Pharmacologic options for generalized anxiety disorder: a systematic review and network meta-analysis

Supplemental Appendix

Contents

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Alaka	2014		F1JMC-HMGF	Alaka KJ, Noble W, Montejo A et al. Efficacy and safety of duloxetine in the treatment of older adult patients with generalized anxiety disorder: a randomized, double-blind, placebo-controlled trial. Int J Geriatr Psychiatry. 2014 Sep;29(9):978-86.		
Allgulander	2001		S378, S3	Allgulander C, Hackett D, Salinas E. Venlafaxine extended release (ER) in the treatment of generalised anxiety disorder: twenty-four-week placebo-controlled dose-ranging study. Br J Psychiatry. 2001 Jul;179:15-22.	Venlefaxine XR, NDA 20-699 accessed from Food and Drug Administration via Freedom of Information Act Appeal	https://www.pfizer medicalinformation. com/en-us/effexor-xr#ClinicalStudies
Allgulander	2004			Allgulander C, Dahl AA, Austin C et al. Efficacy of sertraline in a 12-week trial for generalized anxiety disorder. Am J Psychiatry. 2004 Sep;161(9):1642-9.		
Baldwin	2006		SCT-MD-20	Baldwin DS, Huusom AK, Maehlum E. Escitalopram and paroxetine in the treatment of generalised anxiety disorder: randomised, placebo-controlled, double-blind study. Br J Psychiatry. 2006 Sep;189:264-72.	Study Summary: Lexapro(R) SCT-MD-20. Accessed from www.allerganclinicaltrials.com/	
Ball	2005			Ball SG, Kuhn A, Wall D, Shekhar A, Goddard AW. Selective serotonin reuptake inhibitor treatment for generalized anxiety disorder: a double-blind, prospective comparison between paroxetine and sertraline. J Clin Psychiatry. 2005 Jan;66(1):94-9.		

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Bandelow	2010	NCT00322595	S11 Silver	Bandelow B, Chouinard G, Bobes J et al. Extended-release quetiapine fumarate (quetiapine XR): a once-daily monotherapy effective in generalized anxiety disorder. Data from a randomized, double-blind, placebo- and active-controlled study. Int J Neuropsychopharmacol. 2010 Apr;13(3):305-20.		
Beyazyuz	2013			Beyazyüz M, Albayrak Y, Eğilmez OB, Albayrak N, Beyazyüz E. Relationship between SSRIs and Metabolic Syndrome Abnormalities in Patients with Generalized Anxiety Disorder: A Prospective Study. Psychiatry Investig. 2013 Jun;10(2):148-54.		
Bidzan	2012	NCT00744627	S311	Bidzan L, Mahableshwarkar AR, Jacobsen P, Yan M, Sheehan DV. Vortioxetine (Lu AA21004) in generalized anxiety disorder: results of an 8-week, multinational, randomized, double-blind, placebo-controlled clinical trial. Eur Neuropsychopharmacol. 2012 Dec;22(12):847-57.		
Bielski	2005			Bielski RJ, Bose A, Chang CC. A double-blind comparison of escitalopram and paroxetine in the long-term treatment of generalized anxiety disorder. Ann Clin Psychiatry. 2005 Apr-Jun;17(2):65-9.		
Boerner	2003			Boerner RJ, Sommer H, Berger W, Kuhn U, Schmidt U, Mannel M. Kava-Kava extract LI 150 is as effective as Opipramol and Buspirone in Generalised Anxiety Disorder--an 8-week randomized, double-blind multi-centre clinical trial in 129 out-patients. Phytomedicine. 2003;10 Suppl 4:38-49.		
Bose	2008		SCT-MD-31	Bose A, Korotzer A, Gommoll C, Li D. Randomized placebo-controlled trial of escitalopram and venlafaxine XR in the treatment of generalized anxiety disorder. Depress Anxiety. 2008;25(10):854-61.	Study Summary: Lexapro(R) SCT-MD-20. Accessed from www.allerganclinicaltrials.com/	

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Brawman-Mintzer	2006			Brawman-Mintzer O, Knapp RG, Rynn M, Carter RE, Rickels K. Sertraline treatment for generalized anxiety disorder: a randomized, double-blind, placebo-controlled study. J Clin Psychiatry. 2006 Jun;67(6):874-81.		
Bystritsky	2008		02113	Bystritsky A, Kerwin L, Feusner JD, Vapnik T. A pilot controlled trial of bupropion XL versus escitalopram in generalized anxiety disorder. Psychopharmacol Bull. 2008;41(1):46-51.		
Coric	2010	NCT00481325		Coric V, Feldman HH, Oren DA et al. Multicenter, randomized, double-blind, active comparator and placebo-controlled trial of a corticotropin-releasing factor receptor-1 antagonist in generalized anxiety disorder. *Depress Anxiety* 2010; 27(5):417-25.		
Cvjetkovic-Bosnjak	2015			Cvjetkovic-Bosnjak M, Soldatovic-Stajic B, Babovic SS, Boskovic K, Jovicevic M. Pregabalin versus sertraline in generalized anxiety disorder. An open label study. *Eur Rev Med Pharmacol Sci* 2015; 19(11):2120-4.		
Czobor	2010			Czobor P, Skolnick P, Beer B, Lippa A. A multicenter, placebo-controlled, double-blind, randomized study of efficacy and safety of ocinaplon (DOV 273,547) in generalized anxiety disorder. *CNS Neurosci Ther* 2010; 16(2):63-75.		
Davidson	1999		S214, S2	Davidson JR, DuPont RL, Hedges D, Haskins JT. Efficacy, safety, and tolerability of venlafaxine extended release and buspirone in outpatients with generalized anxiety disorder. J Clin Psychiatry. 1999 Aug;60(8):528-35.	Venlefaxine XR, NDA 20-699 accessed from Food and Drug Administration via Freedom of Information Act Appeal	
Davidson	2004		SCT-MD-07	Davidson JR, Bose A, Korotzer A, Zheng H. Escitalopram in the treatment of generalized anxiety disorder: double-blind, placebo controlled, flexible-dose study. *Depress Anxiety* 2004;19(4):234-40.	Study Summary: Lexapro(R) SCT-MD-07. Accessed from www.allerganclinicaltrials.com/	

