Forests plots and funnel plots for all parameters

Fig. 1 pooled effects of trazodone on TST

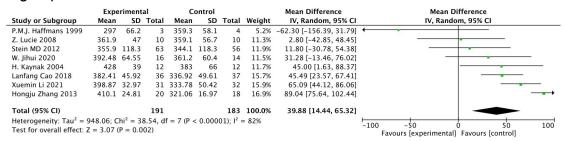


Fig. 2 subgroups analysis to TST (treatment duration)

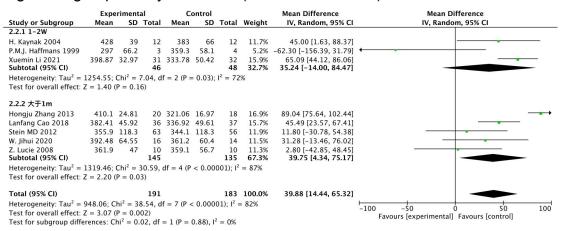


Fig. 3 subgroups analysis to TST (mean age)

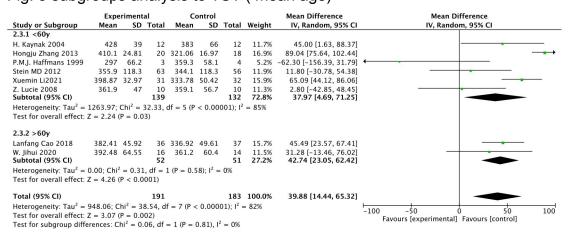


Fig. 4 subgroups analysis to TST(dosage)

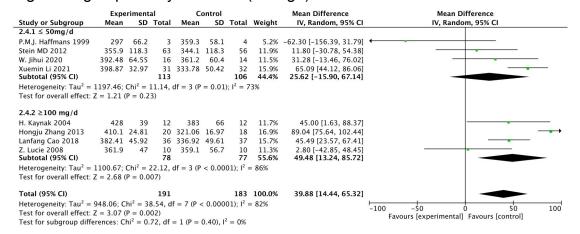


Fig. 5 subgroups analysis to TST(treatment combination or placebo)

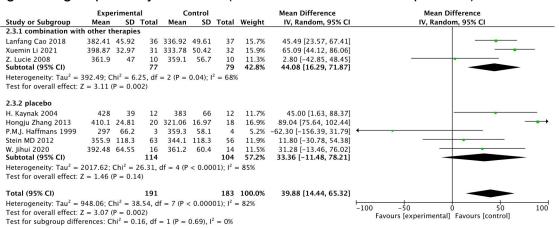


Fig. 6 Funnel plot for TST

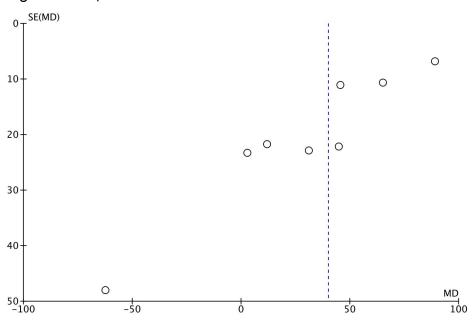


Fig. 7 pooled effects of trazodone on LPS

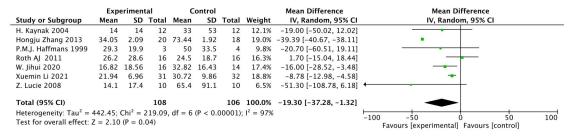


Fig. 8 Sensitivity analysis to LPS

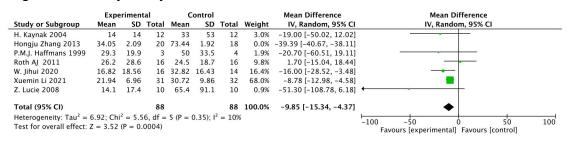


Fig. 9 subgroups analysis to LPS(dosage)

