Forests plots and funnel plots for all parameters

Fig. 1 pooled effects of trazodone on TST

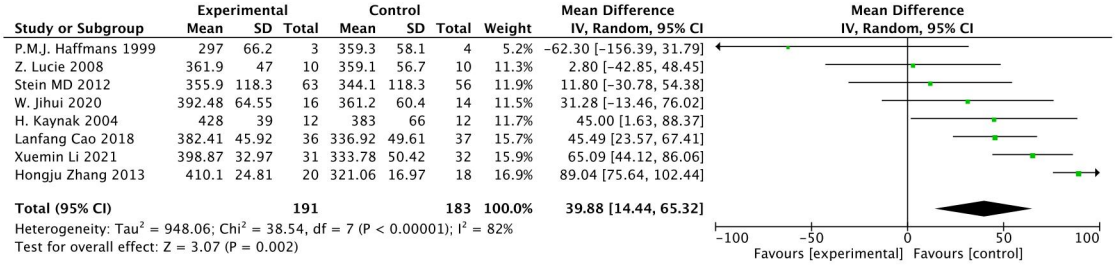


Fig. 2 subgroups analysis to TST (treatment duration)

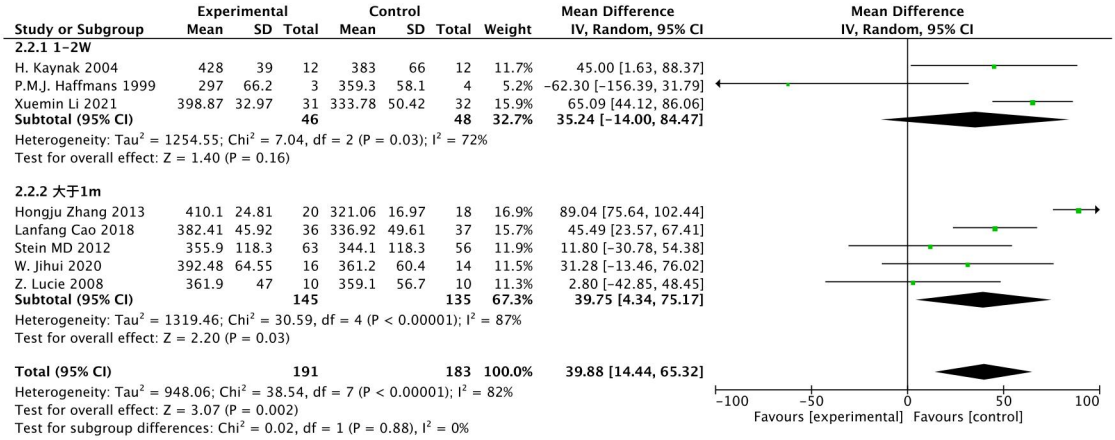


Fig. 3 subgroups analysis to TST (mean age)

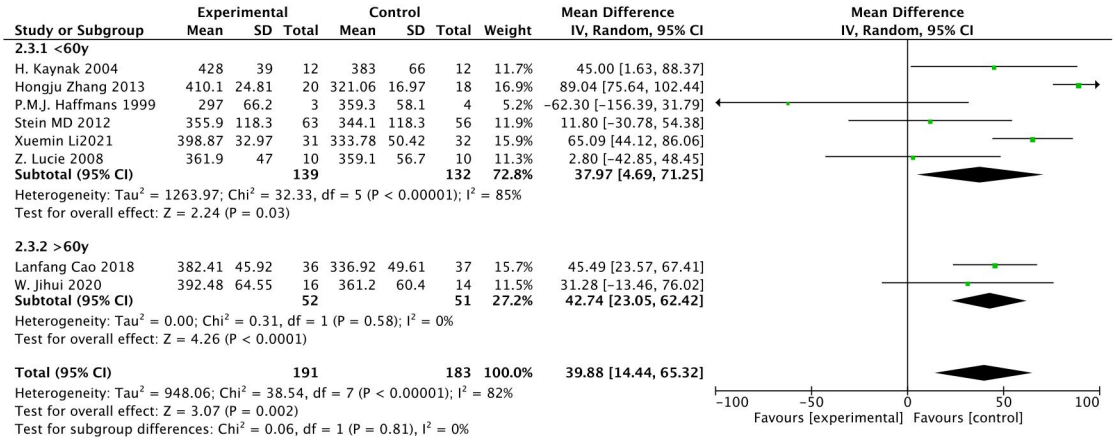


Fig. 4 subgroups analysis to TST(dosage)

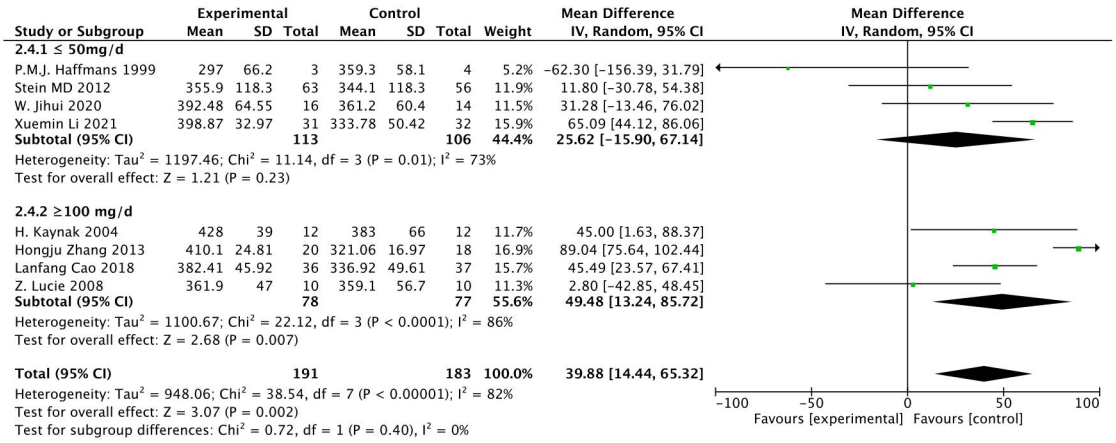


Fig. 5 subgroups analysis to TST(treatment combination or placebo)