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Durgam	2016	NCT01844115	VLZMD07	Durgam S, Gommoll C, Forero G et al. Efficacy and Safety of Vilazodone in Patients With Generalized Anxiety Disorder: A Randomized, Double-Blind, Placebo-Controlled, Flexible-Dose Trial. *J Clin Psychiatry 2016* ; 77(12):1687-1694.		
Feltner	2003		021	Feltner DE, Crockatt JG, Dubovsky SJ et al. A randomized, double-blind, placebo-controlled, fixed-dose, multicenter study of pregabalin in patients with generalized anxiety disorder. *J Clin Psychopharmacol* 2003; 23(3):240-9.		
Fresquet	2000			Fresquet A, Sust M, Lloret A et al. Efficacy and safety of lesopitron in outpatients with generalized anxiety disorder. *Ann Pharmacother* 2000; 34(2):147-53.		
Gao	2009			高润利,赵艳艳.米氮平与劳拉西泮治疗广泛性焦虑症的疗效观察[J].四川精神卫生 *Sichuan Mental Health* 2009; 22(01):59-63.		
Gelenberg	2000		S218, S4	Gelenberg AJ, Lydiard RB, Rudolph RL, Aguiar L, Haskins JT, Salinas E. Efficacy of venlafaxine extended-release capsules in nondepressed outpatients with generalized anxiety disorder: A 6-month randomized controlled trial. *JAMA* 2000; 283(23):3082-8.	https://www.pfizermedicalinformation.com/en-us/effexor-xr#ClinicalStudies	
Gommoll	2015	NCT01629966	VLZMD05	Gommoll C, Durgam S, Mathews M et al. A double-blind, randomized, placebo-controlled, fixed-dose phase III study of vilazodone in patients with generalized anxiety disorder. *Depress Anxiety* 2015; 32(6):451-9.		
Gommoll	2015	NCT01766401	VLZMD06	Gommoll C, Forero G, Mathews M et al. Vilazodone in patients with generalized anxiety disorder: a double-blind, randomized, placebo-controlled, flexible-dose study. Int Clin Psychopharmacol. 2015 Nov;30(6):297-306.		
GSK 637	Unpublished			Clinical Publication and scientific result summary for 29060/637. http://www.gsk-clinicalstudyregister.com		
GSK 791	Unpublished			Scientific result summary for 29060/791. http://www.gsk-clinicalstudyregister.com		
GSK 856	Unpublished			Scientific result summaries for 29060/637. http://www.gsk-clinicalstudyregister.com		

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Hackett	2003		S377	Hackett D, Haudiquet V, Salinas E. A method for controlling for a high placebo response rate in a comparison of venlafaxine XR and diazepam in the short-term treatment of patients with generalised anxiety disorder. *Eur Psychiatry* 2003; 18(4):182-7.	Kelsey JE. Efficacy, safety, and tolerability of venlafaxine XR in generalized anxiety disorder. *Depress Anxiety* 2000; 12 Suppl 1:81-4.	
Hartford	2007	NCT00122850	F1JMCHMDU	Hartford J, Kornstein S, Liebowitz M et al. Duloxetine as an SNRI treatment for generalized anxiety disorder: results from a placebo and active-controlled trial. Int *Clin Psychopharmacol* 2007; 22(3):167-74.	Clinical Study Summary: Study F1J-MC-HMDU, accessed at http://www.lillytrials.com/result s/Cymbalta.pdf	
Huang	2005			黄寅平,朱建中,蒋幸衍,周德怡,张峰.米氮平与阿普唑仑治疗广泛性焦虑的对照研究[J].中国行为医学科学 *Chinese Journal of Behavioral Medical Science* 2005; 10:919.		
Guo (2)	2009			郭慧荣,任玉明,李幼辉.米氮平治疗广泛性焦虑症32例疗效观察[J].郑州大学学报(医学版) *Journal of Zhengzhou University Medical Sciences* 2009; 44(01):206-208.		
Jia	2009			贾裕堂,陈圣侠,朱凤玲.米氮平与帕罗西汀治疗广泛性焦虑障碍的对照研究[J].精神医学杂志 *Journal of Psychiatry* 2009; 22(03):209-210.		
Kasper	2009	NCT00151450		Kasper S, Herman B, Nivoli G et al. Efficacy of pregabalin and venlafaxine-XR in generalized anxiety disorder: results of a double-blind, placebo-controlled 8-week trial. *Int Clin Psychopharmacol* 2009; 24(2):87-96.		
Kasper	2014			Kasper S, Gastpar M, Müller WE et al. Lavender oil preparation Silexan is effective in generalized anxiety disorder--a randomized, double-blind comparison to placebo and paroxetine. *Int J Neuropsychopharmacol* 2014; 17(6):859-69.		
Khan	2011	NCT00329264	S9 Titanium	Khan A, Joyce M, Atkinson S, Eggens I, Baldytcheva I, Eriksson H. A randomized, double-blind study of once-daily extended release quetiapine fumarate (quetiapine XR) monotherapy in patients with generalized anxiety disorder. *J Clin Psychopharmacol* 2011; 4:418-28.	Synopsis for D1448C00009, accessed at http://www.astrazenecaclinicaltr ials.com.	