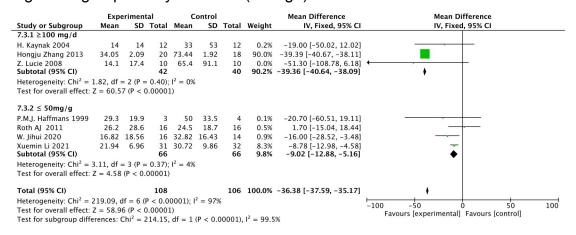
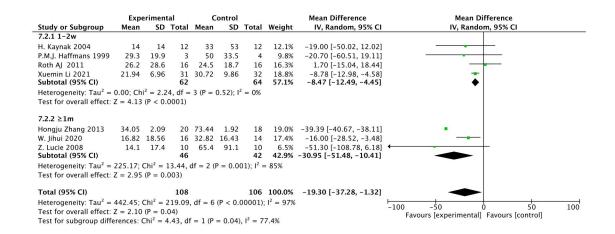


Fig. 10 subgroups analysis to LPS (treatment duration)



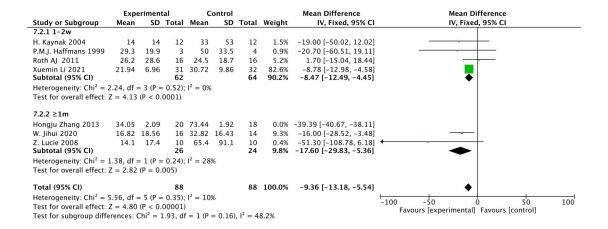


Fig. 11 subgroups analysis to LPS(combination with other therapies or placebo)

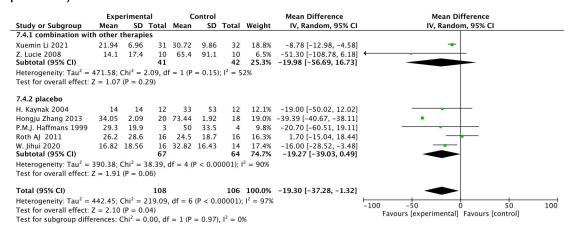


Fig. 12 Funnel plot for LPS

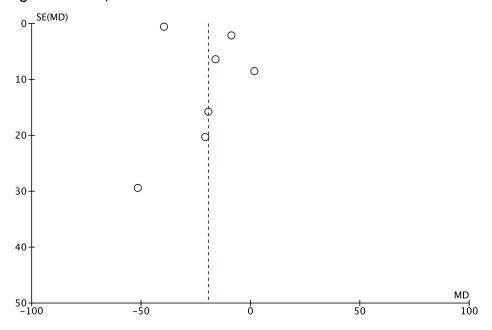


Fig. 13 pooled effects of trazodone on SE

	Expe	Experimental Control						Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
Hongju Zhang 2013	75	2	20	46	3	18	20.9%	29.00 [27.36, 30.64]			
Roth AJ 2011	85.3	11	16	81.7	12	16	20.0%	3.60 [-4.38, 11.58]	 -		
Stein MD 2012	85.8	12.1	63	85.3	12.1	56	20.7%	0.50 [-3.86, 4.86]	+		
W. Jihui 2020	81.67	11.87	16	75.88	22.4	14	18.6%	5.79 [-7.31, 18.89]	 • -		
Z. Lucie 2008	80.8	11.5	10	80.9	8	10	19.8%	-0.10 [-8.78, 8.58]	_		
Total (95% CI)			125				100.0%		-		
Heterogeneity: Tau ² =				6, df =	4 (P <	0.0000	(1) ; $I^2 = 9$	18%	-100 -50 0 50 100		
Test for overall effect	Z = 0.9	2 (P = 0)	0.36)						Favours [experimental] Favours [control]		

Fig. 14 Sensitivity analysis to SE

	Exp	Experimental Control						Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI		
Hongju Zhang 2013	75	2	20	46	3	18	0.0%	29.00 [27.36, 30.64]			
Roth AJ 2011	85.3	11	16	81.7	12	16	18.0%	3.60 [-4.38, 11.58]	+		
Stein MD 2012	85.8	12.1	63	85.3	12.1	56	60.2%	0.50 [-3.86, 4.86]	*		
W. Jihui 2020	81.67	11.87	16	75.88	22.4	14	6.7%	5.79 [-7.31, 18.89]	+-		
Z. Lucie 2008	80.8	11.5	10	80.9	8	10	15.2%	-0.10 [-8.78, 8.58]	+		
Total (95% CI)			105			96	100.0%	1.32 [-2.06, 4.70]	•		
Heterogeneity: Chi ² =); $I^2 = 0$	1%				-100 -50 0 50 100		
Test for overall effect	Z = 0.7	$^{'}6 (P = 0)$	0.44)						Favours [experimental] Favours [control]		

