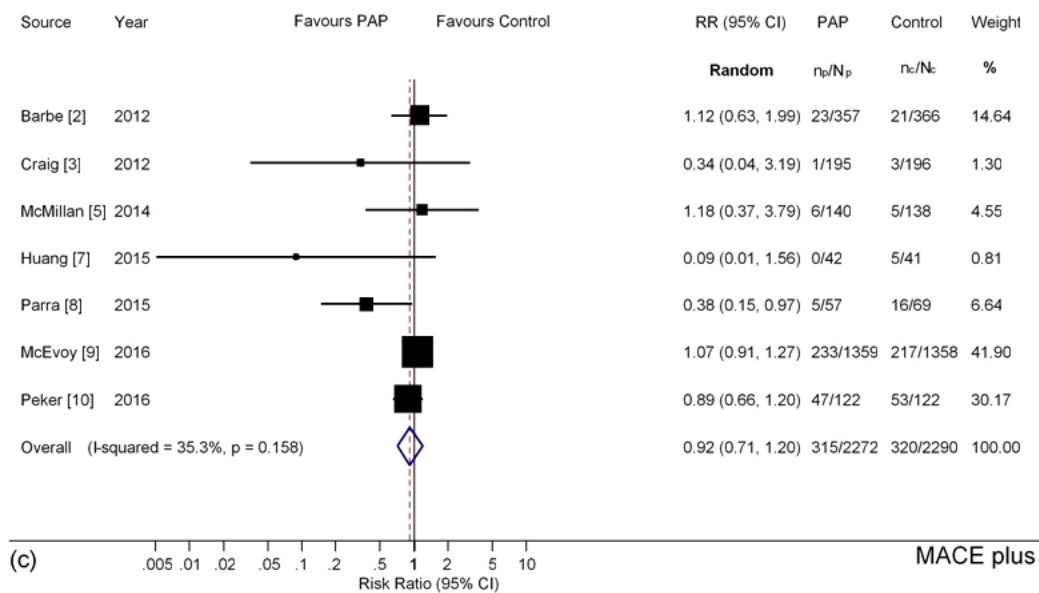
(c) Meta regression on risk ratio of cardiovascular death according to apnea hypopnea index at baseline in 7 included studies^{1,2,6-10} with regression coefficient of -0.00 [-0.10 to 0.09] and p value =0.93.

The size of the circles represents the weight given to each study. The circles are centred on the intersection of the relative risk for MACE on the vertical axis and the mean trial value of the metric of interest on the y-axis.

eFigure 4. Association of Positive Airway Pressure With Major Adverse Cardiovascular Events (MACE) and MACE Plus Hospitalization for Unstable Angina After Exclusion of Outlying Study Using Random-Effects Meta-Analysis



eFigure 4. (continued)



Legend: (a) Pooled relative risks estimated by random-effect model for MACE.

(b) Pooled relative risks estimated by random-effect model for MACE after dropping Huang et al⁷.

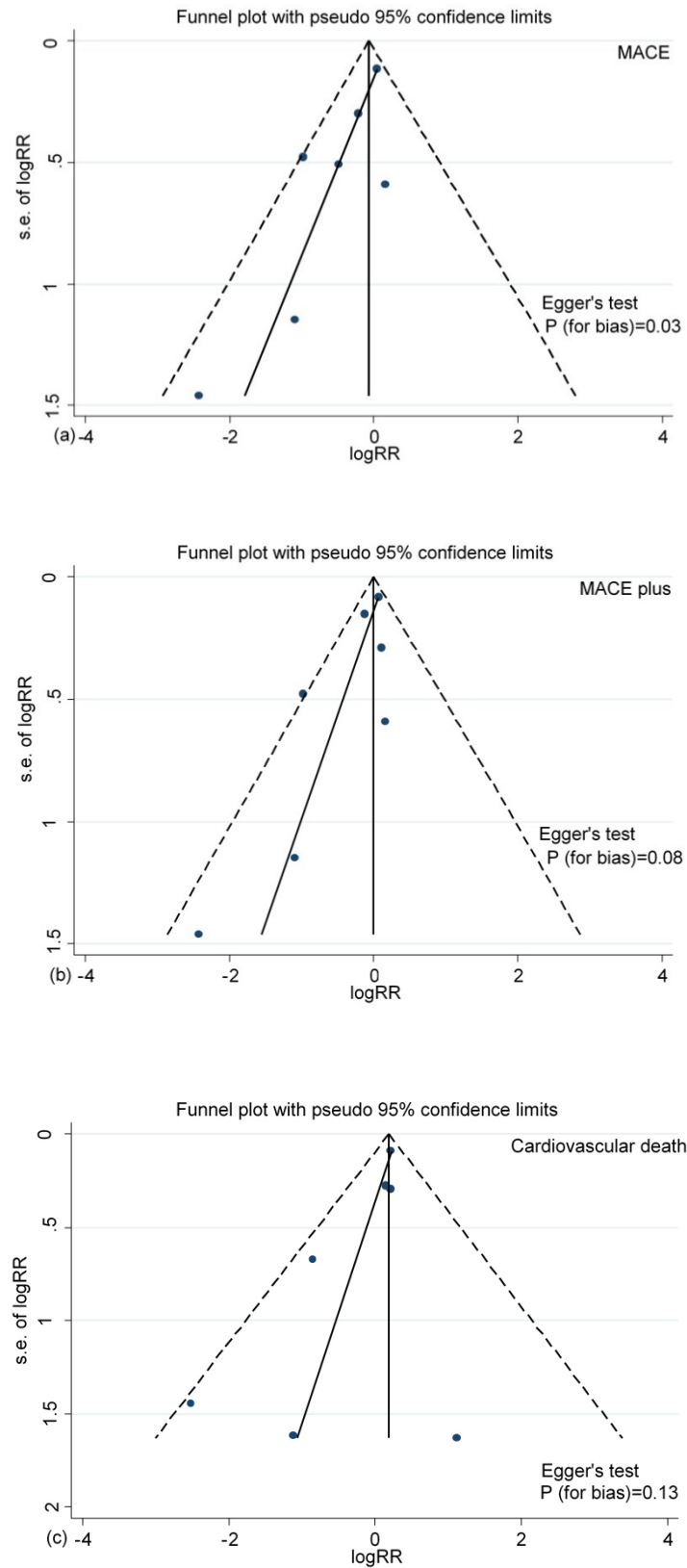
(c) Pooled relative risks estimated by random-effect model for MACE plus.

(d) Pooled relative risk estimated by random-effect model for MACE plus after dropping Huang et al⁷.