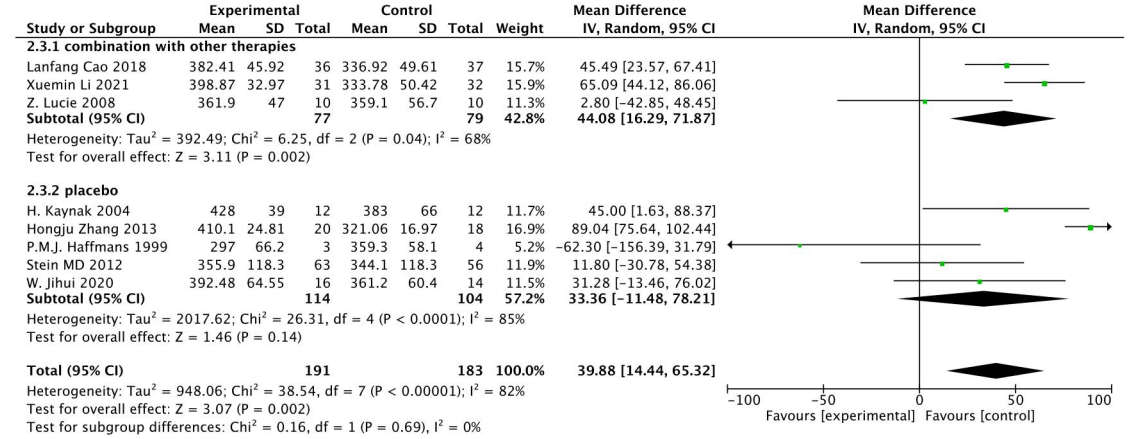


Fig. 6 Funnel plot for TST

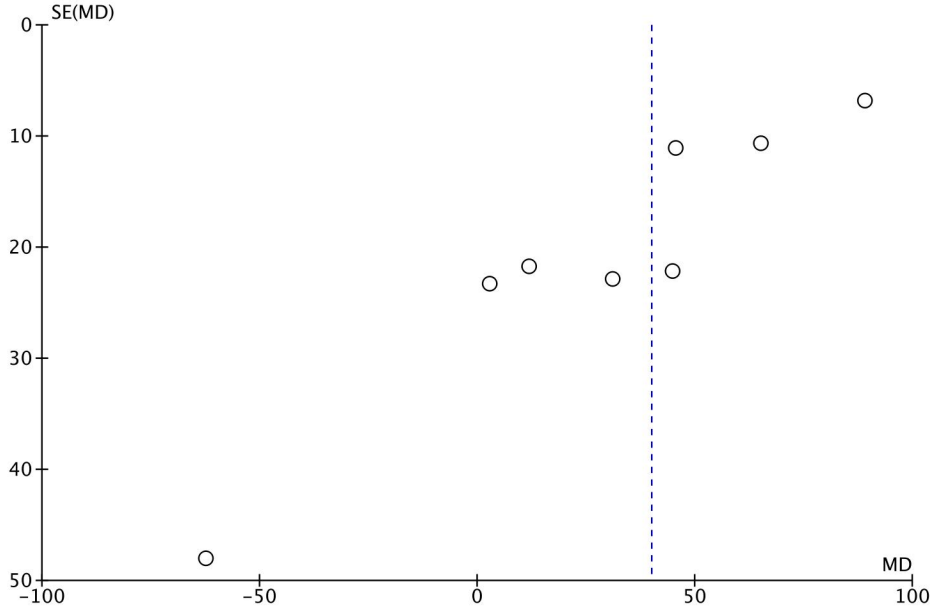


Fig. 7 pooled effects of trazodone on LPS

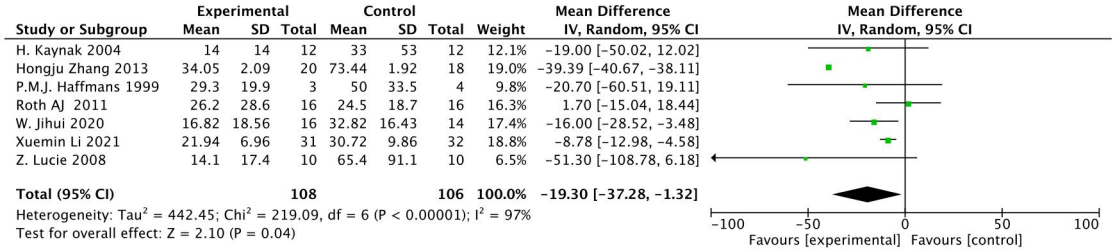


Fig. 8 Sensitivity analysis to LPS

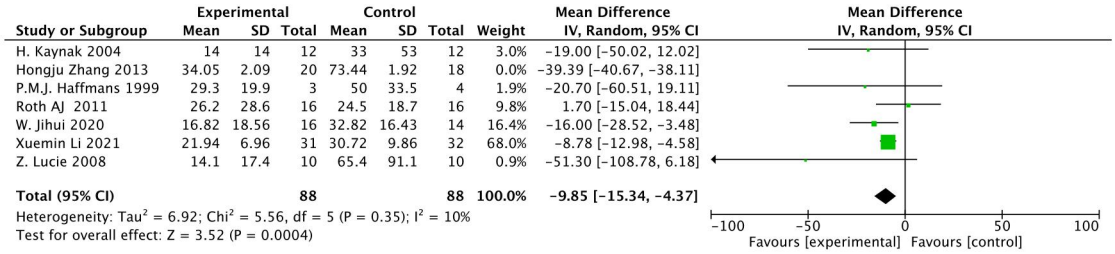


Fig. 9 subgroups analysis to LPS(dosage)

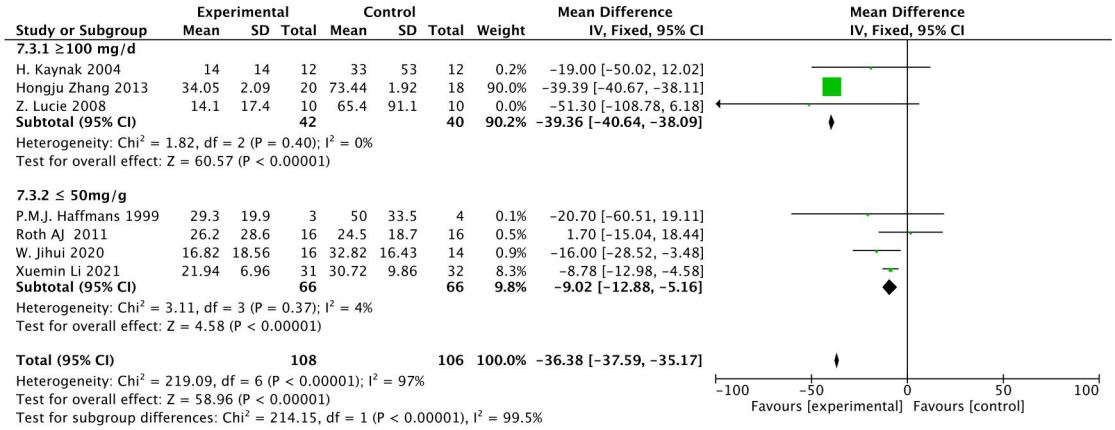
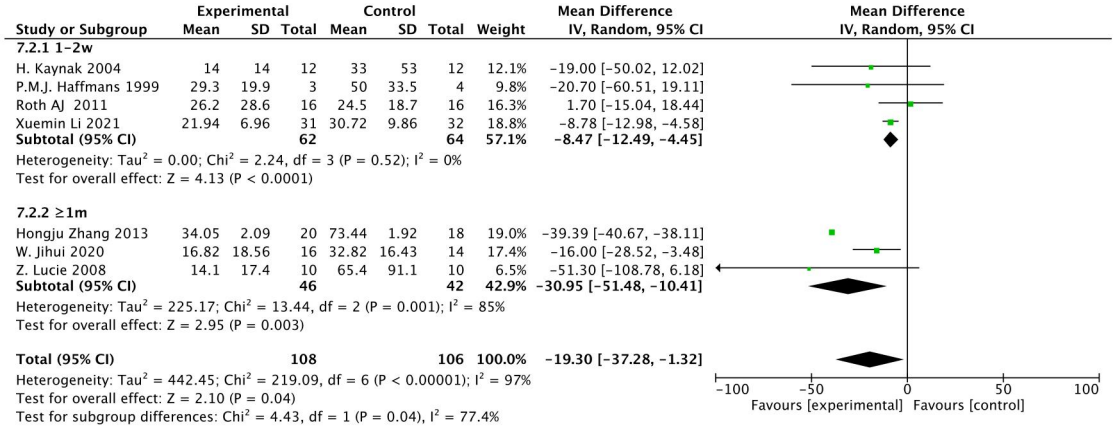


Fig. 10 subgroups analysis to LPS (treatment duration)



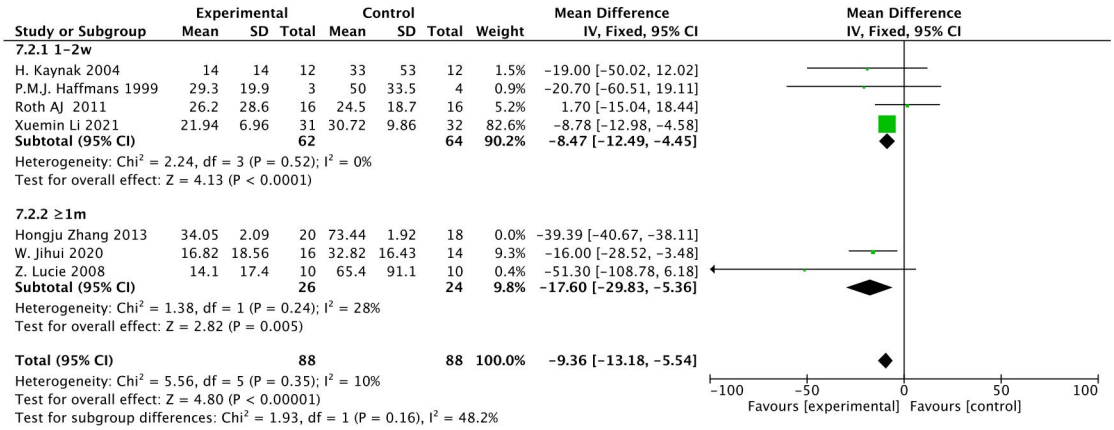


Fig. 11 subgroups analysis to LPS(combination with other therapies or placebo)