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Kim	2006			Kim TS, Pae CU, Yoon SJ et al. Comparison of venlafaxine extended release versus paroxetine for treatment of patients with generalized anxiety disorder. Psychiatry *Clin Neurosci* 2006; 60(3):347-51.		
Koponen	2007	NCT00122824	F1JMCHMBR	Koponen H, Allgulander C, Erickson J et al. Efficacy of duloxetine for the treatment of generalized anxiety disorder: implications for primary care physicians. *Prim Care Companion J Clin Psychiatry* 2007; 9(2):100-7.	Clinical Study Summary: Study F1J-MC-HMBR, accessed at http://www.lillytrials.com/result s/Cymbalta.pdf	
Lader	1998			Lader M, Scotto JC. A multicentre double-blind comparison of hydroxyzine, buspirone and placebo in patients with generalized anxiety disorder. *Psychopharmacology (Berl)* 1998; 139(4):402-6.		
Lenox-Smith	2003			Lenox-Smith AJ, Reynolds A. A double-blind, randomised, placebo controlled study of venlafaxine XL in patients with generalised anxiety disorder in primary care. Br *J Gen Pract* 2003; 53(495):772-7.		
Lenze	2005			Lenze EJ, Mulsant BH, Shear MK et al. Efficacy and tolerability of citalopram in the treatment of late-life anxiety disorders: results from an 8-week randomized, placebo-controlled trial. *Am J Psychiatry* 2005; 162(1):146-50.		
Lenze	2009	NCT00105586		Lenze EJ, Rollman BL, Shear MK et al. Escitalopram for older adults with generalized anxiety disorder: a randomized controlled trial. *JAMA* 2009;301(3):295-303.		
Li	2005			李卫军,刘晓红.米氮平治疗广泛性焦虑症对照研究[J].神经疾病与精神卫生 *Nervous Diseases and Mental Hygiene* 2005; 06:447-448.		
Li	2011			李刚.艾司西酞普兰与氟西汀治疗广泛性焦虑的对照研究[J].现代医药卫生 *Modern Medicine & Health* 2011; 27(09):1287-1289.		
Liu	2004			刘祥臣,陈悦霞,苏荣红.氟西汀与地西泮治疗广泛性焦虑症的对照研究[J].中国行为医学科学 *Chinese Journal of Behavioral Medical Science* 2004; 03:43-44.		
LiuX	2005			刘晓伟,杨雀萍,曹磊明,王进良.米氮平和丁螺环酮治疗广泛性焦虑症的对照研究[J].中国民康医学 *Medical Journal of Chinese People Health* 2005; 09:495-496.		

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Llorca	2002			Llorca PM, Spadone C, Sol O et al. Efficacy and safety of hydroxyzine in the treatment of generalized anxiety disorder: a 3-month double-blind study. *J Clin Psychiatry* 2002; 63(11):1020-7.		
Mahableshwarkar	2014	NCT00730691	S308	Mahableshwarkar AR, Jacobsen PL, Chen Y, Simon JS. A randomised, double-blind, placebo-controlled, duloxetine-referenced study of the efficacy and tolerability of vortioxetine in the acute treatment of adults with generalised anxiety disorder. *Int J Clin Pract* 2014; 68(1):49-59.		
Mahableshwarkar	2014	NCT00731120	S309	Mahableshwarkar AR, Jacobsen PL, Serenko M, Chen Y. A randomized, double-blind, fixed-dose study comparing the efficacy and tolerability of vortioxetine 2.5 and 10 mg in acute treatment of adults with generalized anxiety disorder. *Hum Psychopharmacol* 2014; 29(1):64-72.		
Majercsik	2003			Majercsik E, Haller J, Leveleki C, Baranyi J, Halász J, Rodgers RJ. The effect of social factors on the anxiolytic efficacy of buspirone in male rats, male mice, and men. *Prog Neuropsychopharmacol Biol Psychiatry* 2003; 27(8):1187-99.		
Meredith	2012	NCT00329446	S10 Gold	Merideth C, Cutler AJ, She F, Eriksson H. Efficacy and tolerability of extended release quetiapine fumarate monotherapy in the acute treatment of generalized anxiety disorder: a randomized, placebo controlled and active-controlled study. Int Clin Psychopharmacol. 2012 Jan;27(1):40-54.		
Mezhebovsky	2013	NCT00389064	S15	Mezhebovsky I, Mägi K, She F, Datto C, Eriksson H. Double-blind, randomized study of extended release quetiapine fumarate (quetiapine XR) monotherapy in older patients with generalized anxiety disorder. *Int J Geriatr Psychiatry* 2013; 28(6):615-25.		
Michelson	2013			Michelson D, Hargreaves R, Alexander R et al. Lack of efficacy of L-759274, a novel neurokinin 1 (substance P) receptor antagonist, for the treatment of generalized anxiety disorder. *Int J Neuropsychopharmacol* 2013; 16(1):1-11.		