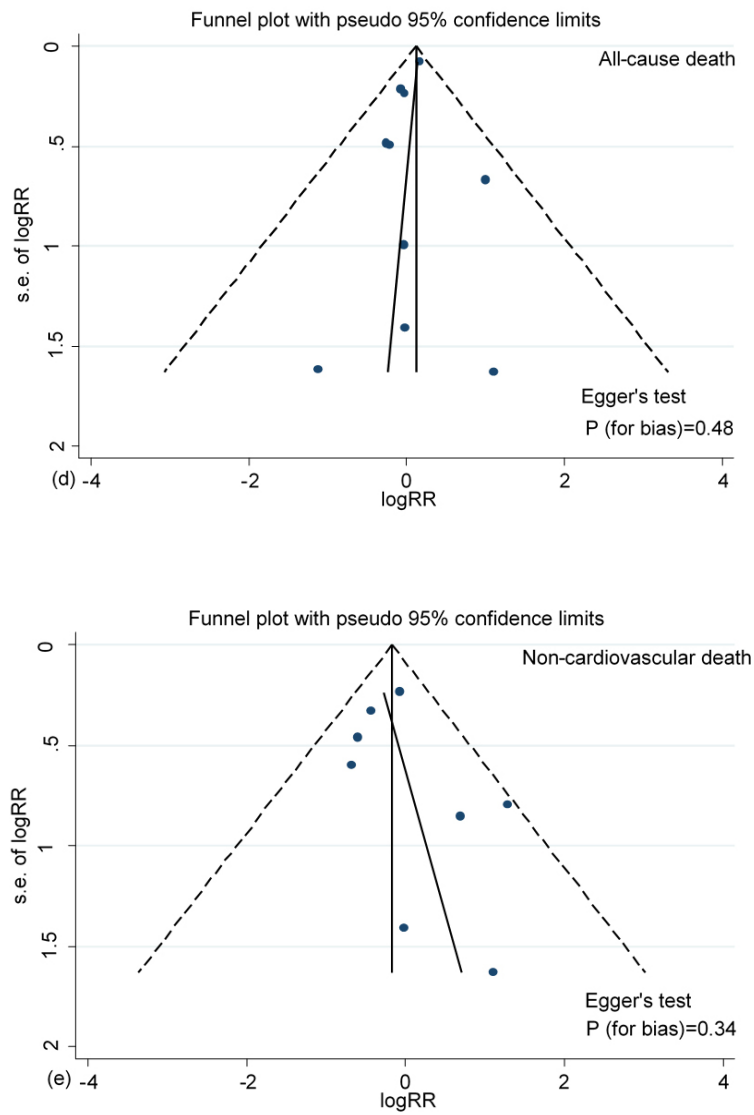
Box sizes are proportional to study weight with the centre of the box placed at the point estimate of effect and the horizontal line extending from the upper to the lower margins of the 95% confidence interval for each individual study. The centre of the diamond is placed at the point estimate of the summary metric of association with the tips of the diamond extending from the upper to the lower margins of the 95% confidence interval. The I-squared value indicates the percentage of variability across the pooled estimates attributable to heterogeneity beyond chance with an I-squared statistic of 0-25% considered to reflect a low likelihood, 26-75% a moderate likelihood, and 76-100% a high likelihood. The p value is for a test of heterogeneity across all studies with a p value of ≤ 0.05 indicating likely variation across pooled estimates beyond chance.

Abbreviations: MACE, major adverse cardiovascular events (consists of cardiovascular death, non-fatal acute coronary syndrome and non-fatal stroke); MACE plus, MACE and hospitalization for unstable angina; n_C : number of cardiovascular events or death in control group; N_C : number of participants in control group; n_P : number of cardiovascular events or death in treatment with positive airway pressure; N_P : number of participants in treatment with positive airway pressure; PAP: positive airway pressure; RR: risk ratio.

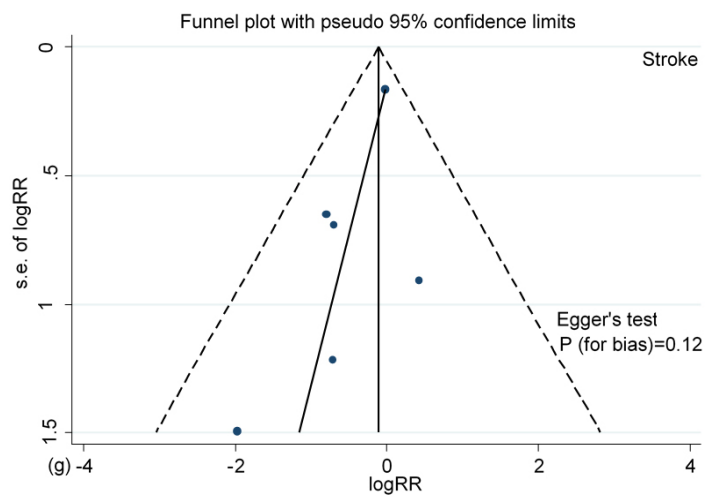
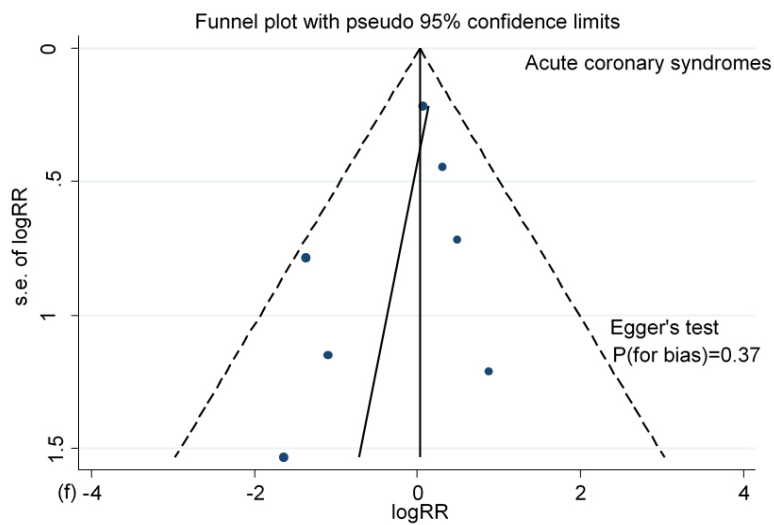
eFigure 5. Assessment of Publication Bias on Vascular Outcomes and Death