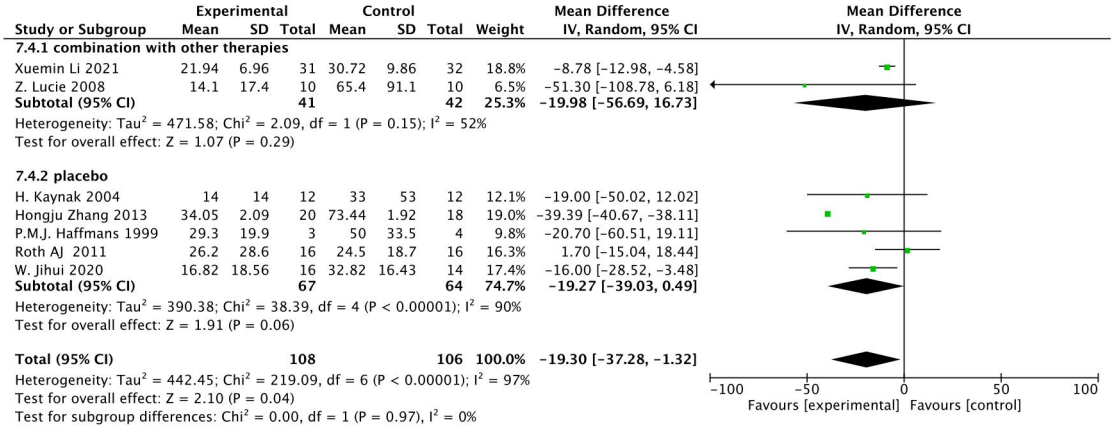


Fig. 12 Funnel plot for LPS

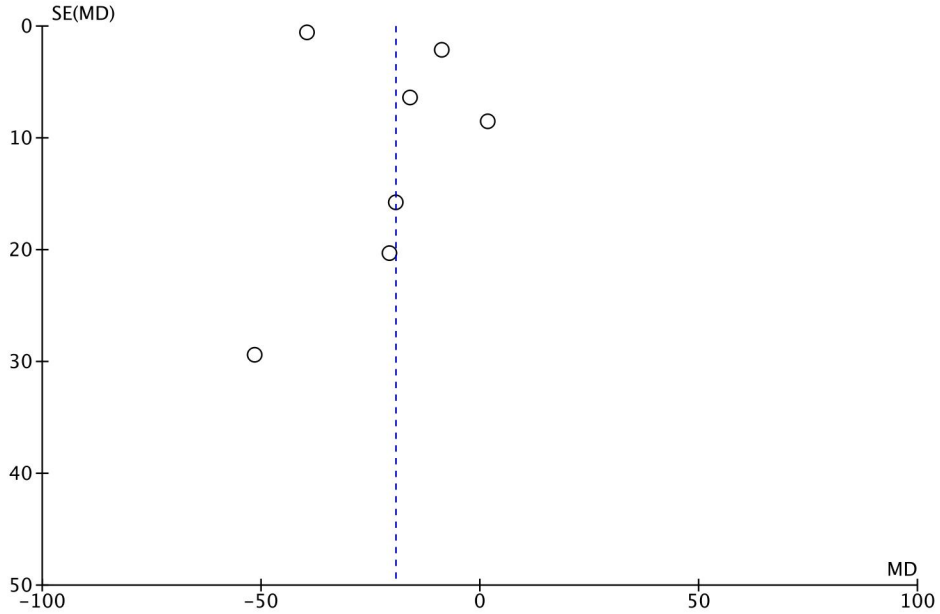


Fig. 13 pooled effects of trazodone on SE

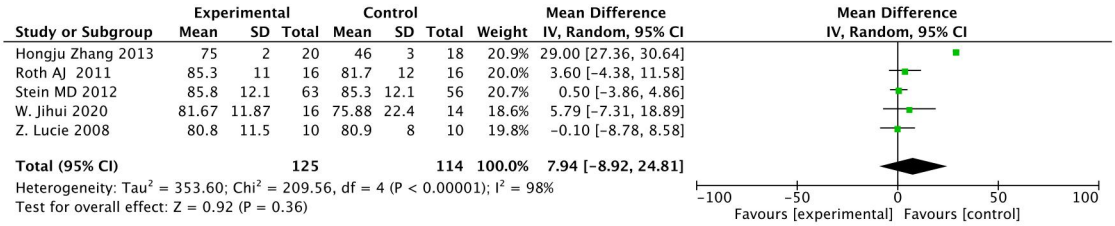


Fig. 14 Sensitivity analysis to SE

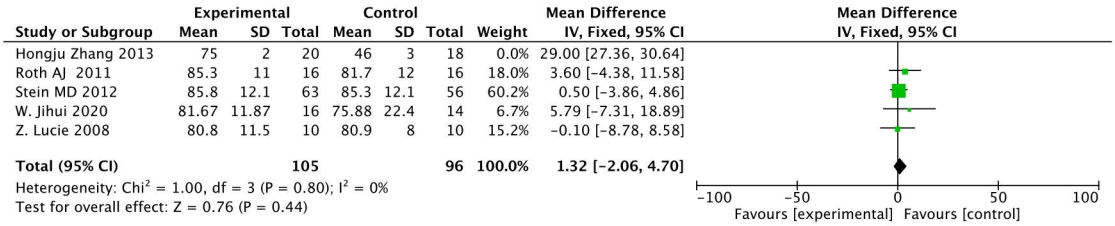


Fig. 15 Funnel plot for SE

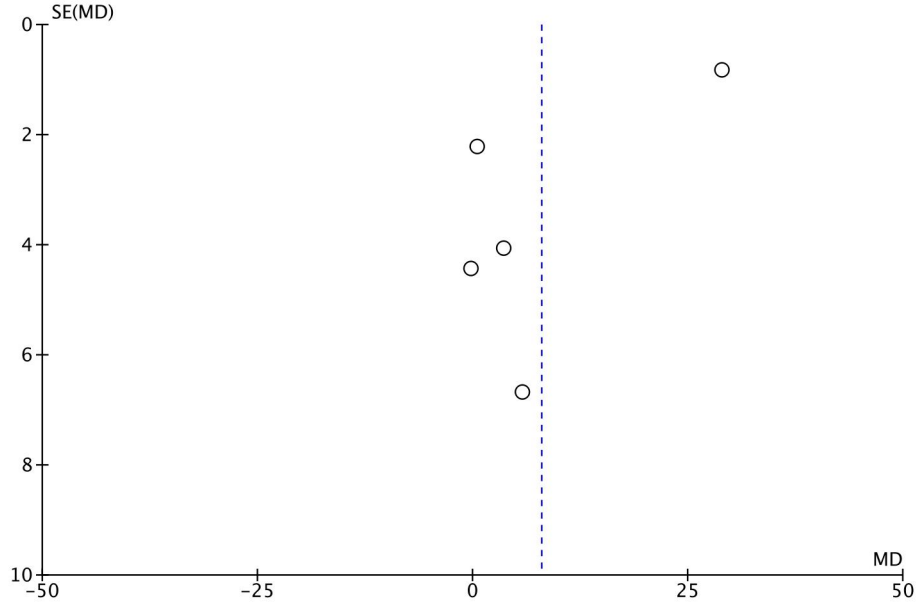


Fig. 16 pooled effects of trazodone on WASO

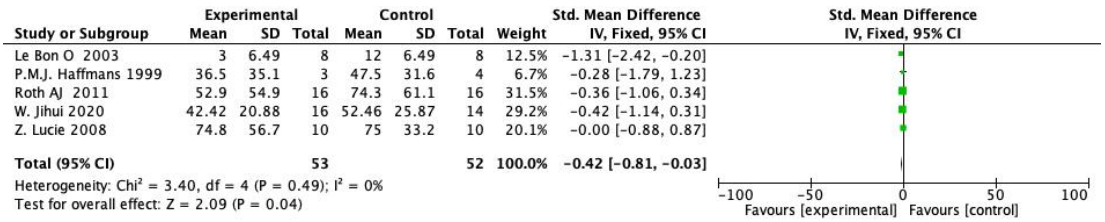


Fig. 17 Sensitivity analysis of WASO to combination of treatment

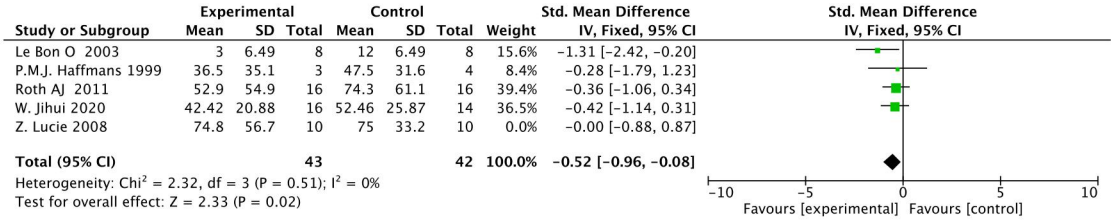


Fig. 18 Funnel plot for WASO

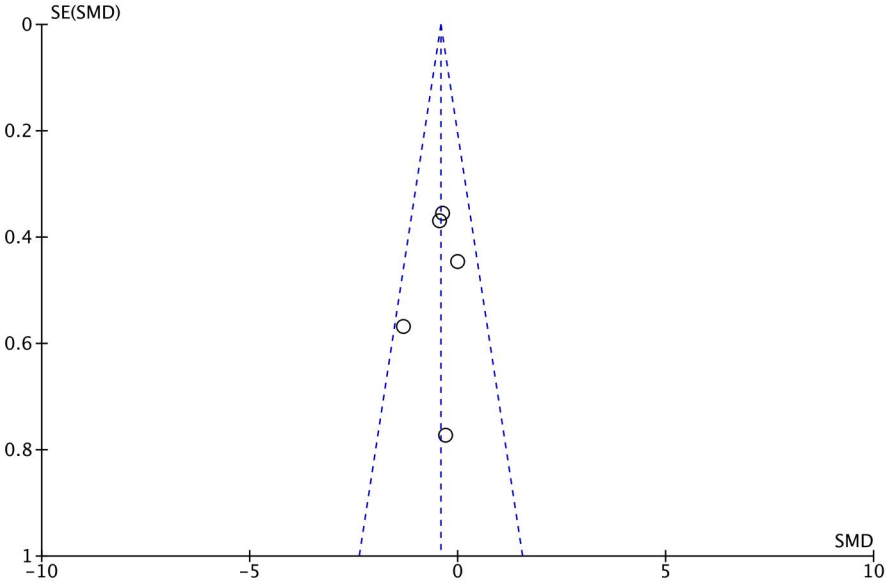


Fig. 19 pooled effects of trazodone on NAs (including both arousal times and arousal index)