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Mokhber	2010			Mokhber N, Azarpazhooh MR, Khajehdaluee M, Velayati A, Hopwood M. Randomized, single-blind, trial of sertraline and buspirone for treatment of elderly patients with generalized anxiety disorder. *Psychiatry Clin Neurosci* 2010; 64(2):128-33.		
Moller	2001			Möller HJ, Volz HP, Reimann IW, Stoll KD. Opipramol for the treatment of generalized anxiety disorder: a placebo-controlled trial including an alprazolam-treated group. *J Clin Psychopharmacol* 2001; 21(1):59-65.		
Montgomery	2006		1008-087	Montgomery SA, Tobias K, Zornberg GL, Kasper S, Pande AC. Efficacy and safety of pregabalin in the treatment of generalized anxiety disorder: a 6-week, multicenter, randomized, double-blind, placebo-controlled comparison of pregabalin and venlafaxine. *J Clin Psychiatry* 2006; 67(5):771-82.		
Montgomery	2008		1008-090	Montgomery S, Chatamra K, Pauer L, Whalen E, Baldinetti F. Efficacy and safety of pregabalin in elderly people with generalised anxiety disorder. *Br J Psychiatry* 2008; 193(5):389-94.		
Nicolini	2009	NCT00122837	F1J-MC-HMDW	Nicolini H, Bakish D, Duenas H et al. Improvement of psychic and somatic symptoms in adult patients with generalized anxiety disorder: examination from a duloxetine, venlafaxine extended-release and placebo-controlled trial. Psychol Med. 2009 Feb;39(2):267-76.	Clinical Study Summary: Study F1J-MC-HMDW, accessed at http://www.lillytrials.com/results/Cymbalta.pdf	
Nimatoudis	2004			Nimatoudis I, Zissis NP, Kogeorgos J, Theodoropoulou S, Vidalis A, Kaprinis G. Remission rates with venlafaxine extended release in Greek outpatients with generalized anxiety disorder. A double-blind, randomized, placebo controlled study. *Int Clin Psychopharmacol* 2004; 6:331-6.		
Niu	2004			钮富荣,沈鑫华,孙松涛.米氮平与氟西汀治疗伴有广泛焦虑障碍的抑郁症各35例的疗效比较[J].中国新药与临床杂志 *Chinese Journal of New Drugs and Clinical Remedies* 2004; 12:853-855.		

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Pande	2003		1008-021	Pande AC, Crockatt JG, Feltner DE et al. Pregabalin in generalized anxiety disorder: a placebo-controlled trial. *Am J Psychiatry* 2003; 160(3):533-40.		
Peng	2012			彭岚,吴东,涂军,廖波,冷小兵,江昆伙.氟西汀与阿普唑仑治疗广泛性焦虑的对照研究[J].中国现代医生 *China Modern Doctor* 2012; 50(31):78-79.		
Pfizer	Unpublished		1008-025	Scientific discussion from EMEA. Accessed from http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion_-_Variation/human/000546/WC500046605.pdf	Stein DJ, Baldwin DS, Baldinetti F, Mandel F. Efficacy of pregabalin in depressive symptoms associated with generalized anxiety disorder: a pooled analysis of 6 studies. *Eur Neuropsychopharmacol* 2008; 18(6):422-30.	
Pfizer	Unpublished	NCT00368745	A0081092	Results from https://clinicaltrials.gov		
Pfizer	Unpublished	NCT00624780	A0081147	Public Disclosure Synopsis for protocol A0081147. Accessed from https://www.pfizermedicalinformation.com		
Pohl	2005		1008-085	Pohl RB, Feltner DE, Fieve RR, Pande AC. Efficacy of pregabalin in the treatment of generalized anxiety disorder: double-blind, placebo-controlled comparison of BID versus TID dosing. *J Clin Psychopharmacol* 2005; 25(2):151-8.		
Pollack	2001		S642	Pollack MH, Zaninelli R, Goddard A et al. Paroxetine in the treatment of generalized anxiety disorder: results of a placebo-controlled, flexible-dosage trial. *J Clin Psychiatry* 2001; 62(5):350-7.	Food and Drug Administration Application 20-031/S-026. Accessed at Drugs@FDA.gov	
Pollack	2005			Pollack MH, Roy-Byrne PP, Van Ameringen M et al. The selective GABA reuptake inhibitor tiagabine for the treatment of generalized anxiety disorder: results of a placebo-controlled study. *J Clin Psychiatry* 2005; 66(11):1401-8.		
Pollack	2008		S1, S2, S3	Pollack MH, Tiller J, Xie F, Trivedi MH. Tiagabine in adult patients with generalized anxiety disorder: results from 3 randomized, double-blind, placebo-controlled, parallel-group studies. *J Clin Psychopharmacol* 2008; 28(3):308-16.		