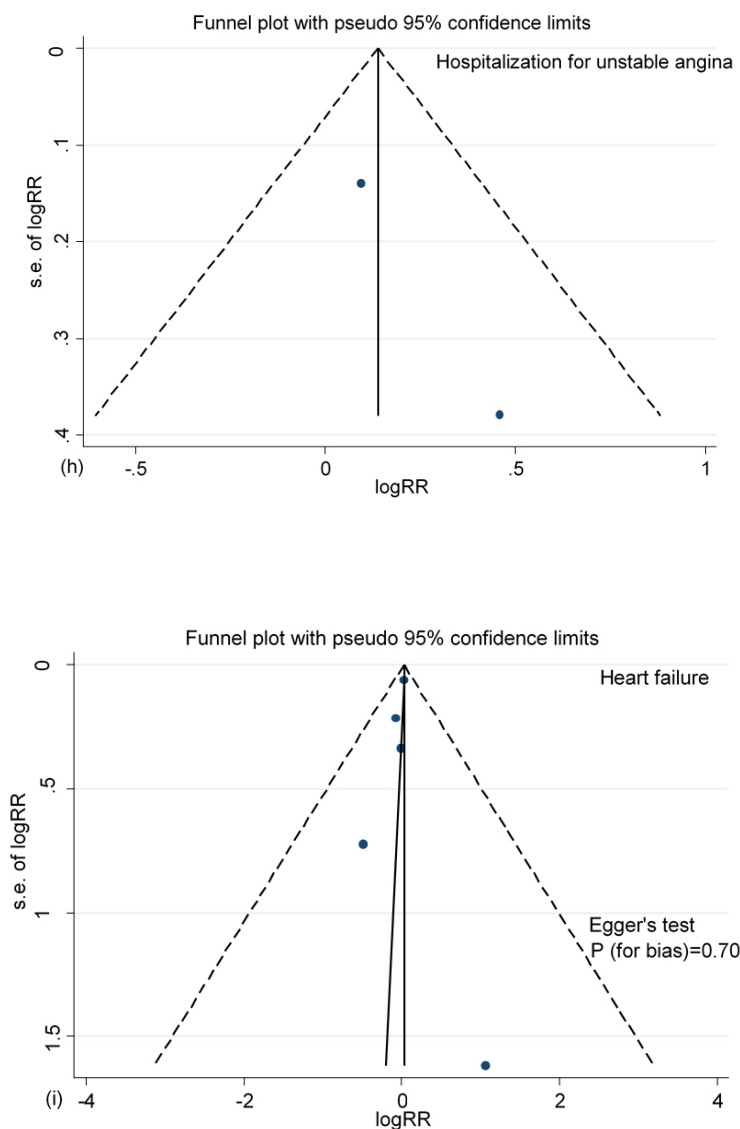
eFigure 5. (continued)



eFigure 5. (continued)



eFigure 5. (continued)



Legend: Funnel plot and Egger's regression test for (a) MACE ($p=0.03$); (b) MACE plus ($p=0.08$); (c) cardiovascular death ($p=0.13$); (d) all-cause death ($p=0.48$); (e) non-cardiovascular death ($p=0.34$); (f) acute coronary syndromes ($p=0.37$); (g) stroke ($p=0.12$); (h) hospitalization for unstable angina (Egger's regression test was not applicable since only two included studies); (i) heart failure ($p=0.70$).

The contour lines (dashed) define the region within which 95% of points would be expected to lie in the absence of both heterogeneity and publication bias. The total overall estimate for the meta-analysis is represented by the vertical line. The linear

eFigure 5. *(continued)*

regression is represented by the diagonal line.

Abbreviations: MACE, major adverse cardiovascular events (consists of cardiovascular death, non-fatal acute coronary syndrome and non-fatal stroke); MACE plus, MACE plus hospitalization for unstable angina.

eTable 1. Individual Trial Data and Pooled Outcomes Using Random-Effects Model

Study	PAP		Control		Risk Ratio Random, 95% CI	Weight* (%)	Risk difference Random, 95% CI	Weight† (%)
	n _P	N _P	n _C	N _C				
MACE								
Barbe 2012 [2]	6	357	10	366	0.62 [0.23 to 1.68]	11.17	-0.01 [-0.03 to 0.01]	26.07
Craig 2012 [3]	1	195	3	196	0.34 [0.04 to 3.19]	2.71	-0.01 [-0.03 to 0.01]	27.25
McMillan 2014 [5]	6	140	5	138	1.18 [0.37 to 3.79]	8.81	0.01 [-0.04 to 0.05]	12.03
Huang 2015 [7]	0	42	5	41	0.09 [0.01 to 1.56]	1.72	-0.12 [-0.23 to -0.02]	2.96
Parra 2015 [8]	5	57	16	69	0.38 [0.15 to 0.97]	12.28	-0.14 [-0.27 to -0.02]	2.25
McEvoy 2016 [9]	134	1359	127	1358	1.05 [0.84 to 1.33]	40.84	0.01 [-0.02 to 0.03]	25.45
Peker 2016 [10]	17	122	21	122	0.81 [0.45 to 1.46]	22.46	-0.03 [-0.12 to 0.06]	3.98
Total (95% CI)	169	2272	187	2290	0.77 [0.53 to 1.13]	100.00	-0.01 [-0.03 to 0.01]	100.00
					Heterogeneity: Tau ² =0.08; Chi ² =9.11; P=0.17; I ² =34.10% Overall effect: z=1.31; P=0.19		Heterogeneity: Tau ² <0.01; Chi ² =11.15; P=0.08; I ² =46.20% Overall effect: z=1.19; P=0.23	
MACE plus								
Barbe 2012 [2]	23	357	21	366	1.12 [0.63 to 1.99]	14.64	0.01 [-0.03 to 0.04]	20.42
Craig 2012 [3]	1	195	3	196	0.34 [0.04 to 3.19]	1.30	-0.01 [-0.03 to 0.01]	28.07
McMillan 2014 [5]	6	140	5	138	1.18 [0.37 to 3.79]	4.55	0.01 [-0.04 to 0.05]	15.79
Huang 2015 [7]	0	42	5	41	0.09 [0.01 to 1.56]	0.81	-0.12 [-0.23 to -0.02]	4.64
Parra 2015 [8]	5	57	16	69	0.38 [0.15 to 0.97]	6.64	-0.14 [-0.27 to -0.02]	3.59
McEvoy 2016 [9]	233	1359	217	1358	1.07 [0.91 to 1.27]	41.90	0.01 [-0.02 to 0.04]	23.87
Peker 2016 [10]	47	122	53	122	0.89 [0.66 to 1.20]	30.17	-0.05 [-0.17 to 0.07]	3.62
Total (95% CI)	315	2272	320	2290	0.92 [0.71 to 1.20]	100.00	-0.01 [-0.03 to 0.01]	100.00
					Heterogeneity: Tau ² =0.03; Chi ² =9.28;		Heterogeneity: Tau ² <0.01; Chi ² =12.53;	

eTable 1. Individual Trial Data and Pooled Outcomes Using Random-Effects Model
(continued)