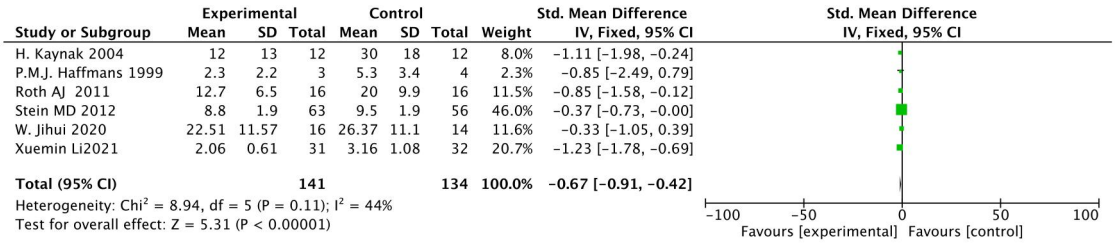


Fig. 20 Sensitivity analysis of NAs to combination of treatment

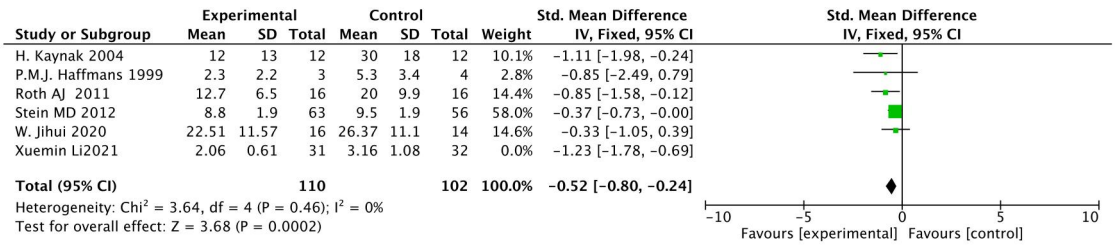


Fig. 21 Funnel plot for NAs

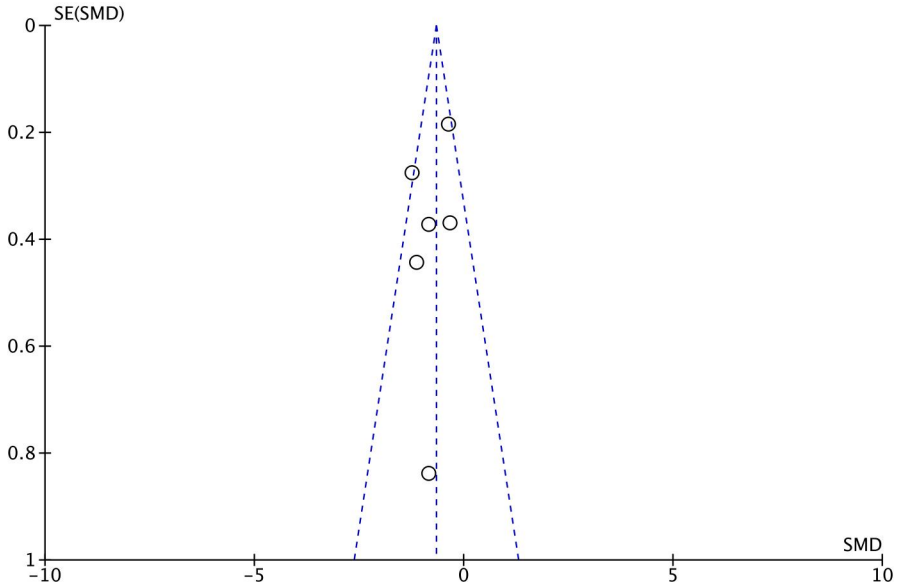


Fig. 22 pooled effects of trazodone on AHI

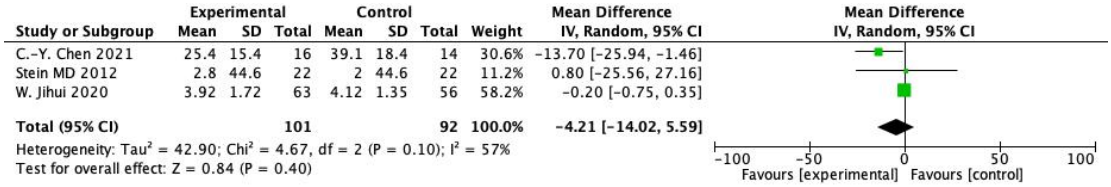


Fig. 23 pooled effects of trazodone on REML

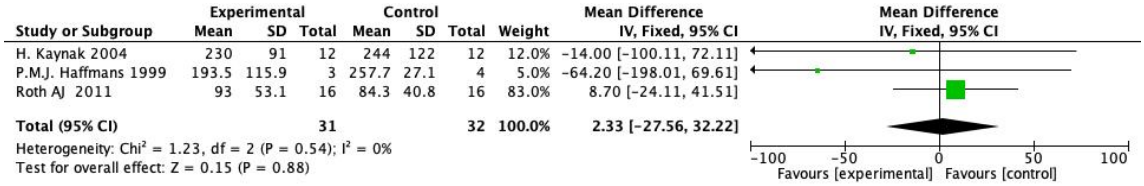


Fig. 24 pooled effects of trazodone on REM

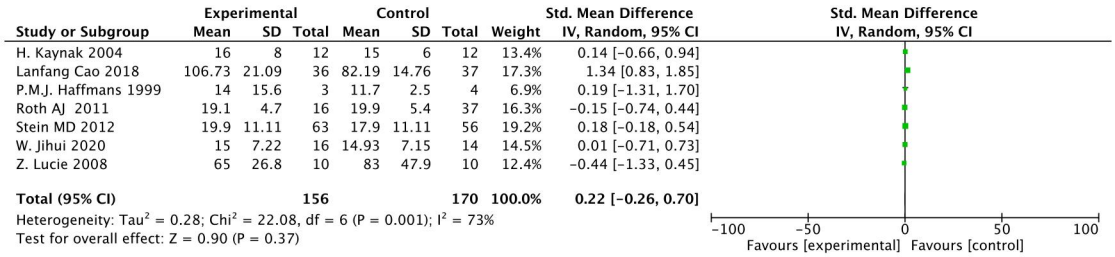


Fig. 25 Sensitivity analysis to REM

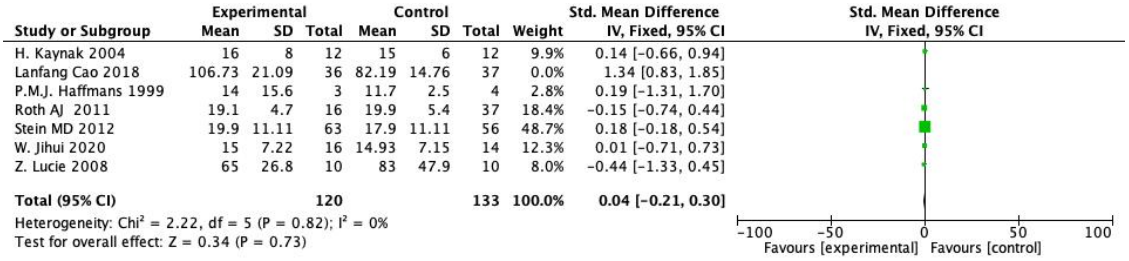


Fig. 26 subgroups analysis to REM (treatment duration)

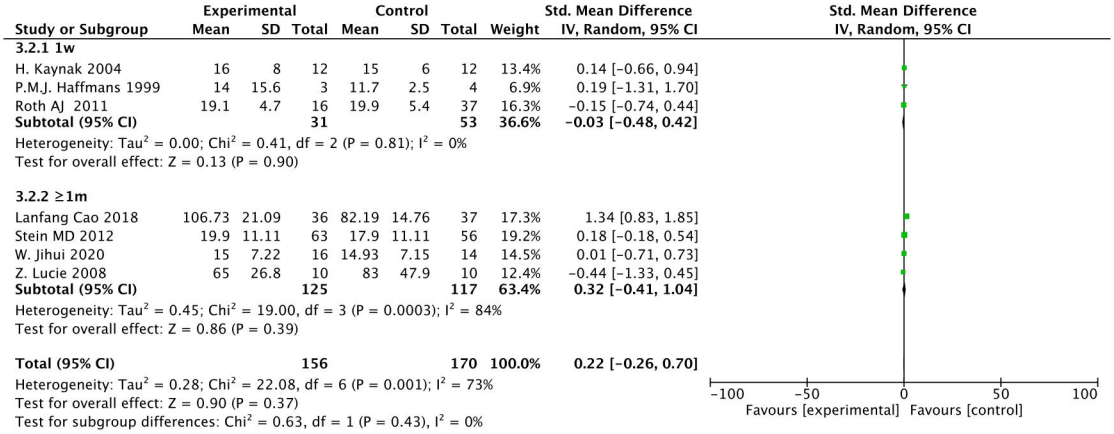


Fig. 27 subgroups analysis to REM(dosage)

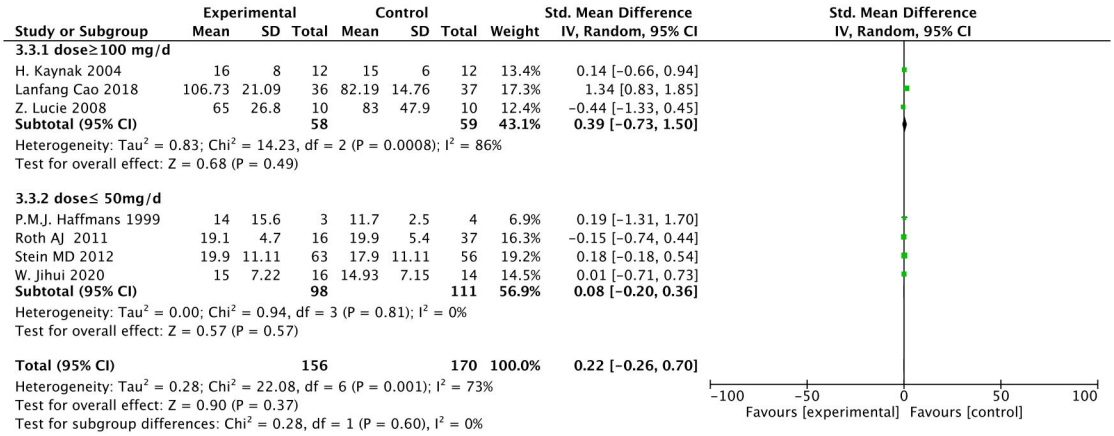


Fig. 28 subgroups analysis to REM (treatment combination or placebo)