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Rickles	2000		S210 S1	Rickels K, Pollack MH, Sheehan DV, Haskins JT. Efficacy of extended-release venlafaxine in nondepressed outpatients with generalized anxiety disorder. *Am J Psychiatry* 2000; 157(6):968-74.	Venlefaxine XR, NDA 20-699 accessed from Food and Drug Administration via Freedom of Information Act Appeal	
Rickles	2003		S641	Rickels K, Zaninelli R, McCafferty J, Bellew K, Iyengar M, Sheehan D. Paroxetine treatment of generalized anxiety disorder: a double-blind, placebo-controlled study. *Am J Psychiatry* 2003; 160(4):749-56.		
Rickles	2005		1008-083	Rickels K, Pollack MH, Feltner DE et al. Pregabalin for treatment of generalized anxiety disorder: a 4-week, multicenter, double-blind, placebo-controlled trial of pregabalin and alprazolam. *Arch Gen Psychiatry* 2005; 62(9):1022-30.		
Rocca	1997			Rocca P, Fonzo V, Scotta M, Zanalda E, Ravizza L. Paroxetine efficacy in the treatment of generalized anxiety disorder. *Acta Psychiatr Scand* 1997; 95(5):444-50.		
Rosenthal	2003			Rosenthal M. Tiagabine for the treatment of generalized anxiety disorder: a randomized, open-label, clinical trial with paroxetine as a positive control. *J Clin Psychiatry* 2003; 64(10):1245-9.		
Rothschild	2012	NCT00734071	S310	Rothschild AJ, Mahableshwarkar AR, Jacobsen P, Yan M, Sheehan DV. Vortioxetine (Lu AA21004) 5 mg in generalized anxiety disorder: results of an 8-week randomized, double-blind, placebo-controlled clinical trial in the United States. *Eur Neuropsychopharmacol* 2012; 22(12):858-66.		
Rynn	2008	NCT00475969	F1JMCHMDT	Rynn M, Russell J, Erickson J et al. Efficacy and safety of duloxetine in the treatment of generalized anxiety disorder: a flexible-dose, progressive-titration, placebo-controlled trial. *Depress Anxiety* 2008; 25(3):182-9.	Clinical Study Summary: Study F1J-MC-HMDT accessed at http://www.lillytrials.com/results/Cymbalta.pdf	
SCTMD05	Unpublished		SCT-MD-05	Study Summary: Lexapro(R) SCT-MD-05. Accessed from www.allerganclinicaltrials.com/		
SCTMD06	Unpublished		SCT-MD-06	Study Summary: Lexapro(R) SCT-MD-06. Accessed from www.allerganclinicaltrials.com/		

Appendix 1 Included studies

Author	Year	Reg. No.	Other names	Source 1	Source 2	Source 3
Silverstone	2001			Silverstone PH, Salinas E. Efficacy of venlafaxine extended release in patients with major depressive disorder and comorbid generalized anxiety disorder. *J Clin Psychiatry* 2001; 62(7):523-9.		
Song	2007			宋传福,陶忠,武慎彬.米氮平治疗广泛性焦虑对照研究[J].临床精神医学杂志 *Journal of Clinical Psychiatry* 2007; 05:323-324.		
Stein	2008		CL2-040	Stein DJ, Ahokas AA, de Bodinat C. Efficacy of agomelatine in generalized anxiety disorder: a randomized, double-blind, placebo-controlled study. *J Clin Psychopharmacol* 2008; 28(5):561-6.		
Stein	2014	ISRCTN03554974	CL3-071	Stein DJ, Ahokas A, Márquez MS et al. Agomelatine in generalized anxiety disorder: an active comparator and placebo-controlled study. *J Clin Psychiatry* 2014; 75(4):362-8.		
Tang	2012			唐锴,叶庆红,陈志斌,阳春.度洛西汀片与氟西汀片治疗广泛性焦虑症对照观察[J].中国民康医学 *Journal of Clinical Psychiatry* 2012; 24(01):60-61.		
Wang	2009			王树元,李丛梅.米氮平与帕罗西汀治疗广泛性焦虑的对照研究[J].临床精神医学杂志 *Journal of Clinical Psychiatry* 2009; 19(02):76.		
Wu	2011		F1J-MC-HMFJ	Wu WY, Wang G, Ball SG, Desaiah D, Ang QQ. Duloxetine versus placebo in the treatment of patients with generalized anxiety disorder in China. *Chin Med J* 2011; 124(20):3260-8.		
Wu	2012			吴逢春,李烜,黄杏娟.盐酸安非他酮缓释片治疗焦虑症的临床观察[J].中国医药指南 *Guide of China Medicine* 2012; 10(21):114-116.		
Yang	2005			杨福收,王新法,王新友.米氮平治疗广泛性焦虑症的疗效及安全性[J].中国新药杂志 *Chinese New Drugs Journal* 2005; 05:113-115.		