Study	PAP		Control		Risk Ratio Random, 95% CI	Weight* (%)	Risk difference Random, 95% CI	Weight† (%)
	n _P	N _P	n _C	N _C				
					P=0.16; I ² =35.30% Overall effect: z=0.61; P=0.54		P=0.05; I ² =52.10% Overall effect: z=0.81; P=0.42	
Cardiovascular death								
Bradley 2005 [1]	23	128	20	130	1.17 [0.68 to 2.02]	18.21	0.03 [-0.07 to 0.12]	4.61
Barbe 2012 [2]	1	357	0	366	3.08 [0.13 to 75.24]	0.68	0.00 [-0.00 to 0.01]	29.25
Cowie 2015 [6]	199	666	158	659	1.25 [1.04 to 1.49]	59.28	0.06 [0.01 to 0.11]	11.99
Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.69	-0.02 [-0.09 to 0.04]	7.95
Parra 2015 [8]	0	57	7	69	0.08 [0.00 to 1.38]	0.86	-0.10 [-0.18 to -0.03]	6.16
McEvoy 2016 [9]	2 5	1359	20	1358	1.25 [0.70 to 2.24]	16.48	0.00 [-0.01 to 0.01]	28.63
Peker 2016 [10]	3	122	7	122	0.43 [0.11 to 1.62]	3.79	-0.03 [-0.08 to 0.02]	11.42
Total (95% CI)	251	2731	213	2745	1.15 [0.88 to 1.50]	100.00	-0.00 [-0.02 to 0.02]	100.00
					Heterogeneity: Tau ² =0.02; Chi ² =7.08; P=0.31; I ² =15.30% Overall effect: z=1.05; P=0.30		Heterogeneity: Tau ² <0.01; Chi ² =28.59; P<0.001; I ² =79.00% Overall effect: z=0.17; P=0.87	
All-cause death								
Bradley 2005 [1]	27	128	28	130	0.98 [0.61 to 1.57]	8.48	-0.00 [-0.10 to 0.10]	0.93
Barbe 2012 [2]	8	357	3	366	2.73 [0.73 to 10.22]	1.07	0.01 [-0.00 to 0.03]	14.72
Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	0.18	0.01 [-0.01 to 0.02]	18.15
Kushida 2012 [4]	2	556	2	542	0.97 [0.14 to 6.90]	0.49	-0.00 [-0.01 to 0.01]	25.22
McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	0.24	-0.00 [-0.02 to 0.02]	13.21
Cowie 2015 [6]	232	666	193	659	1.19 [1.02 to 1.39]	74.96	0.06 [0.01 to 0.11]	3.36
Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.19	-0.02 [-0.09 to 0.04]	2.12
Parra 2015 [8]	6	57	9	69	0.81 [0.31 to 2.13]	1.97	-0.03 [-0.14 to 0.09]	0.73

eTable 1. Individual Trial Data and Pooled Outcomes Using Random-Effects Model
(continued)

Study	PAP		Control		Risk Ratio Random, 95% CI	Weight* (%)	Risk difference Random, 95% CI	Weight† (%)
	n _P	N _P	n _C	N _C				
McEvoy 2016 [9]	40	1359	43	1358	0.93 [0.61 to 1.42]	10.37	-0.00 [-0.02 to 0.01]	19.28
Peker 2016 [10]	7	122	9	122	0.78 [0.30 to 2.02]	2.04	-0.02 [-0.08 to 0.05]	2.28
Total (95% CI)	324	3622	289	3621	1.13 [0.99 to 1.29]	100.00	0.00 [-0.01 to 0.01]	100.00
					Heterogeneity: Tau ² <0.01; Chi ² =5.35; P=0.80; I ² =0.00% Overall effect: z=1.75; P=0.08		Heterogeneity: Tau ² <0.01; Chi ² =17.19; P=0.05; I ² =47.60% Overall effect: z=0.66; P=0.51	
Non-cardiovascular death								
Bradley 2005 [1]	4	128	8	130	0.51 [0.16 to 1.64]	8.00	-0.03 [-0.08 to 0.02]	2.17
Barbe 2012 [2]	7	357	13	366	0.55 [0.22 to 1.37]	13.11	-0.02 [-0.04 to 0.01]	9.18
Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	1.12	0.01 [-0.01 to 0.02]	22.00
McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	1.49	-0.00 [-0.02 to 0.02]	12.61
Cowie 2015 [6]	33	666	35	659	0.93 [0.59 to 1.48]	43.23	-0.00 [-0.03 to 0.02]	9.21
Parra 2015 [8]	6	57	2	69	3.63 [0.76 to 17.31]	4.60	0.08 [-0.01 to 0.17]	0.73
McEvoy 2016 [9]	15	1359	23	1358	0.65 [0.34 to 1.24]	24.47	-0.01 [-0.01 to 0.00]	40.42
Peker 2016 [10]	4	122	2	122	2.00 [0.37 to 10.72]	3.99	0.02 [-0.02 to 0.06]	3.69
Total (95% CI)	71	3024	84	3038	0.85 [0.60 to 1.19]	100.00	-0.00 [-0.01 to 0.01]	100.00
					Heterogeneity: Tau ² =0.01; Chi ² =7.35; P=0.39; I ² =4.80% Overall effect: z=0.97; P=0.33		Heterogeneity: Tau ² <0.01; Chi ² =8.12; P=0.32; I ² =13.80% Overall effect: z=0.66; P=0.51	
Acute coronary syndromes								
Barbe 2012 [2]	2	357	8	366	0.26 [0.05 to 1.20]	7.42	-0.02 [-0.03 to 0.00]	26.74
Craig 2012 [3]	1	195	3	196	0.34 [0.04 to 3.19]	3.59	-0.01 [-0.03 to 0.01]	21.46
McMillan 2014 [5]	5	140	3	138	1.64 [0.40 to 6.74]	8.75	0.01 [-0.03 to 0.05]	7.11

eTable 1. Individual Trial Data and Pooled Outcomes Using Random-Effects Model
(continued)