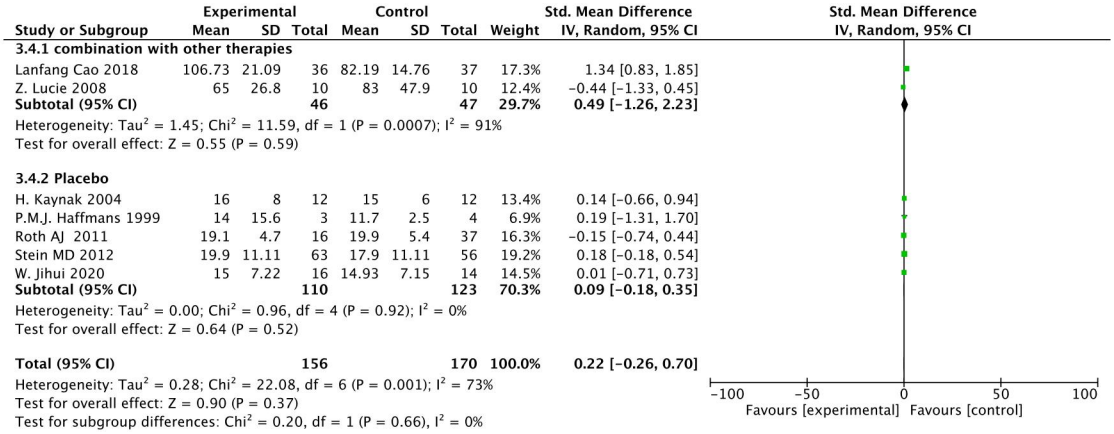


Fig. 29 Funnel plot for REM

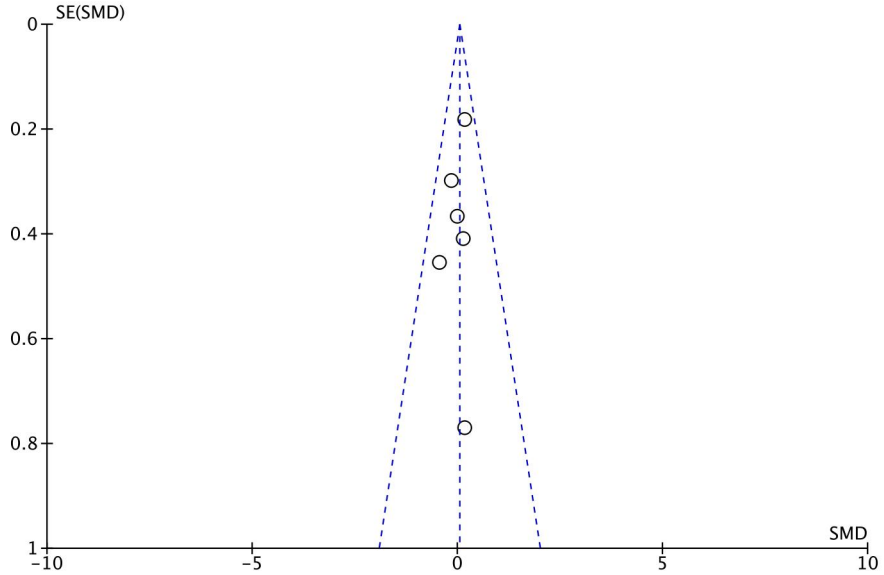


Fig. 30 pooled effects of trazodone on N1

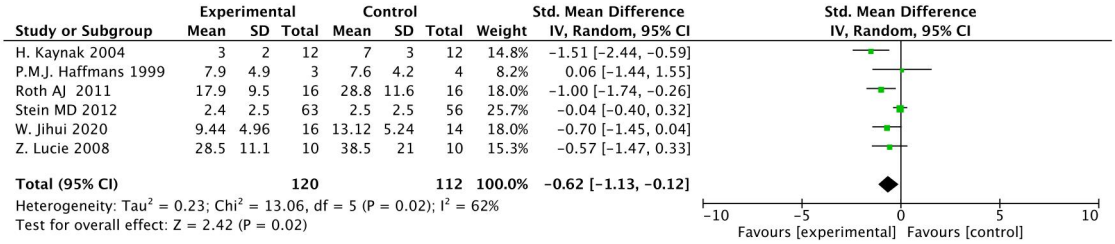


Fig. 31 Sensitivity analysis of heterogeneity to N1

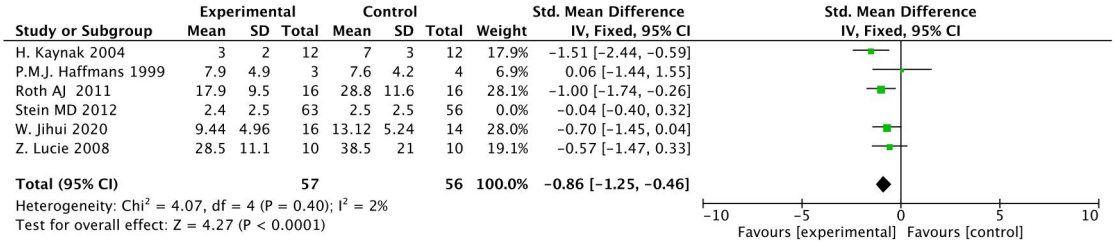


Fig. 32 Analysis on combination of treatment to N1

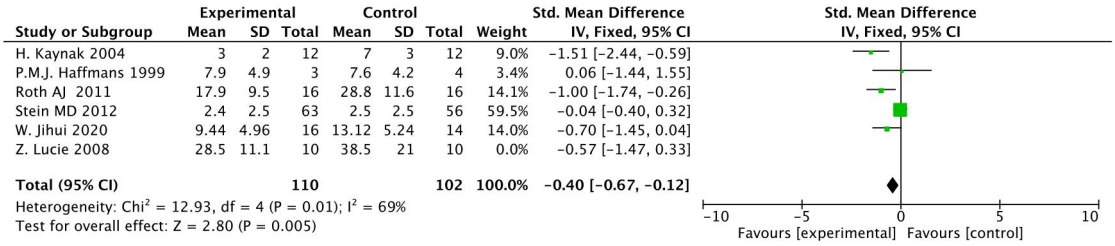


Fig. 33 subgroups analysis to N1 (treatment duration)

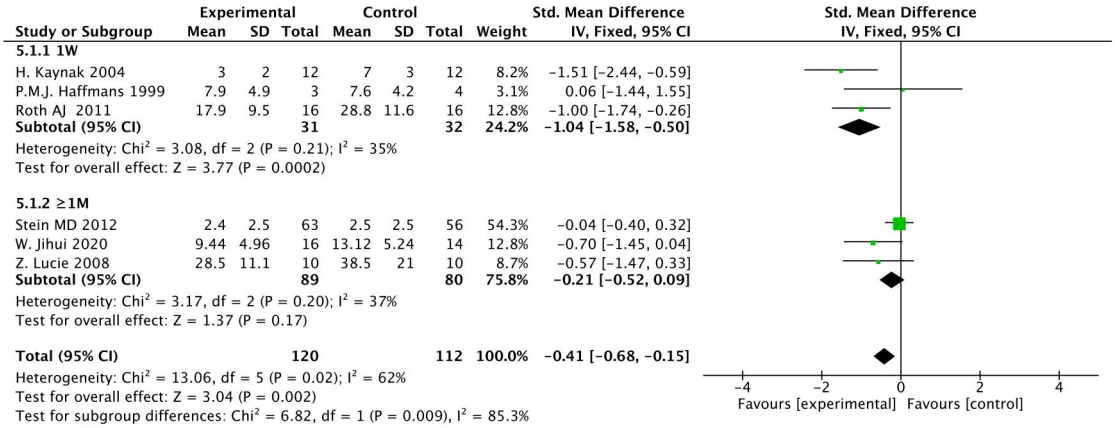


Fig. 34 subgroups analysis to N1(dosage)

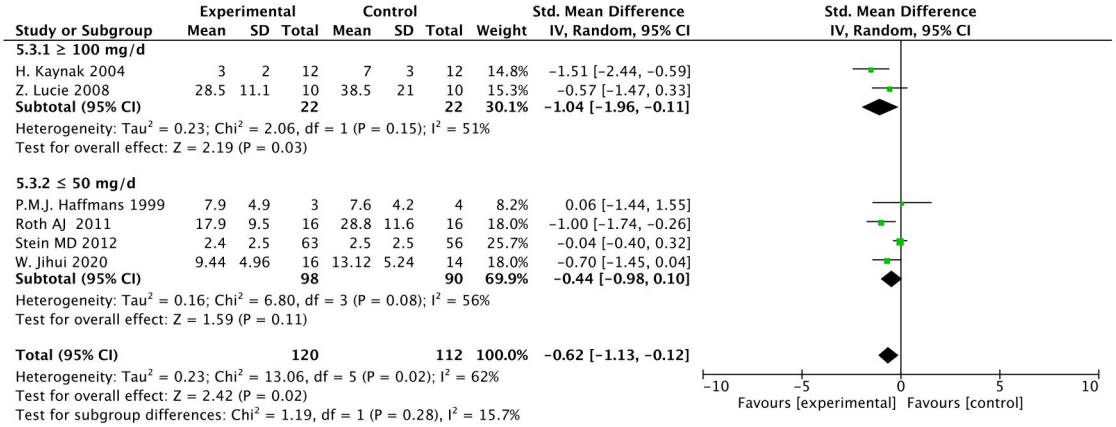


Fig. 35 Funnel plot for N1

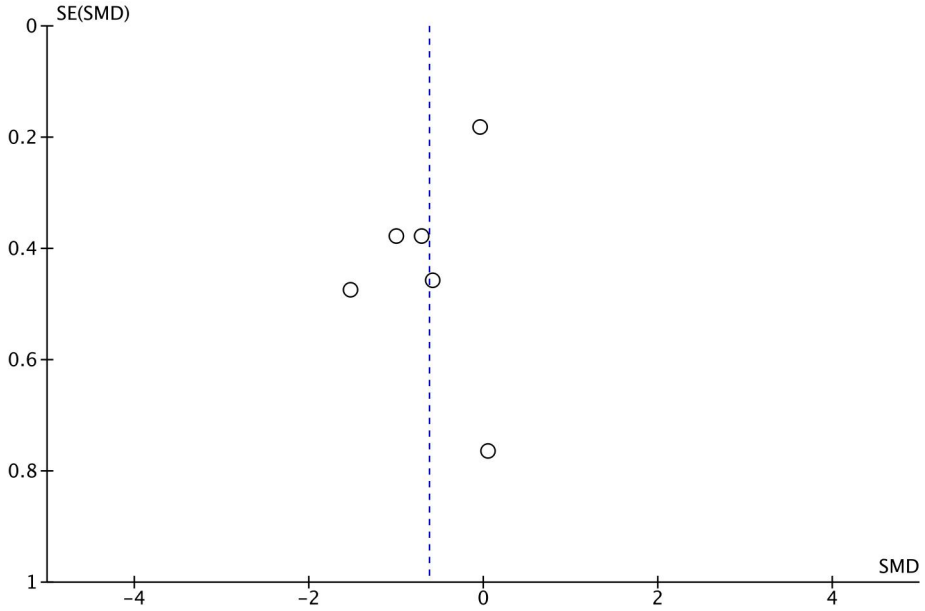


Fig. 36 pooled effects of trazodone on N2

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
H. Kaynak 2004	50	16	12	59	9	12	9.9%	−0.67 [−1.50, 0.16]
P.M.J. Haffmans 1999	41.8	13.5	3	45.7	6.9	4	2.9%	−0.33 [−1.85, 1.19]
Roth AJ 2011	223.1	47.2	16	216	58.2	16	14.1%	0.13 [−0.56, 0.82]
Stein MD 2012	63.3	13	63	63.3	13	56	52.3%	0.00 [−0.36, 0.36]
W. Jihui 2020	59.72	13.59	16	61.31	11.56	14	13.2%	−0.12 [−0.84, 0.60]
Z. Lucie 2008	148.2	60.5	10	197.4	20.9	10	7.6%	−1.04 [−1.99, −0.09]
Total (95% CI)			**120**			**112**	**100.0%**	**−0.15 [−0.41, 0.11]**