Appendix 2 Description of included studies

Select Inclusion Criteria

Author	Year	Other names	Duration (weeks)	Double Blind	n Rand.	GadDx	Age Min	Age Max	Min BL HAM-A	Max BL MADRS	Max BL HAM-D
Alaka	2014	F1JMC-HMGF	10	Yes	291	GAD IV-TR	65				
Allgulander	2001	S378, S3	24	Yes	541	GAD IV	18		20		
Allgulander	2004		12	Yes	378	GAD IV	18		18		
Baldwin	2006	SCTMD20	12	Yes	682	GAD IV-TR	18	65	20	16	
Ball	2005		8	Yes	53	GAD IV	18		18		
Bandelow	2010	S11 Silver	8	Yes	873	GAD IV-TR	18	65	20	16	
Beyazyuz	2013		16	Unk	100	GAD IV	20	41			
Bidzan	2012	S311	8	Yes	301	GAD IV-TR	18		20		16
Bielski	2005		8	Yes	123	GAD IV	18	65	18		17
Boerner	2003		8	Yes	86	ICD-10	25	65	19		12
Bose	2008	SCT-MD-31	8	Yes	404	GAD IV	18	65	20		15
Brawman-Mintzer	2006		10	Yes	338	GAD IV	18		20		
Bystritsky	2008	02113	12	Yes	24	GAD IV	18	64	20		17
Coric	2010		8	Yes	260	GAD IV-TR	18	65	18		
Cvjetkovic-Bosnjak	2015		4	No	107	GAD IV	20	60	21		
Czobor	2010		4	Yes	60	GAD IV	18	60	20		15
Davidson	1999	S214, S2	8	Yes	405	GAD IV	18		18		
Davidson	2004	SCTMD07	8	Yes	315	GAD IV	18	80	16		17
Durgam	2016	VLZMD07	8	Yes	415	GAD IV-TR	18	70	20		17
Feltner	2003	021	4	Yes	271	GAD IV	18				
Fresquet	2000		6	Yes	68	GAD IV	18	65	18		15
Gao	2009		6	Unk	54	CCMD-3			14		
Gelenberg	2000	S218, S4	26	Yes	251	GAD IV	18		18		
Gommoll	2015	VLZMD05	8	Yes	680	GAD IV-TR	18	70	20		17
Gommoll	2015	VLZMD06	8	Yes	402	GAD IV-TR	18	70	20		17
GSK 637	Unpublished		8	Yes	374	GAD IV	18		20		
GSK 791	Unpublished		8	Yes	335	GAD IV	18		20		
GSK 856	Unpublished		8	Yes	361	GAD IV	18		20		
Hackett	2003	S377	8	Yes	556	GAD IV	18		20		
Hartford	2007	F1JMCHMDU	10	Yes	487	GAD IV	18				

Appendix 2 Description of included studies

Author	Year	Other names	Duration (weeks)	Double Blind	n Rand.	GadDx	Age Min	Age Max	Min BL HAM-A	Max BL MADRS	Max BL HAM-D
Huang	2005		6	Unk	60	CCMD-3	20	52	15		
Guo (2)	2009	2009	2009	Unk	62	CCMD-3	16	60	14		8
Jia	2009		8	Unk	76	CCMD-3			14		
Kasper	2009		8	Yes	374	GAD IV	18	65	20		
Kasper	2014		10	Yes	273	GAD IV-TR	18	65	18		
Khan	2011	S9 Titanium	8	Yes	951	GAD IV-TR	18	65	20	16	
Kim	2006		8	Yes	60	GAD IV	18	65			
Koponen	2007	F1JMCHMBR	9	Yes	513	GAD IV	18				
Lader	1998		4	Yes	246	GAD IV	18	65	20		
Lenox-Smith	2003		24	Yes	244	GAD IV	18		20	22	
Lenze	2005		8	Yes	34	GAD IV	60		17		
Lenze	2009		12	Yes	179	GAD IV	60		17		
Li	2005		6	Unk	60	CCMD-3			16		
Li	2011		8	Unk	60	CCMD-3	18	60	14		16
Liu	2004		4	Unk	112	CCMD-3			15		
LiuX	2005		6	Unk	64	CCMD-3	18	65	15		
Llorca	2002		12	Yes	334	GAD IV	18	65	20		
Mahableshwarkar	2014	S308	8	Yes	781	GAD IV-TR	18	65	20	16	
Mahableshwarkar	2014	S309	8	Yes	457	GAD IV-TR	18		20	15	
Majercsik	2003		6	Yes	52	GAD IV	65		16		
Meredith	2012	S10 Gold	8	Yes	854	GAD IV-TR	18	65	20	16	
Mezhebovsky	2013	S15	9	Yes	450	GAD IV	66		20	16	
Michelson	2013		6	Yes	140	GAD IV	18	60	20		
Mokhber	2010		8	No	46	GAD IV	60		20		
Moller	2001		4	Yes	313	ICD-10	18	65	17		20
Montgomery	2006	1008-087	5	Yes	421	GAD IV	18		20		
Montgomery	2008	1008-090	8	Yes	273	GAD IV	65		20		
Nicolini	2009	F1J-MC-HMDW	10	Yes	581	GAD IV	18				
Nimatoudis	2004		8	Yes	46	GAD IV	18		18		12
Niu	2004		8	Unk	70	GAD IV	18	71			18