Study	PAP		Control		Risk Ratio Random, 95% CI	Weight [*] (%)	Risk difference Random, 95% CI	Weight [†] (%)
	n _P	N _P	n _C	N _C				
Huang 2015 [7]	0	42	2	41	0.20 [0.01 to 3.95]	2.05	-0.05 [-0.13 to 0.03]	1.92
Parra 2015 [8]	2	57	1	69	2.42 [0.23 to 26.02]	3.25	0.02 [-0.03 to 0.08]	3.74
McEvoy 2016 [9]	42	1359	39	1358	1.08 [0.70 to 1.65]	54.63	0.00 [-0.01 to 0.01]	36.43
Peker 2016 [10]	11	122	8	122	1.38 [0.57 to 3.30]	20.32	0.02 [-0.04 to 0.09]	2.59
Total (95% CI)	63	2272	64	2290	1.00 [0.65 to 1.55]	100.00	-0.00 [-0.02 to 0.01]	100.00
					Heterogeneity: Tau ² =0.04; Chi ² =6.68; P=0.35; I ² =10.20% Overall effect: z=0.01; P=0.99		Heterogeneity: Tau ² <0.01; Chi ² =7.58; P=0.27; I ² =20.90% Overall effect: z=0.76; P=0.45	
Stroke								
Barbe 2012 [2]	3	357	2	366	1.54 [0.26 to 9.15]	2.86	0.00 [-0.01 to 0.02]	42.63
McMillan 2014 [5]	1	140	2	138	0.49 [0.05 to 5.37]	1.59	-0.01 [-0.03 to 0.02]	17.72
Huang 2015 [7]	0	42	3	41	0.14 [0.01 to 2.62]	1.06	-0.07 [-0.16 to 0.02]	1.65
Parra 2015 [8]	3	57	8	69	0.45 [0.13 to 1.63]	5.55	-0.06 [-0.16 to 0.03]	1.46
McEvoy 2016 [9]	67	1359	68	1358	0.98 [0.71 to 1.37]	84.05	-0.00 [-0.02 to 0.02]	30.90
Peker 2016 [10]	3	122	6	122	0.50 [0.13 to 1.95]	4.89	-0.02 [-0.07 to 0.02]	5.64
Total (95% CI)	77	2077	89	2094	0.90 [0.66 to 1.21]	100.00	-0.00 [-0.02 to 0.01]	100.00
					Heterogeneity: Tau ² <0.01; Chi ² =4.26; P=0.51; I ² =0.00% Overall effect: z=0.72; P=0.47		Heterogeneity: Tau ² <0.01; Chi ² =6.37; P=0.27; I ² =21.50% Overall effect: z=0.64; P=0.52	
Hospitalization for unstable angina								
Barbe 2012 [2]	17	357	11	366	1.58 [0.75 to 3.34]	12.04	0.02 [-0.01 to 0.05]	31.55
McEvoy 2016 [9]	99	1359	90	1358	1.10 [0.83 to 1.45]	87.96	0.01 [-0.01 to 0.03]	68.45
Total (95% CI)	116	1716	101	1724	1.15 [0.89 to 1.49]	100.00	0.01 [-0.01 to 0.03]	100.00

eTable 1. Individual Trial Data and Pooled Outcomes Using Random-Effects Model
(continued)

Study	PAP		Control		Risk Ratio Random, 95% CI	Weight [*] (%)	Risk difference Random, 95% CI	Weight [†] (%)
	n _P	N _P	n _C	N _C				
					Heterogeneity: Tau ² <0.01; Chi ² =0.82; P=0.37; I ² =0.00% Overall effect: z=1.05; P=0.29		Heterogeneity: Tau ² <0.01; Chi ² =0.42; P=0.52; I ² =0.00% Overall effect: z=1.24; P=0.21	
Heart failure								
Barbe 2012 [2]	3	357	5	366	0.62 [0.15 to 2.55]	0.69	-0.01 [-0.02 to 0.01]	22.40
Cowie 2015 [6]	287	666	272	659	1.04 [0.92 to 1.18]	88.42	0.02 [-0.03 to 0.07]	1.83
Huang 2015 [7]	1	42	0	41	2.93 [0.12 to 69.92]	0.14	0.02 [-0.04 to 0.09]	1.27
McEvoy 2016 [9]	17	1359	17	1358	1.00 [0.51 to 1.95]	3.15	-0.00 [-0.01 to 0.01]	74.07
Peker 2016 [10]	30	122	32	122	0.94 [0.61 to 1.44]	7.60	-0.02 [-0.13 to 0.09]	0.43
Total (95% CI)	338	2546	326	2546	1.03 [0.92 to 1.16]	100.00	-0.00 [-0.01 to 0.01]	100.00
					Heterogeneity: Tau ² <0.01; Chi ² =1.16; P=0.88; I ² =0.00% Overall effect: z=0.52; P=0.60		Heterogeneity: Tau ² <0.01; Chi ² =2.81; P=0.59; I ² =0.00% Overall effect: z=0.17; P=0.87	

*Weight of risk ratio.

†Weight of risk difference.

Abbreviations: MACE, major adverse cardiovascular events (consists of cardiovascular death, non-fatal acute coronary syndrome and non-fatal stroke); MACE plus, MACE and hospitalization for unstable angina; n_C: number of cardiovascular events or death in control group; N_C: number of participants in control group; n_P: number of cardiovascular events or death in treatment with positive airway pressure; N_P: number of participants in treatment with positive airway pressure; PAP: positive airway pressure.

eTable 2. Individual Trial Data and Pooled Outcomes in Subgroups Using Random-Effects Model

Subgroup		Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
			n _P	N _P	n _C	N _C		
MACE								
Adherence<4 hours/day	Craig 2012 [3]	1	195	3	196	0.34 [0.04 to 3.19]	2.71	
	McMillan 2014 [5]	6	140	5	138	1.18 [0.37 to 3.79]	8.81	
	McEvoy 2016 [9]	134	1359	127	1358	1.05 [0.84 to 1.33]	40.84	
	Subtotal (95% CI)	141	1694	135	1692	1.05 [0.84 to 1.31]	52.36	
		Heterogeneity: Tau ² <0.01; Chi ² =1.03; P=0.60; I ² =0.00% Subgroup effect: z=0.40; P=0.69						
Adherence≥4 hours/day	Barbe 2012 [2]	6	357	10	366	0.62 [0.23 to 1.67]	11.17	
	Huang 2015 [7]	0	42	5	41	0.09 [0.01 to 1.56]	1.72	
	Parra 2015 [8]	5	57	16	69	0.38 [0.15 to 0.97]	12.28	
	Peker 2016 [10]	17	122	21	122	0.81 [0.45 to 1.46]	22.46	
	Subtotal (95% CI)	28	578	52	598	0.58 [0.34 to 0.99]	47.64	
		Heterogeneity: Tau ² =0.06; Chi ² =3.74; P=0.29; I ² =19.70% Subgroup effect: z=1.99; P=0.05						
Specify [†]	Barbe 2012 [2]	6	357	10	366	0.62 [0.23 to 1.67]	11.17	
	Huang 2015 [7]	0	42	5	41	0.09 [0.01 to 1.56]	1.72	
	Parra 2015 [8]	5	57	16	69	0.38 [0.15 to 0.97]	12.28	
	McEvoy 2016 [9]	134	1359	127	1358	1.05 [0.84 to 1.33]	40.84	
	Peker 2016 [10]	17	122	21	122	0.81 [0.45 to 1.46]	22.46	
	Subtotal (95% CI)	162	1937	179	1956	0.73 [0.46 to 1.16]	88.47	
		Heterogeneity: Tau ² =0.12; Chi ² =8.15; P=0.09; I ² =50.90% Subgroup effect: z=1.35; P=0.18						
Not specify [†]	Craig 2012 [3]	1	195	3	196	0.34 [0.04 to 3.19]	2.71	
	McMillan 2014 [5]	6	140	5	138	1.18 [0.37 to 3.79]	8.81	
	Subtotal (95% CI)	7	335	8	334	0.91 [0.32 to 2.55]	11.53	
		Heterogeneity: Tau ² <0.01; Chi ² =0.96; P=0.33; I ² =0.00% Subgroup effect: z=0.18; P=0.85						

eTable 2. (continued)