Fig. 15 Funnel plot for SE

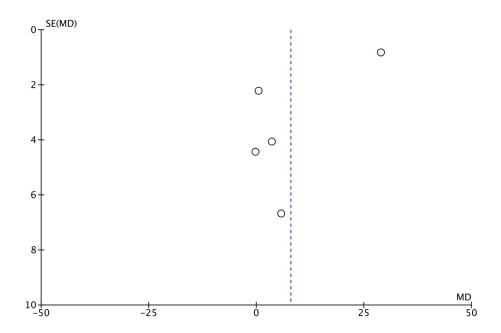


Fig. 16 pooled effects of trazodone on WASO

	Exp	eriment	tal	(Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Le Bon O 2003	3	6.49	8	12	6.49	8	12.5%	-1.31 [-2.42, -0.20]	•
P.M.J. Haffmans 1999	36.5	35.1	3	47.5	31.6	4	6.7%	-0.28 [-1.79, 1.23]	†
Roth AJ 2011	52.9	54.9	16	74.3	61.1	16	31.5%	-0.36 [-1.06, 0.34]	•
W. Jihui 2020	42.42	20.88	16	52.46	25.87	14	29.2%	-0.42 [-1.14, 0.31]	*
Z. Lucie 2008	74.8	56.7	10	75	33.2	10	20.1%	-0.00 [-0.88, 0.87]	*
Total (95% CI)			53			52	100.0%	-0.42 [-0.81, -0.03]	
Heterogeneity: $Chi^2 = 3$.40, df =	= 4 (P =	0.49);	$I^2 = 0\%$					100 100 100
Test for overall effect: 2	2 = 2.09	(P = 0.0)	04)						Favours [experimental] Favours [control]

Fig. 17 Sensitivity analysis of WASO to combination of treatment

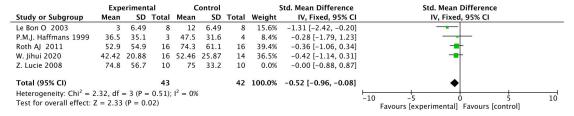


Fig. 18 Funnel plot for WASO

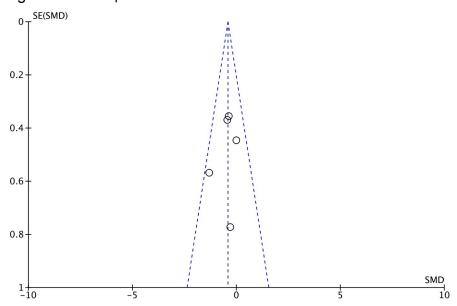


Fig. 19 pooled effects of trazodone on NAs (including both arousal times and arousal index)

	Experimental Control					Std. Mean Difference	Std. Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed	, 95% CI	
H. Kaynak 2004	12	13	12	30	18	12	8.0%	-1.11 [-1.98, -0.24]			
P.M.J. Haffmans 1999	2.3	2.2	3	5.3	3.4	4	2.3%	-0.85 [-2.49, 0.79]			
Roth AJ 2011	12.7	6.5	16	20	9.9	16	11.5%	-0.85 [-1.58, -0.12]			
Stein MD 2012	8.8	1.9	63	9.5	1.9	56	46.0%	-0.37 [-0.73, -0.00]			
W. Jihui 2020	22.51	11.57	16	26.37	11.1	14	11.6%	-0.33 [-1.05, 0.39]			
Xuemin Li2021	2.06	0.61	31	3.16	1.08	32	20.7%	-1.23 [-1.78, -0.69]			
Total (95% CI)			141			134	100.0%	-0.67 [-0.91, -0.42]			
Heterogeneity: $Chi^2 = 8$					%				-100 -50	50 1	00
Test for overall effect: 2	Z = 5.31	(P < 0.	00001)						Favours [experimental]		00