Heterogeneity: Chi² = 6.27, df = 5 (P = 0.28); I² = 20%
Test for overall effect: Z = 1.15 (P = 0.25)

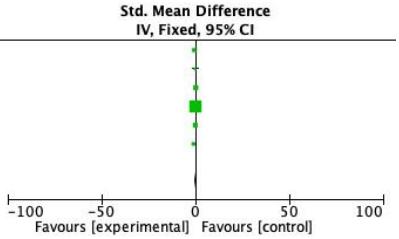


Fig. 37 Analysis on combination of treatment to N2

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
H. Kaynak 2004	0.5	0.16	12	0.59	0.09	12	10.7%	−0.67 [−1.50, 0.16]
P.M.J. Haffmans 1999	0.418	0.135	3	0.457	0.069	4	3.2%	−0.33 [−1.85, 1.19]
Roth AJ 2011	223.1	47.2	16	216	58.2	16	15.2%	0.13 [−0.56, 0.82]
Stein MD 2012	0.633	0.13	63	0.633	0.13	56	56.6%	0.00 [−0.36, 0.36]
W. Jihui 2020	0.5972	0.1359	16	0.6131	0.1156	14	14.2%	−0.12 [−0.84, 0.60]
Z. Lucie 2008	148.2	60.5	10	197.4	20.9	10	0.0%	−1.04 [−1.99, −0.09]
Total (95% CI)			**110**			**102**	**100.0%**	**−0.08 [−0.35, 0.19]**

Heterogeneity: Chi² = 2.61, df = 4 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.58 (P = 0.56)

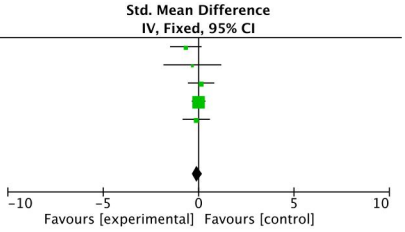


Fig. 38 subgroups analysis to N2 (treatment duration:1 week)

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
H. Kaynak 2004	50	16	12	59	9	12	36.8%	−0.67 [−1.50, 0.16]
P.M.J. Haffmans 1999	41.8	13.5	3	45.7	6.9	4	10.9%	−0.33 [−1.85, 1.19]
Roth AJ 2011	223.1	47.2	16	216	58.2	16	52.3%	0.13 [−0.56, 0.82]
Stein MD 2012	63.3	13	63	63.3	13	56	0.0%	0.00 [−0.36, 0.36]
W. Jihui 2020	59.72	13.59	16	61.31	11.56	14	0.0%	−0.12 [−0.84, 0.60]
Z. Lucie 2008	148.2	60.5	10	197.4	20.9	10	0.0%	−1.04 [−1.99, −0.09]
Total (95% CI)			**31**			**32**	**100.0%**	**−0.21 [−0.72, 0.29]**

Heterogeneity: Chi² = 2.14, df = 2 (P = 0.34); I² = 6%
Test for overall effect: Z = 0.84 (P = 0.40)

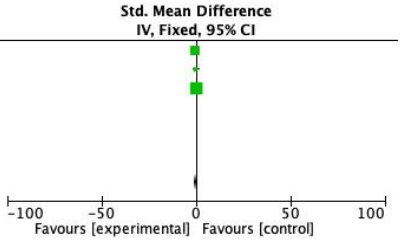
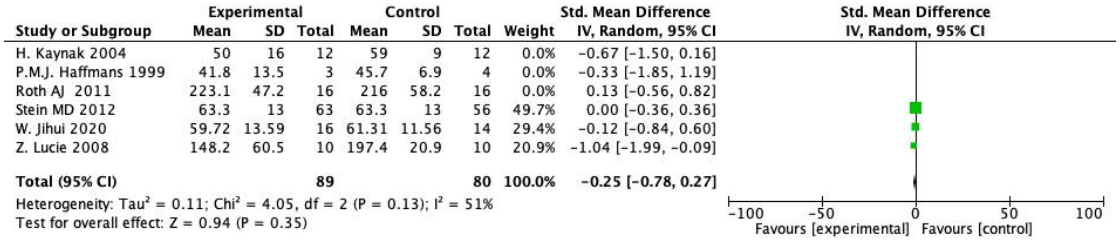


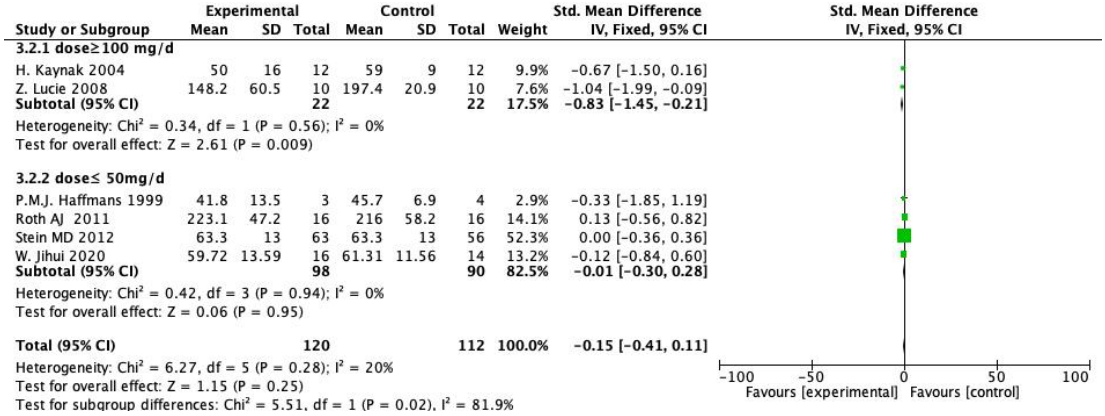
Fig. 39 subgroups analysis to N2 (treatment duration:≥1 month)



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
H. Kaynak 2004	50	16	12	59	9	12	0.0%	−0.67 [−1.50, 0.16]
P.M.J. Haffmans 1999	41.8	13.5	3	45.7	6.9	4	0.0%	−0.33 [−1.85, 1.19]
Roth AJ 2011	223.1	47.2	16	216	58.2	16	0.0%	0.13 [−0.56, 0.82]
Stein MD 2012	63.3	13	63	63.3	13	56	49.7%	0.00 [−0.36, 0.36]
W. Jihui 2020	59.72	13.59	16	61.31	11.56	14	29.4%	−0.12 [−0.84, 0.60]
Z. Lucie 2008	148.2	60.5	10	197.4	20.9	10	20.9%	−1.04 [−1.99, −0.09]
Total (95% CI)			**89**			**80**	**100.0%**	**−0.25 [−0.78, 0.27]**

Heterogeneity: Tau² = 0.11; Chi² = 4.05, df = 2 (P = 0.13); I² = 51%
Test for overall effect: Z = 0.94 (P = 0.35)

Fig. 40 subgroups analysis to N2(dosage)



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
3.2.1 dose≥100 mg/d								
H. Kaynak 2004	50	16	12	59	9	12	9.9%	−0.67 [−1.50, 0.16]
Z. Lucie 2008	148.2	60.5	10	197.4	20.9	10	7.6%	−1.04 [−1.99, −0.09]
Subtotal (95% CI)			**22**			**22**	**17.5%**	**−0.83 [−1.45, −0.21]**
Heterogeneity: Chi² = 0.34, df = 1 (P = 0.56); I² = 0%								
Test for overall effect: Z = 2.61 (P = 0.009)								
3.2.2 dose≤ 50mg/d								
P.M.J. Haffmans 1999	41.8	13.5	3	45.7	6.9	4	2.9%	−0.33 [−1.85, 1.19]
Roth AJ 2011	223.1	47.2	16	216	58.2	16	14.1%	0.13 [−0.56, 0.82]
Stein MD 2012	63.3	13	63	63.3	13	56	52.3%	0.00 [−0.36, 0.36]
W. Jihui 2020	59.72	13.59	16	61.31	11.56	14	13.2%	−0.12 [−0.84, 0.60]
Subtotal (95% CI)			**98**			**90**	**82.5%**	**−0.01 [−0.30, 0.28]**
Heterogeneity: Chi² = 0.42, df = 3 (P = 0.94); I² = 0%								
Test for overall effect: Z = 0.06 (P = 0.95)								
Total (95% CI)			**120**			**112**	**100.0%**	**−0.15 [−0.41, 0.11]**
Heterogeneity: Chi² = 6.27, df = 5 (P = 0.28); I² = 20%								
Test for overall effect: Z = 1.15 (P = 0.25)								
Test for subgroup differences: Chi² = 5.51, df = 1 (P = 0.02), I² = 81.9%								