Subgroup	Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
		n _p	N _p	n _c	N _c		
MACE plus							
Adherence<4 hours/day	Craig 2012 [3]	1	195	3	196	0.34 [0.04 to 3.19]	1.30
	McMillan 2014 [5]	6	140	5	138	1.18 [0.37 to 3.79]	4.55
	McEvoy 2016 [9]	233	1359	217	1358	1.07 [0.91 to 1.27]	41.90
	Subtotal (95% CI)	240	1694	225	1692	1.07 [0.90 to 1.26]	47.74
		Heterogeneity: Tau ² <0.01; Chi ² =1.05; P=0.59; I ² =0.00% effect: z=0.78; P=0.44					Subgroup
Adherence≥4 hours/day	Barbe 2012 [2]	23	357	21	366	1.12 [0.63 to 1.99]	14.64
	Huang 2015 [7]	0	42	5	41	0.09 [0.01 to 1.56]	0.81
	Parra 2015 [8]	5	57	16	69	0.38 [0.15 to 0.97]	6.64
	Peker 2016 [10]	47	122	53	122	0.89 [0.66 to 1.20]	30.17
	Subtotal (95% CI)	75	578	95	598	0.76 [0.45 to 1.27]	52.26
		Heterogeneity: Tau ² =0.13; Chi ² =6.37; P=0.09; I ² =52.90% effect: z=1.06; P=0.29					Subgroup
Specify [†]	Barbe 2012 [2]	23	357	21	366	1.12 [0.63 to 1.99]	14.64
	Huang 2015 [7]	0	42	5	41	0.09 [0.01 to 1.56]	0.81
	Parra 2015 [8]	5	57	16	69	0.38 [0.15 to 0.97]	6.64
	McEvoy 2016 [9]	233	1359	217	1358	1.07 [0.91 to 1.27]	41.90
	Peker 2016 [10]	47	122	53	122	0.89 [0.66 to 1.20]	30.17
	Subtotal (95% CI)	308	1937	312	1956	0.91 [0.68 to 1.22]	94.16
		Heterogeneity: Tau ² =0.05; Chi ² =8.29; P=0.08; I ² =51.70% effect: z=0.63; P=0.53					Subgroup
Not specify [†]	Craig 2012 [3]	1	195	3	196	0.34 [0.04 to 3.19]	1.30
	McMillan 2014 [5]	6	140	5	138	1.18 [0.37 to 3.79]	4.55
	Subtotal (95% CI)	7	335	8	334	0.91 [0.32 to 2.55]	5.84
		Heterogeneity: Tau ² <0.01; Chi ² =0.96; P=0.33; I ² =0.00% effect: z=0.18; P=0.85					Subgroup

eTable 2. (continued)

Subgroup	Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
		n _p	N _p	n _c	N _c		
Cardiovascular death							
Adherence<4 hours/day	Bradley 2005 [1]	23	128	20	130	1.17 [0.68 to 2.02]	18.21
	Cowie 2015 [6]	199	666	158	659	1.25 [1.04 to 1.49]	59.28
	McEvoy 2016 [9]	25	1359	20	1358	1.25 [0.70 to 2.24]	16.48
	Subtotal (95% CI)	247	2153	198	2147	1.24 [1.05 to 1.46]	93.97
		Heterogeneity: Tau ² <0.01; Chi ² =0.05; P=0.98; I ² =0.00% Subgroup effect: z=2.58; P=0.01					
Adherence≥4 hours/day	Barbe 2012 [2]	1	357	0	366	3.08 [0.13 to 75.24]	0.68
	Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.69
	Parra 2015 [8]	0	57	7	69	0.08 [0.00 to 1.38]	0.86
	Peker 2016 [10]	3	122	7	122	0.43 [0.11 to 1.62]	3.79
	Subtotal (95% CI)	4	578	15	598	0.41 [0.14 to 1.18]	6.03
		Heterogeneity: Tau ² <0.01; Chi ² =2.89; P=0.41; I ² =0.00% Subgroup effect: z=1.65; P=0.10					
OSA	Barbe 2012 [2]	1	357	0	366	3.08 [0.13 to 75.24]	0.68
	Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.69
	Parra 2015 [8]	0	57	7	69	0.08 [0.00 to 1.38]	0.86
	McEvoy 2016 [9]	25	1359	20	1358	1.25 [0.70 to 2.24]	16.48
	Peker 2016 [10]	3	122	7	122	0.43 [0.11 to 1.62]	3.79
	Subtotal (95% CI)	29	1937	35	1956	0.70 [0.27 to 1.80]	22.51
		Heterogeneity: Tau ² =0.40; Chi ² =6.30; P=0.18; I ² =36.50% Subgroup effect: z=0.75; P=0.45					
CSA	Bradley 2005 [1]	23	128	20	130	1.17 [0.68 to 2.02]	18.21
	Cowie 2015 [6]	199	666	158	659	1.25 [1.04 to 1.49]	59.28
	Subtotal (95% CI)	222	794	178	789	1.24 [1.04 to 1.47]	77.49
		Heterogeneity: Tau ² <0.01; Chi ² =0.05; P=0.82; I ² =0.00% Subgroup effect: z=2.46; P=0.01					

eTable 2. (continued)

Subgroup	Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
		n _P	N _P	n _C	N _C		
CPAP	Bradley 2005 [1]	23	128	20	130	1.17 [0.68 to 2.02]	18.21
	Barbe 2012 [2]	1	357	0	366	3.08 [0.13 to 75.24]	0.68
	Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.69
	Parra 2015 [8]	0	57	7	69	0.08 [0.00 to 1.38]	0.86
	McEvoy 2016 [9]	25	1359	20	1358	1.25 [0.70 to 2.24]	16.48
	Peker 2016 [10]	3	122	7	122	0.43 [0.11 to 1.62]	3.79
	Subtotal (95% CI)	52	2065	55	2086	0.96 [0.57 to 1.61]	40.72
		Heterogeneity: $\text{Tau}^2=0.09$; $\text{Chi}^2=6.54$; $P=0.26$; $I^2=23.60\%$ effect: $z=0.14$; $P=0.89$					Subgroup
ASV	Cowie 2015 [6]	199	666	158	659	1.25 [1.04 to 1.49]	59.28
All-cause death							
Adherence<4 hours/day	Bradley 2005 [1]	27	128	28	130	0.98 [0.61 to 1.57]	8.48
	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	0.18
	Kushida 2012 [4]	2	556	2	542	0.97 [0.14 to 6.90]	0.49
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	0.24
	Cowie 2015 [6]	232	666	193	659	1.19 [1.02 to 1.39]	74.96
	McEvoy 2016 [9]	40	1359	43	1358	0.93 [0.61 to 1.42]	10.37
	Subtotal (95% CI)	303	3044	267	3023	1.14 [0.99 to 1.31]	94.73
		Heterogeneity: $\text{Tau}^2<0.01$; $\text{Chi}^2=1.98$; $P=0.85$; $I^2=0.00\%$ effect: $z=1.81$; $P=0.07$					Subgroup
Adherence≥4 hours/day	Barbe 2012 [2]	8	357	3	366	2.73 [0.73 to 10.22]	1.07
	Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.19
	Parra 2015 [8]	6	57	9	69	0.81 [0.31 to 2.13]	1.97
	Peker 2016 [10]	7	122	9	122	0.78 [0.30 to 2.02]	2.04
	Subtotal (95% CI)	21	578	22	598	0.99 [0.53 to 1.85]	5.27

eTable 2. (continued)