Fig. 20 Sensitivity analysis of NAs to combination of treatment

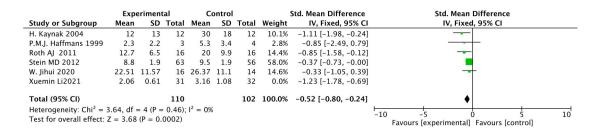


Fig. 21 Funnel plot for NAs

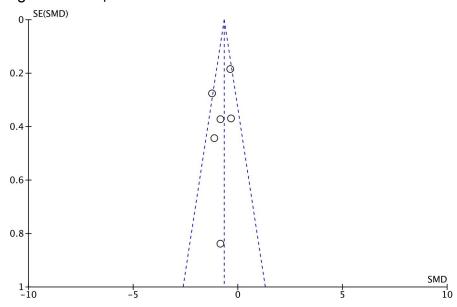


Fig. 22 pooled effects of trazodone on AHI

	Expe	erimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
CY. Chen 2021	25.4	15.4	16	39.1	18.4	14	30.6%	-13.70 [-25.94, -1.46]	
Stein MD 2012	2.8	44.6	22	2	44.6	22	11.2%	0.80 [-25.56, 27.16]	- +
W. Jihui 2020	3.92	1.72	63	4.12	1.35	56	58.2%	-0.20 [-0.75, 0.35]	•
Total (95% CI)			101			92	100.0%	-4.21 [-14.02, 5.59]	•
Heterogeneity: Tau ² =	= 42.90;	Chi ² =	4.67,	df = 2	(P = 0)	.10); I2	= 57%		-100 -50 0 50 100
Test for overall effect	Z = 0.8	84 (P =	0.40)						Favours [experimental] Favours [control]

Fig. 23 pooled effects of trazodone on REML

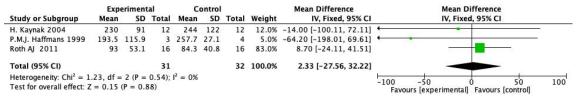


Fig. 24 pooled effects of trazodone on REM

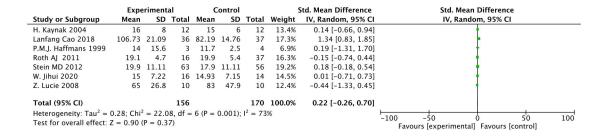


Fig. 25 Sensitivity analysis to REM

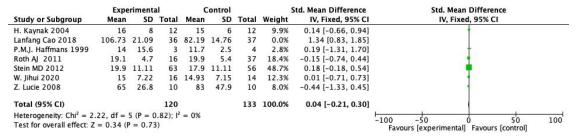


Fig. 26 subgroups analysis to REM (treatment duration)

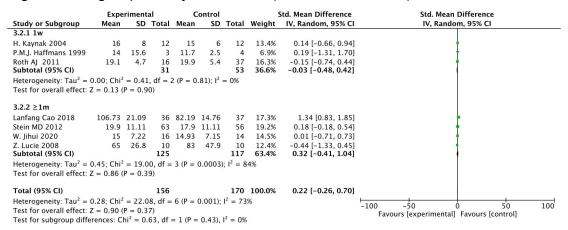


Fig. 27 subgroups analysis to REM(dosage)

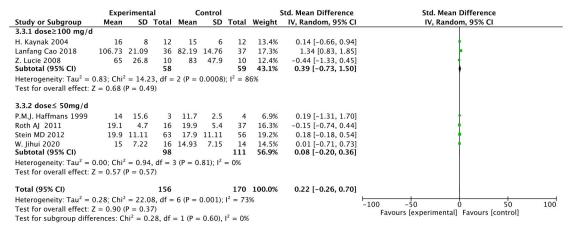


Fig. 28 subgroups analysis to REM (treatment combination or placebo)