Appendix 2 Description of included studies   **Select Inclusion Criteria**

Author	Year	Other names	Duration (weeks)	Double Blind	n Rand.	GadDx	Age Min	Age Max	Min BL HAM-A	Max BL MADRS	Max BL HAM-D
Pande	2003	1008-021	4	Yes	276	GAD IV	18		20		
Peng	2012		6	Unk	60	CCMD-3			14		
Pfizer	Unpublished	1008-025	4	Yes	262	GAD IV	18				
Pfizer	Unpublished	A0081092	6	Yes	108	GAD IV-TR	18	65			
Pfizer	Unpublished	A0081147	12	Yes	615	GAD IV	18	65	18		
Pohl	2005	1008-085	6	Yes	341	GAD IV	18		20		
Pollack	2001	S642	8	Yes	326	GAD IV	18		20	16	
Pollack	2005		8	Yes	272	GAD IV	18	64	18	19	
Pollack	2008	S1	10	Yes	910	GAD IV-TR	18	64	20	20	
Pollack	2008	S2	10	Yes	468	GAD IV-TR	18	64	20	20	
Pollack	2008	S3	10	Yes	452	GAD IV-TR	18	64	20	20	
Rickles	2000	S210 S1	8	Yes	349	GAD IV	18		18		
Rickles	2003	S641	8	Yes	566	GAD IV	18		20	16	
Rickles	2005	1008-083	4	Yes	454	GAD IV	18		20		
Rocca	1997		8	No	56	GAD IV	18	65	18		14
Rosenthal	2003		10	No	40	GAD IV	18	65	18		14
Rothschild	2012	S310	8	Yes	304	GAD IV-TR	18		20	16	
Rynn	2008	F1JMCHMDT	10	Yes	327	GAD IV	18				
SCTMD05	Unpublished		8	Yes	254	GAD IV	18		18		17
SCTMD06	Unpublished		8	Yes	287	GAD IV	18		18		17
Silverstone	2001		12	Yes	92	GAD IV	18				
Song	2007		6	Unk	66	CCMD-3			14		
Stein	2008	CL2-040	12	Yes	121	GAD IV-TR	18	65	22	16	
Stein	2014	CL3-071	12	Yes	412	GAD IV-TR	18	65	22	16	
Tang	2012		6	Unk	60	CCMD-3	20	55	21		
Wang	2009		8	Unk	59	CCMD-3					
Wu	2011	F1J-MC-HMFJ	15	Yes	210	GAD IV	18				
Wu	2012		6	Yes	59	CCMD-3	18		14		
Yang	2005		6	Unk	60	CCMD-3			14		

Appendix 3 Description of included studies

Author	Year	Arms	Mean Age	Majority Race/ Country	% Female	Mean HAM-A
Alaka	2014	Group 1 N= 140 Placebo Group 2 N= 151 Duloxetine 30-120 mg	71.5	85% Caucasian	78%	24.5
Allgulander	2001	Group 1 N= 130 Placebo Group 2 N= 138 Venlafaxine ER 37.5mg Group 3 N= 134 Venlafaxine ER 75mg Group 4 N= 137 Venlafaxine ER 150mg	45.1	Europe	61%	26.5
Allgulander	2004	Group 1 N= 188 Placebo Group 2 N= 182 Sertraline 50 - 150mg	41.4	98% Caucasian	54%	24.8
Baldwin	2006	Group 1 N= 139 Placebo Group 2 N= 139 Paroxetine 20 mg Group 3 N= 134 Escitalopram 5 mg Group 4 N= 136 Escitalopram 10 mg Group 5 N= 133 Escitalopram 20 mg	41.4	99% caucasian	64%	27.0
Ball	2005	Group 1 N= 28 Sertraline 25-100mg Group 2 N= 25 Paroxetine 10-40mg	39.5	90% Caucasian	77%	21.1
Bandelow	2010	Group 1 N= 217 Placebo Group 2 N= 214 Paroxetine 20 mg Group 3 N= 219 Quetiapine XR 50 mg Group 4 N= 216 Quetiapine XR 150 mg	41.4	94% Caucasian	65%	27.0
Beyazyuz	2013	Group 1 N= 20 Sertraline Group 2 N= 20 Fluoxetine Group 3 N= 20 Paroxetine Group 4 N= 18 Citalopram	27.3	Turkey	100%	26.2
Bidzan	2012	Group 1 N= 151 Placebo Group 2 N= 150 Vortioxetine 5mg	45.2	100% Caucasian	65%	26.6
Bielski	2005	Group 1 N= 60 Paroxetine 20-50mg Group 2 N= 61 Escitalopram 10-20mg	37.1	75% Caucasian	62%	23.6
Boerner	2003	Group 1 N= 43 Buspirone Group 2 N= 43 Opipramol		Germany	84%	23.7
Bose	2008	Group 1 N= 140 Placebo Group 2 N= 133 Venlafaxine 75mg-225mg Group 3 N= 131 Escitalopram 10-20mg	37.6	76% Caucasian	62%	23.9
Brawman-Mintzer	2006	Group 1 N= 162 Placebo Group 2 N= 164 Sertraline 50-200mg	40.5	75% Caucasian	56%	24.3