Subgroup	Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
		n _P	N _P	n _C	N _C		
		Heterogeneity: Tau ² =0.02; Chi ² =3.18; P=0.36; I ² =5.70% effect: z=0.02; P=0.98					Subgroup
OSA	Barbe 2012 [2]	8	357	3	366	2.73 [0.73 to 10.22]	1.07
	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	0.18
	Kushida 2012 [4]	2	556	2	542	0.97 [0.14 to 6.90]	0.49
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	0.24
	Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.19
	Parra 2015 [8]	6	57	9	69	0.81 [0.31 to 2.13]	1.97
	McEvoy 2016 [9]	40	135 9	43	1358	0.93 [0.61 to 1.42]	10.37
	Peker 2016 [10]	7	122	9	122	0.78 [0.30 to 2.02]	2.04
	Subtotal (95% CI)	65	282 8	68	2832	0.96 [0.69 to 1.35]	16.56
		Heterogeneity: Tau ² <0.01; Chi ² =3.70; P=0.81; I ² =0.00% effect: z=0.23; P=0.82					Subgroup
CSA	Bradley 2005 [1]	27	128	28	130	0.98 [0.61 to 1.57]	8.48
	Cowie 2015 [6]	232	666	193	659	1.19 [1.02 to 1.39]	74.96
	Subtotal (95% CI)	259	794	221	789	1.17 [1.00 to 1.35]	83.44
		Heterogeneity: Tau ² <0.01; Chi ² =0.59; P=0.44; I ² =0.00% effect: z=2.02; P=0.04					Subgroup
CPAP	Bradley 2005 [1]	27	128	28	130	0.98 [0.61 to 1.57]	8.48
	Barbe 2012 [2]	8	357	3	366	2.73 [0.73 to 10.22]	1.07
	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	0.18
	Kushida 2012 [4]	2	556	2	542	0.97 [0.14 to 6.90]	0.49
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	0.24
	Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.19
	Parra 2015 [8]	6	57	9	69	0.81 [0.31 to 2.13]	1.97
	McEvoy 2016 [9]	40	135 9	43	1358	0.93 [0.61 to 1.42]	10.37

eTable 2. (continued)

Subgroup	Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
		n _p	N _P	n _c	N _C		
CPAP	Peker 2016 [10]	7	122	9	122	0.78 [0.30 to 2.02]	2.04
	Subtotal (95% CI)	92	295 6	96	2962	0.97 [0.74 to 1.27]	25.04
		Heterogeneity: Tau ² <0.01; Chi ² =3.70; P=0.88; I ² =0.00% Subgroup effect: z=0.23; P=0.81					
ASV	Cowie 2015 [6]	232	666	193	659	1.19 [1.02 to 1.39]	74.96
Specify [†]	Bradley 2005 [1]	27	128	28	130	0.98 [0.61 to 1.57]	8.48
	Barbe 2012 [2]	8	357	3	366	2.73 [0.73 to 10.22]	1.07
	Cowie 2015 [6]	232	666	193	659	1.19 [1.02 to 1.39]	74.96
	Huang 2015 [7]	0	42	1	41	0.33 [0.01 to 7.77]	0.19
	Parra 2015 [8]	6	57	9	69	0.81 [0.31 to 2.13]	1.97
	McEvoy 2016 [9]	40	135 9	43	1358	0.93 [0.61 to 1.42]	10.37
	Peker 2016 [10]	7	122	9	122	0.78 [0.30 to 2.02]	2.04
	Subtotal (95% CI)	320	273 1	286	2745	1.13 [0.98 to 1.29]	99.09
		Heterogeneity: Tau ² <0.01; Chi ² =4.96; P=0.55; I ² =0.00% Subgroup effect: z=1.73; P=0.08					
Not specify [†]	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	0.18
	Kushida 2012 [4]	2	556	2	542	0.97 [0.14 to 6.90]	0.49
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	0.24
	Subtotal (95% CI)	4	891	3	876	1.23 [0.29 to 5.11]	0.91
		Heterogeneity: Tau ² <0.01; Chi ² =0.38; P=0.82; I ² =0.00% Subgroup effect: z=0.28; P=0.78					
Non-cardiovascular death							
Adherence<4 hours/day	Bradley 2005 [1]	4	128	8	130	0.51 [0.16 to 1.64]	8.00
	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	1.12
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	1.49
	Cowie 2015 [6]	33	666	35	659	0.93 [0.59 to 1.48]	43.23
	McEvoy 2016 [9]	15	135 9	23	1358	0.65 [0.34 to 1.24]	24.47

eTable 2. (continued)