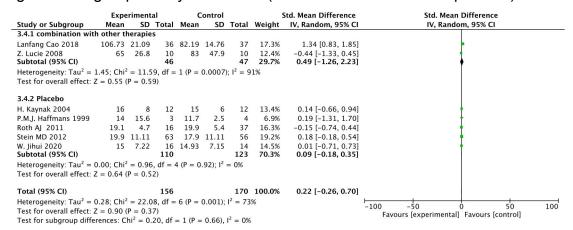


Fig. 29 Funnel plot for REM

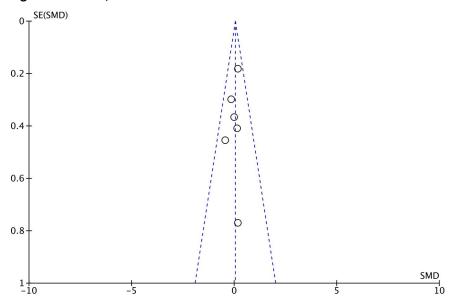


Fig. 30 pooled effects of trazodone on N1

	Expe	Experimental Control					9	Std. Mean Difference	Std. Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI			
H. Kaynak 2004	3	2	12	7	3	12	14.8%	-1.51 [-2.44, -0.59]	-			
P.M.J. Haffmans 1999	7.9	4.9	3	7.6	4.2	4	8.2%	0.06 [-1.44, 1.55]	- 			
Roth AJ 2011	17.9	9.5	16	28.8	11.6	16	18.0%	-1.00 [-1.74, -0.26]	-			
Stein MD 2012	2.4	2.5	63	2.5	2.5	56	25.7%	-0.04 [-0.40, 0.32]	†			
W. Jihui 2020	9.44	4.96	16	13.12	5.24	14	18.0%	-0.70 [-1.45, 0.04]				
Z. Lucie 2008	28.5	11.1	10	38.5	21	10	15.3%	-0.57 [-1.47, 0.33]	-			
Total (95% CI)			120				100.0%	-0.62 [-1.13, -0.12]	◆			
Heterogeneity: $Tau^2 =$				f = 5 (P)	= 0.0	2); $I^2 =$	62%		$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			
Test for overall effect:	Z = 2.42	(P = 0)	0.02)						Favours [experimental] Favours [control]			

Fig. 31 Sensitivity analysis of heterogeneity to N1

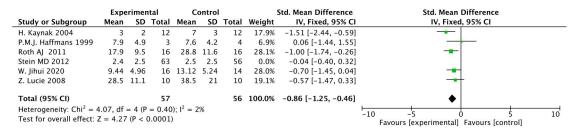


Fig. 32 Analysis on combination of treatment to N1

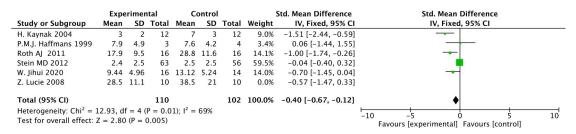


Fig. 33 subgroups analysis to N1 (treatment duration)

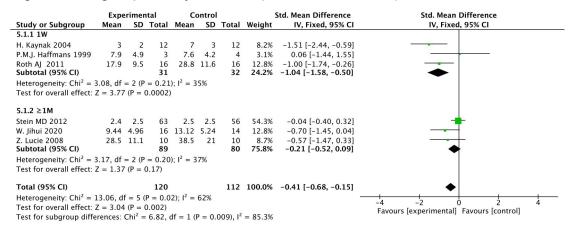


Fig. 34 subgroups analysis to N1(dosage)

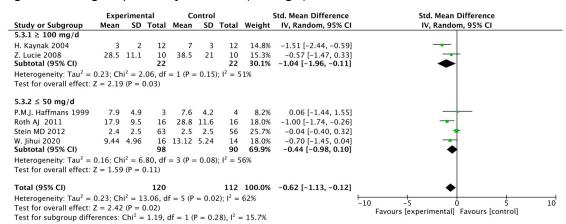


Fig. 35 Funnel plot for N1

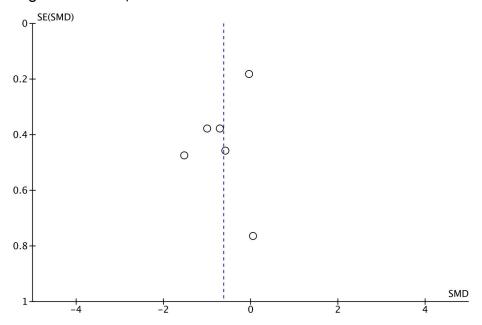


Fig. 36 pooled effects of trazodone on N2

	Exp	eriment	al	(Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	I 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]	1 †
Roth AJ 2011	223.1	47.2	16	216	58.2	16	14.1%	0.13 [-0.56, 0.82]	1 +
Stein MD 2012	63.3	13	63	63.3	13	56	52.3%	0.00 [-0.36, 0.36]	i]
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]	1
Total (95% CI)			120			112	100.0%	-0.15 [-0.41, 0.11]	1
Heterogeneity: $Chi^2 = 6$.27, df =	5 (P =	0.28);	$I^2 = 209$	6				-100 -50 0 50 1
Test for overall effect: 2	z = 1.15	(P = 0.2)	25)						Favours [experimental] Favours [control]

Fig. 37 Analysis on combination of treatment to N2

	Exp	Experimental			Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	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: Chi ² = 7 Test for overall effect:				= 0%					-10 -5 0 5 10
rest for overall effect:	Z = 0.58 ((r = 0.50)	"						Favours [experimental] Favours [control]