Fig. 41 Funnel plot for N2

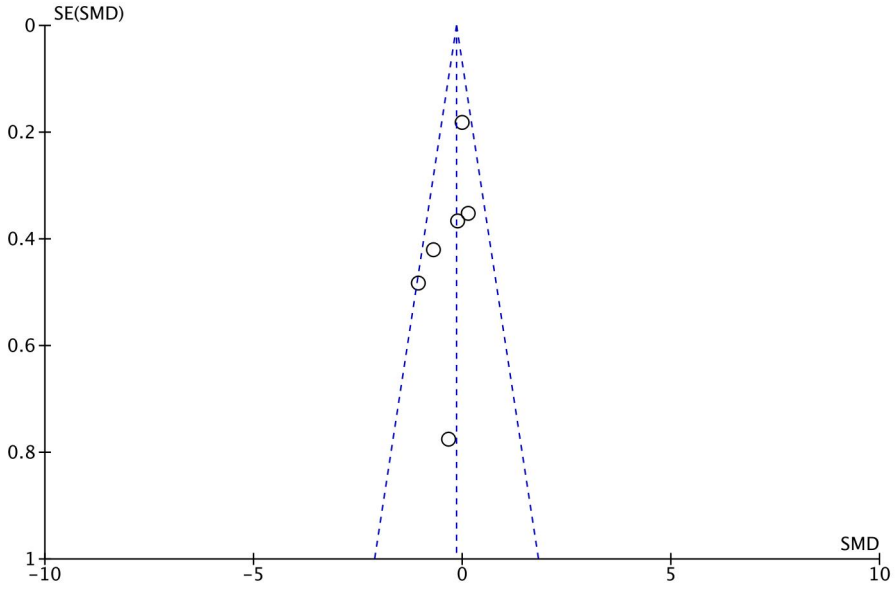


Fig. 42 pooled effects of trazodone on N3

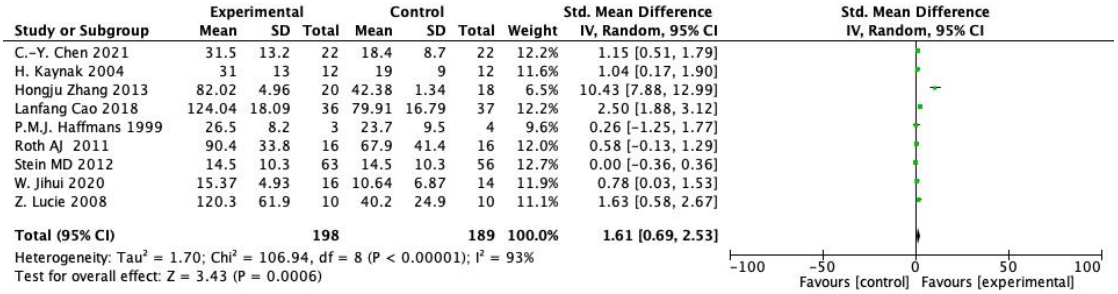


Fig. 43 subgroups analysis to N3 (mean age)

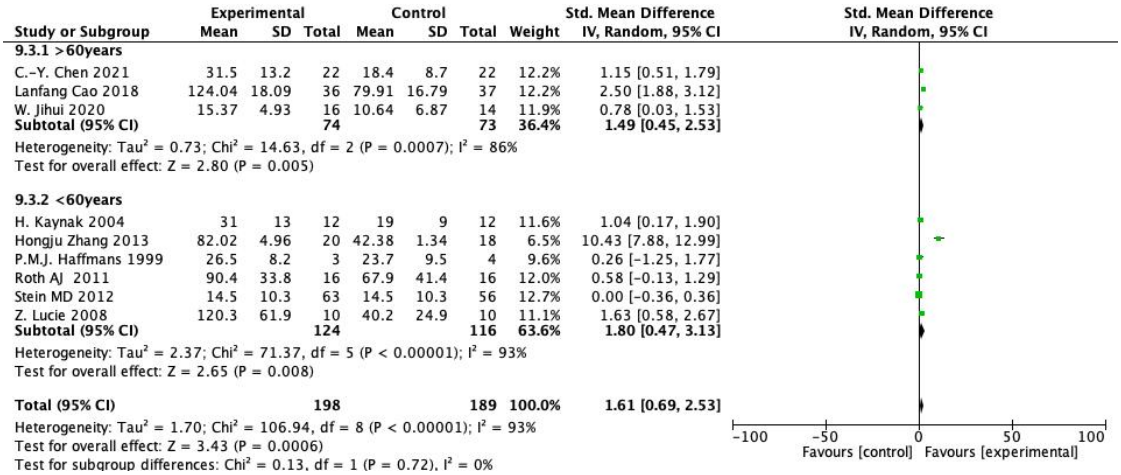


Fig. 44 subgroups analysis to N3(dosage)

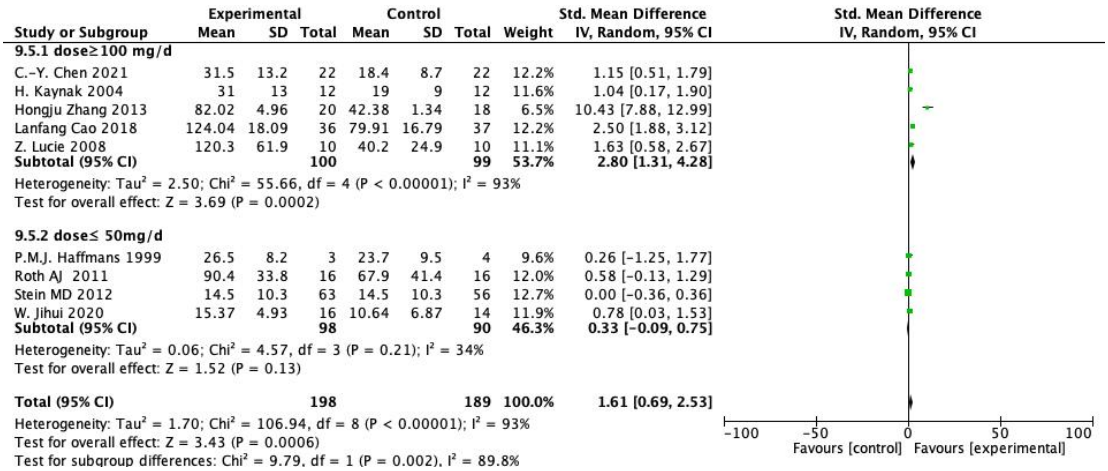


Fig. 45 subgroups analysis to N3 (treatment combination or placebo)

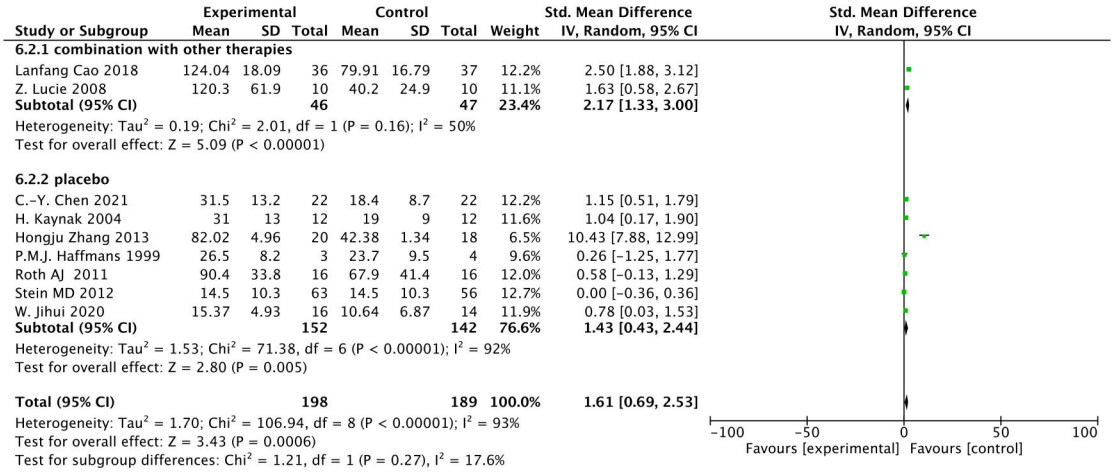


Fig. 46 subgroups analysis to N3 (treatment duration)