Subgroup	Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
		n _P	N _P	n _C	N _C		
	Subtotal (95% CI)	54	248 8	67	2481	0.81 [0.57 to 1.15]	78.31
		Heterogeneity: $\text{Tau}^2 < 0.01$; $\text{Chi}^2 = 2.07$; $P = 0.72$; $I^2 = 0.00\%$ Subgroup effect: $z = 1.20$; $P = 0.23$					
Adherence ≥ 4 hours/day	Barbe 2012 [2]	7	357	13	366	0.55 [0.22 to 1.37]	13.11
	Parra 2015 [8]	6	57	2	69	3.63 [0.76 to 17.31]	4.60
	Peker 2016 [10]	4	122	2	122	2.00 [0.37 to 10.72]	3.99
	Subtotal (95% CI)	17	536	17	557	1.37 [0.40 to 4.69]	21.69
		Heterogeneity: $\text{Tau}^2 = 0.70$; $\text{Chi}^2 = 4.93$; $P = 0.08$; $I^2 = 59.40\%$ Subgroup effect: $z = 0.50$; $P = 0.62$					
OSA	Barbe 2012 [2]	7	357	13	366	0.55 [0.22 to 1.37]	13.11
	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	1.12
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	1.49
	Parra 2015 [8]	6	57	2	69	3.63 [0.76 to 17.31]	4.60
	McEvoy 2016 [9]	15	135 9	23	1358	0.65 [0.34 to 1.24]	24.47
	Peker 2016 [10]	4	122	2	122	2.00 [0.37 to 10.72]	3.99
	Subtotal (95% CI)	34	223 0	41	2249	0.94 [0.51 to 1.72]	48.77
		Heterogeneity: $\text{Tau}^2 = 0.13$; $\text{Chi}^2 = 6.46$; $P = 0.26$; $I^2 = 22.60\%$ Subgroup effect: $z = 0.20$; $P = 0.84$					
CSA	Bradley 2005 [1]	4	128	8	130	0.51 [0.16 to 1.64]	8.00
	Cowie 2015 [6]	33	666	35	659	0.93 [0.59 to 1.48]	43.23
	Subtotal (95% CI)	37	794	43	789	0.86 [0.56 to 1.32]	51.23
		Heterogeneity: $\text{Tau}^2 < 0.01$; $\text{Chi}^2 = 0.89$; $P = 0.34$; $I^2 = 0.00\%$ Subgroup effect: $z = 0.69$; $P = 0.49$					
CPAP	Bradley 2005 [1]	4	128	8	130	0.51 [0.16 to 1.64]	8.00
	Barbe 2012 [2]	7	357	13	366	0.55 [0.22 to 1.37]	13.11
	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	1.12
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	1.49
	Parra 2015 [8]	6	57	2	69	3.63 [0.76 to 17.31]	4.60

eTable 2. (continued)

Subgroup	Study	PAP		Control		Risk Ratio Random, 95% CI	Weight (%)
		n _P	N _P	n _C	N _C		
CPAP	McEvoy 2016 [9]	15	1359	23	1358	0.65 [0.34 to 1.24]	24.47
	Peker 2016 [10]	4	122	2	122	2.00 [0.37 to 10.72]	3.99
	Subtotal (95% CI)	38	2358	49	2379	0.82 [0.49 to 1.36]	56.77
		Heterogeneity: $\text{Tau}^2=0.07$; $\text{Chi}^2=7.04$; $P=0.32$; $I^2=14.70\%$ effect: $z=0.77$; $P=0.44$					Subgroup
ASV	Cowie 2015 [6]	33	666	35	659	0.93 [0.59 to 1.48]	43.23
Specify [†]	Bradley 2005 [1]	4	128	8	130	0.51 [0.16 to 1.64]	8.00
	Barbe 2012 [2]	7	357	13	366	0.55 [0.22 to 1.37]	13.11
	Cowie 2015 [6]	33	666	35	659	0.93 [0.59 to 1.48]	43.23
	Parra 2015 [8]	6	57	2	69	3.63 [0.76 to 17.31]	4.60
	McEvoy 2016 [9]	15	1359	23	1358	0.65 [0.34 to 1.24]	24.47
	Peker 2016 [10]	4	122	2	122	2.00 [0.37 to 10.72]	3.99
	Subtotal (95% CI)	69	2689	83	2704	0.84 [0.55 to 1.27]	97.39
		Heterogeneity: $\text{Tau}^2=0.07$; $\text{Chi}^2=6.72$; $P=0.24$; $I^2=25.60\%$ effect: $z=0.85$; $P=0.40$					Subgroup
Not specify [†]	Craig 2012 [3]	1	195	0	196	3.02 [0.12 to 73.57]	1.12
	McMillan 2014 [5]	1	140	1	138	0.99 [0.06 to 15.60]	1.49
	Subtotal (95% CI)	2	335	1	334	1.59 [0.20 to 12.85]	2.61
		Heterogeneity: $\text{Tau}^2<0.01$; $\text{Chi}^2=0.27$; $P=0.60$; $I^2=0.00\%$ effect: $z=0.44$; $P=0.66$					Subgroup

[†]Trials that specified or did not specify vascular outcomes or death as primary outcome.

Abbreviations: ASV, adaptive servo ventilation; CPAP, continuous positive airways pressure; CSA, central sleep apnea; MACE, major adverse cardiovascular events (consists of cardiovascular death, non-fatal acute coronary syndrome and non-fatal stroke); MACE plus, MACE and hospitalization for unstable angina; n_C: number of cardiovascular events or death in control group; N_C: number of participants in control group; n_P: number of cardiovascular events or death in treatment with positive airway pressure; N_P: number of participants in treatment with positive airway pressure; OSA: obstructive sleep apnea; PAP: positive airway pressure.

eReferences.

1. Bradley TD, Logan AG, Kimoff RJ, et al. Continuous positive airway pressure for central sleep apnea and heart failure. *N Engl J Med*. 2005;353(19):2025-2033.
2. Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, et al. Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. *JAMA*. 2012; 307(20): 2161-2168.
3. Craig SE, Kohler M, Nicoll D, et al. Continuous positive airway pressure improves sleepiness but not calculated vascular risk in patients with minimally symptomatic obstructive sleep apnoea: the MOSAIC randomised controlled trial. *Thorax*. 2012; 67(12): 1090-1096.
4. Kushida CA, Nichols DA, Holmes TH, et al. Effects of continuous positive airway pressure on neurocognitive function in obstructive sleep apnea patients: The Apnea Positive Pressure Long-term Efficacy Study (APPLES). *Sleep*. 2012;35(12):1593-1602.
5. McMillan A, Bratton DJ, Faria R, et al. Continuous positive airway pressure in older people with obstructive sleep apnoea syndrome (PREDICT): a 12-month, multicenter, randomised trial. *Lancet Respir Med*. 2014; 2(10): 804-812.
6. Cowie MR, Woehrle H, Wegscheider K, et al. Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure. *N Engl J Med*. 2015; 373(12): 1095-1105.
7. Huang Z, Liu Z, Luo Q, et al. Long-term effects of continuous positive airway pressure on blood pressure and prognosis in hypertensive patients with coronary heart disease and obstructive sleep apnea: a randomized controlled trial. *Am J Hypertens*. 2015; 28(3): 300-306.
8. Parra O, Sánchez-Armengol Á, Capote F, et al. Efficacy of continuous positive airway pressure treatment on 5-year survival in patients with ischaemic stroke and obstructive sleep apnea: a randomized controlled trial. *J Sleep Res*. 2015; 24(1):

47-53.

9. McEvoy RD, Antic NA, Heeley E, et al. CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea. *N Engl J Med*. 2016; 375(10): 919-931.
10. Peker Y, Glantz H, Eulenburg C, Wegscheider K, Herlitz J, Thunström E. Effect of Positive Airway Pressure on Cardiovascular Outcomes in Coronary Artery Disease Patients with Nonsleepy Obstructive Sleep Apnea. The RICCADSA Randomized Controlled Trial. *Am J Respir Crit Care Med*. 2016; 194(5): 613-620.