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

	Exp	eriment	al	(Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	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: $Chi^2 = 2$.14, df =	2 (P =	0.34);	$I^2 = 6\%$					
Test for overall effect: 2	Z = 0.84	(P = 0.4)	10)						-100 -50 0 50 100 Favours [experimental] Favours [control]

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

	Exp	eriment	al	(Control			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	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: Tau ² = 0	0.11; Chi	$^{2} = 4.0$	5, df =	2 (P = 0	0.13); I ²	= 51%			1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Test for overall effect: 2	Z = 0.94	(P = 0.3)	35)						Favours [experimental] Favours [control]

Fig. 40 subgroups analysis to N2(dosage)

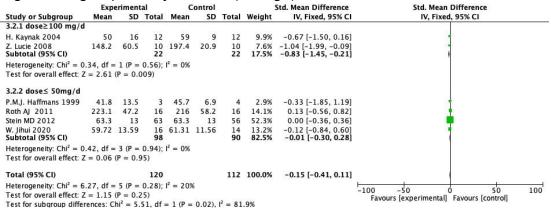


Fig. 41 Funnel plot for N2

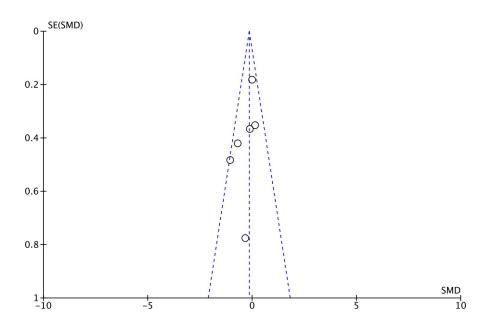


Fig. 42 pooled effects of trazodone on N3

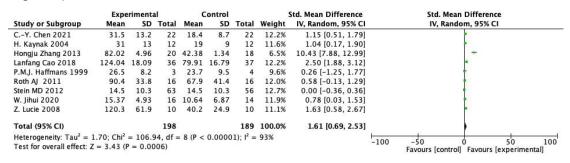


Fig. 43 subgroups analysis to N3 (mean age)

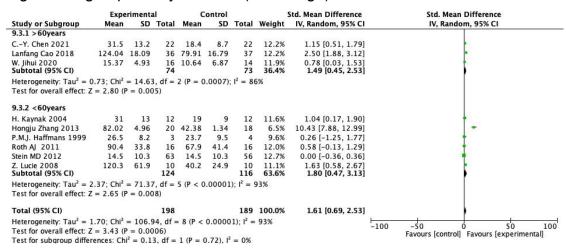


Fig. 44 subgroups analysis to N3(dosage)

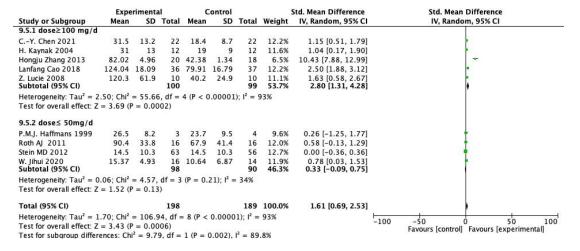


Fig. 45 subgroups analysis to N3 (treatment combination or placebo)

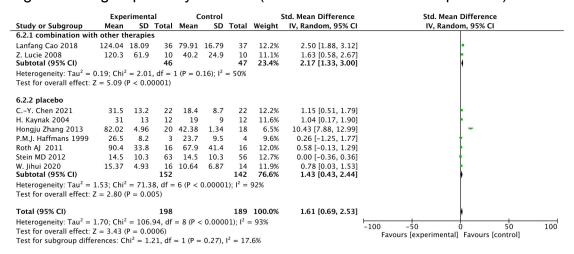


Fig. 46 subgroups analysis to N3 (treatment duration)