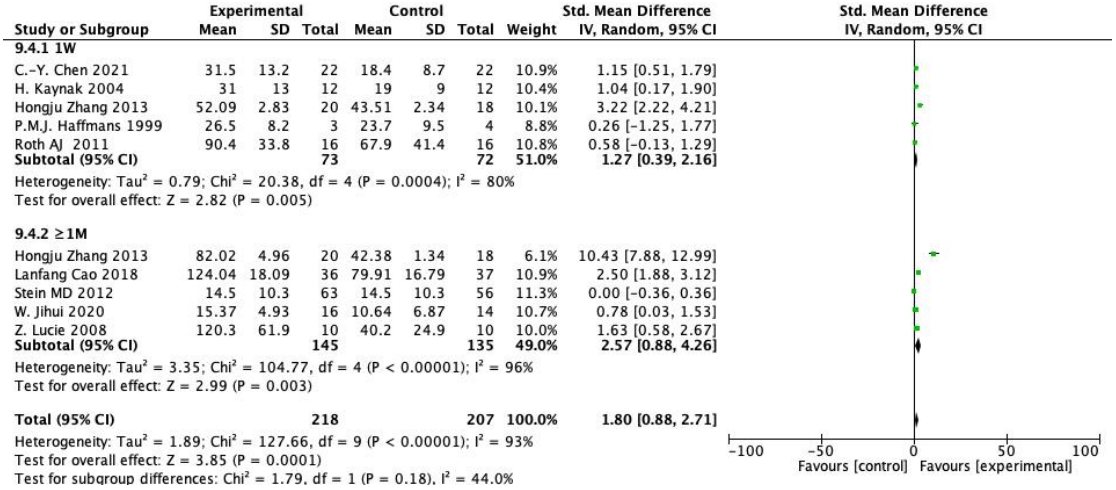


Fig. 47 Funnel plot for N3

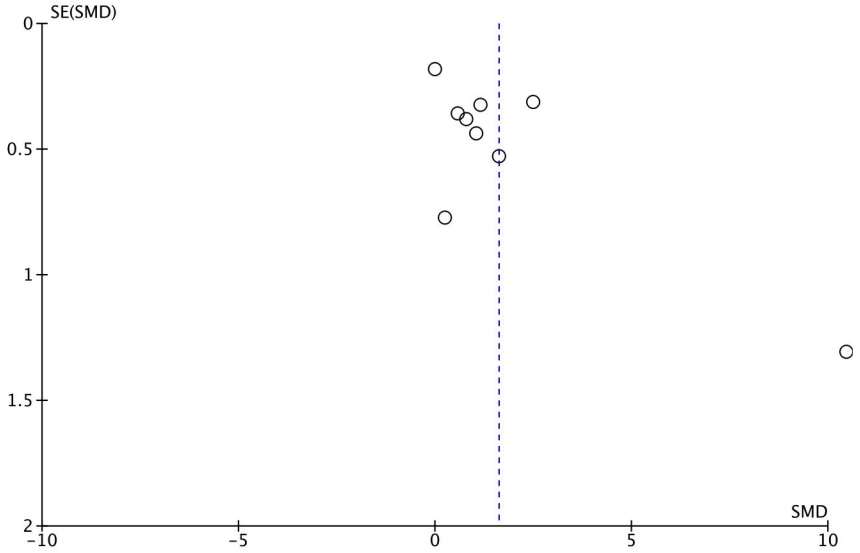


Fig. 48 discontinuation for all causes

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
C.-Y. Chen 2021	2	24	2	24	7.5%	1.00 [0.13, 7.75]
H. Kaynak 2004	0	12	0	12		Not estimable
Hongju Zhang 2013	0	20	2	20	10.0%	0.18 [0.01, 4.01]
Lanfang Cao 2018	0	36	0	37		Not estimable
Le Bon O 2003	1	9	1	9	3.6%	1.00 [0.05, 18.91]
P.M.J. Haffmans 1999	0	3	0	4		Not estimable
Roth AJ 2011	0	16	0	16		Not estimable
Stein MD 2012	6	69	12	68	45.2%	0.44 [0.16, 1.26]
W. Jihui 2020	4	20	6	20	19.6%	0.58 [0.14, 2.50]
Xuemin Li 2021	5	36	4	36	14.1%	1.29 [0.32, 5.26]
Z. Lucie 2008	0	10	0	10		Not estimable
Total (95% CI)		**255**		**256**	**100.0%**	**0.63 [0.33, 1.18]**
Total events	18		27			

Heterogeneity: Chi² = 2.36, df = 5 (P = 0.80); I² = 0%
Test for overall effect: Z = 1.44 (P = 0.15)

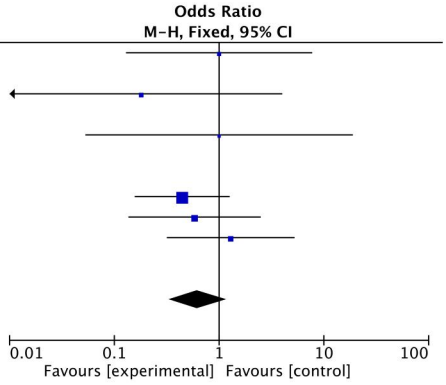


Fig. 49 Adverse event: dizziness

Study or Subgroup	trazodone Events	trazodone Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
C.-Y. Chen 2021	0	24	0	24		Not estimable
H. Kaynak 2004	0	12	0	12		Not estimable
Hongju Zhang 2013	0	20	0	20		Not estimable
Lanfang Cao 2018	0	36	0	37		Not estimable
Le Bon O 2003	2	9	0	9	3.7%	6.33 [0.26, 152.86]
P.M.J. Haffmans 1999	0	3	0	4		Not estimable
Roth AJ 2011	0	16	0	16		Not estimable
Stein MD 2012	16	67	7	67	53.2%	2.69 [1.03, 7.05]
W. Jihui 2020	3	20	4	20	33.9%	0.71 [0.14, 3.66]
Xuemin Li 2021	2	31	1	32	9.2%	2.14 [0.18, 24.86]
Z. Lucie 2008	0	10	0	10		Not estimable
Total (95% CI)		**248**		**251**	**100.0%**	**2.10 [1.00, 4.41]**
Total events	23		12			

Heterogeneity: Chi² = 2.40, df = 3 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.97 (P = 0.05)

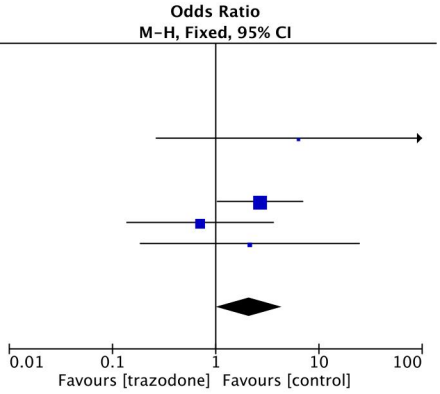


Fig. 50 Adverse event: headache

Study or Subgroup	trazodone Events	trazodone Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
C.-Y. Chen 2021	0	24	0	24		Not estimable
H. Kaynak 2004	0	12	0	12		Not estimable
Hongju Zhang 2013	0	20	0	20		Not estimable
Lanfang Cao 2018	0	36	0	37		Not estimable
Le Bon O 2003	0	9	2	9	22.5%	0.16 [0.01, 3.81]
P.M.J. Haffmans 1999	0	3	0	4		Not estimable
Roth AJ 2011	0	16	0	16		Not estimable
Stein MD 2012	8	67	4	67	33.4%	2.14 [0.61, 7.47]
W. Jihui 2020	1	20	2	20	18.0%	0.47 [0.04, 5.69]
Xuemin Li 2021	2	31	3	32	26.2%	0.67 [0.10, 4.29]
Z. Lucie 2008	0	10	0	10		Not estimable
Total (95% CI)		**248**		**251**	**100.0%**	**1.01 [0.43, 2.36]**
Total events	11		11			

Heterogeneity: Chi² = 3.23, df = 3 (P = 0.36); I² = 7%
Test for overall effect: Z = 0.02 (P = 0.99)

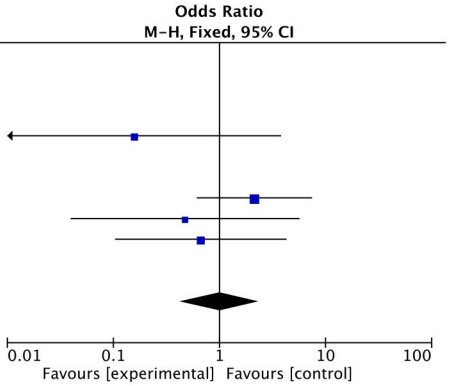


Fig. 51 Adverse event: daytime drowsiness

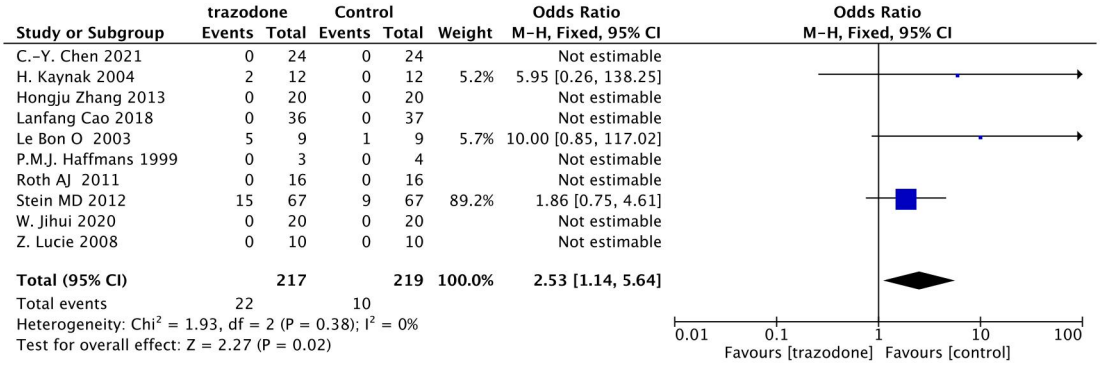
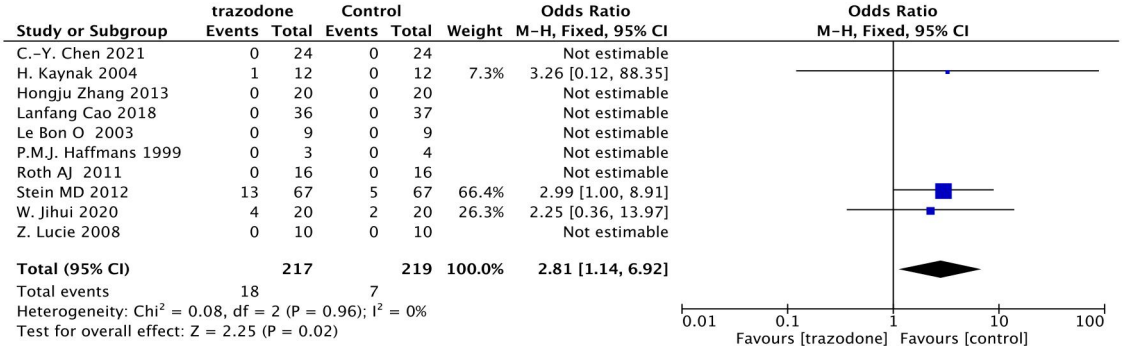


Fig. 52 Adverse event: decreased appetite



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