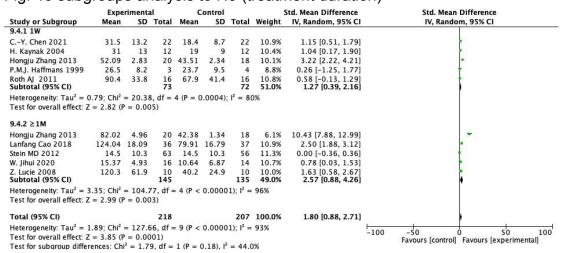


Fig. 47 Funnel plot for N3

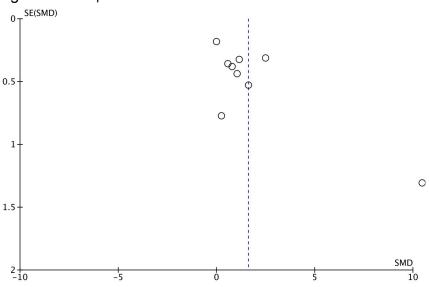


Fig. 48 discontinuation for all causes

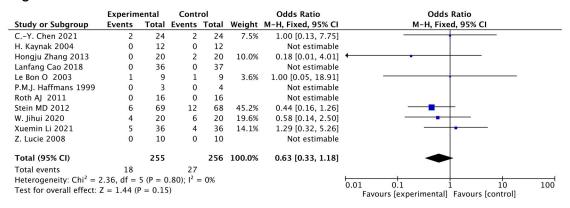


Fig. 49 Adverse event: dizziness

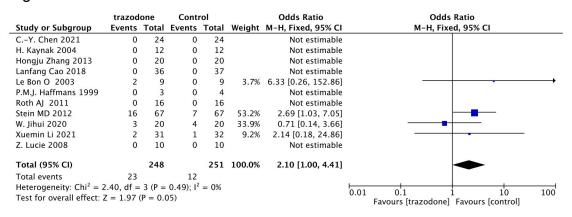


Fig. 50 Adverse event: headache

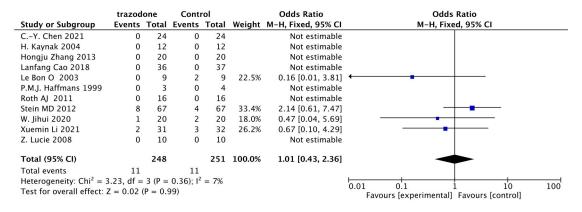


Fig. 51 Adverse event: daytime drowsiness

	trazod	one	Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
CY. Chen 2021	0	24	0	24		Not estimable	
H. Kaynak 2004	2	12	0	12	5.2%	5.95 [0.26, 138.25]	- ·
Hongju Zhang 2013	0	20	0	20		Not estimable	
Lanfang Cao 2018	0	36	0	37		Not estimable	
Le Bon O 2003	5	9	1	9	5.7%	10.00 [0.85, 117.02]	
P.M.J. Haffmans 1999	0	3	0	4		Not estimable	
Roth AJ 2011	0	16	0	16		Not estimable	
Stein MD 2012	15	67	9	67	89.2%	1.86 [0.75, 4.61]	+
W. Jihui 2020	0	20	0	20		Not estimable	
Z. Lucie 2008	0	10	0	10		Not estimable	
Total (95% CI)		217		219	100.0%	2.53 [1.14, 5.64]	•
Total events	22		10				
Heterogeneity: $Chi^2 = 1$.93, df =	2 (P =	0.38); I ²	= 0%			0.01 0.1 1 10 100
Test for overall effect: 2	z = 2.27	(P = 0.0)	02)				Favours [trazodone] Favours [control]

Fig. 52 Adverse event: decreased appetite

	trazod	one	Conti	rol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
CY. Chen 2021	0	24	0	24		Not estimable	
H. Kaynak 2004	1	12	0	12	7.3%	3.26 [0.12, 88.35]	· · · · · · · · · · · · · · · · · · ·
Hongju Zhang 2013	0	20	0	20		Not estimable	
Lanfang Cao 2018	0	36	0	37		Not estimable	
Le Bon O 2003	0	9	0	9		Not estimable	
P.M.J. Haffmans 1999	0	3	0	4		Not estimable	
Roth AJ 2011	0	16	0	16		Not estimable	
Stein MD 2012	13	67	5	67	66.4%	2.99 [1.00, 8.91]	
W. Jihui 2020	4	20	2	20	26.3%	2.25 [0.36, 13.97]	- •
Z. Lucie 2008	0	10	0	10		Not estimable	
Total (95% CI)		217		219	100.0%	2.81 [1.14, 6.92]	-
Total events	18		7				
Heterogeneity: $Chi^2 = 0$	0.08, df =	2 (P =	0.96); I ²	= 0%			
Test for overall effect: 2	Z = 2.25	(P = 0.0)	02)				6.01 0.1 1 10 100 Favours [trazodone] Favours [control]

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