Appendix 3 Description of included studies

Author	Year	Arms	Mean Age	Majority Race/ Country	% Female	Mean HAM-A
Bystritsky	2008	Group 1 N= 11 Bupropion XL 150-300 mg Group 2 N= 13 Escitalopram 10 -20mg	35.0	UCLA	63%	26.0
Coric	2010	Group 1 N= 104 Placebo Group 2 N= 53 Escitalopram 20mg	38.9	78% Caucasian	0%	24.2
Cvjetkovic-Bosnjak	2015	Group 1 N= 47 Pregabalin 225 mg Group 2 N= 60 Sertraline 150 mg	37.6	Serbia	68%	23.6
Czobor	2010	Group 1 N= 29 Placebo Group 2 N= 31 Ocinaplon 90 mg	44.8	Europe	65%	31.5
Davidson	1999	Group 1 N= 104 Placebo Group 2 N= 98 Buspirone 30 mg Group 3 N= 102 Venlafaxine ER 75mg Group 4 N= 101 Venlafaxine ER dose 150 mg	37.8	89% Caucasian	55%	23.5
Davidson	2004	Group 1 N= 157 Placebo Group 2 N= 158 Escitalopram 10-20 mg	39.5	71% Caucasian	53%	23.4
Durgam	2016	Group 1 N= 207 Placebo Group 2 N= 208 Vilazodone 20-40mg	39.9	76% Caucasian	64%	24.7
Feltner	2003	Group 1 N= 67 Placebo Group 2 N= 68 Lorazepam 6 mg Group 3 N= 70 Pregabalin 150mg Group 4 N= 66 Pregabalin 600mg	37.8	72% Caucasian	53%	24.9
Fresquet	2000	Group 1 N= 20 Placebo Group 2 N= 18 Lesopitron 40-80mg Group 3 N= 30 Lorazepam 2-4mg	36.6	65% Caucasian	51%	21.2
Gao	2009	Group 1 N= 27 Lorazepam Group 2 N= 27 Mirtazepine	36.3	China	52%	31.0
Gelenberg	2000	Group 1 N= 127 Placebo Group 2 N= 124 Venlafaxine ER 75-225mg	39.5	91% Caucasian	56%	25.0
Gommoll	2015	Group 1 N= 223 Placebo Group 2 N= 230 Vilazodone 20mg Group 3 N= 227 Vilazodone 40mg	40.2	76% Caucasian	64%	24.5
Gommoll	2015	Group 1 N= 201 Placebo Group 2 N= 202 Vilazodone 20-40mg	40.3	81% Caucasian	69%	25.4
GSK 637	Unpublished	Group 1 N= 185 Placebo Group 2 N= 187 Paroxetine 20-50mg	46.0	99% Caucasian	70%	27.7

Appendix 3 Description of included studies

Author	Year	Arms	Mean Age	Majority Race/ Country	% Female	Mean HAM-A
GSK 791	Unpublished	Group 1 N= 167 Placebo Group 2 N= 168 Paroxetine 12.5-37.5mg	39.0	78% Caucasian	62%	24.6
GSK 856	Unpublished	Group 1 N= 182 Placebo Group 2 N= 179 Paroxetine 20mg	40.1	Japan	59%	
Hackett	2003	Group 1 N= 97 Placebo Group 2 N= 89 Diazepam 15mg Group 3 N= 191 Venlafaxine ER 75mg Group 4 N= 179 Venlafaxine ER 150mg	44.2		66%	27.9
Hartford	2007	Group 1 N= 161 Placebo Group 2 N= 164 Venlafaxine XR 75mg-225mg Group 3 N= 162 Duloxetine 60mg-120mg	40.8	70% Caucasian	63%	25.2
Huang	2005	Group 1 N= 30 Alprazolam Group 2 N= 30 Mirtazepine	36.5	China	57%	24.9
Guo (2)	2009	Group 1 N= 30 Paroxetine Group 2 N= 32 Mirtazepine	38.0	China	48%	21.8
Jia	2009	Group 1 N= 38 Paroxetine Group 2 N= 38 Mirtazepine	42.8	China	50%	17.7
Kasper	2009	Group 1 N= 128 Placebo Group 2 N= 125 Venlafaxine ER 75-225mg Group 3 N= 121 Pregabalin 300-600mg	40.8	71% Caucasian	49%	27.3
Kasper	2014	Group 1 N= 128 Placebo Group 2 N= 125 Venlafaxine ER 75-225mg Group 3 N= 121 Pregabalin 300-600mg	45.2	Germany	74%	25.4
Khan	2011	Group 1 N= 235 Placebo Group 2 N= 234 Quetiapine XR 50mg Group 3 N= 241 Quetiapine XR 150mg Group 4 N= 241 Quetiapine XR 300mg	40.0	81% Caucasian	58%	24.6
Kim	2006	Group 1 N= 30 Paroxetine 10-40 mg Group 2 N= 30 Venlafaxine XR 37.5-225 mg	44.2	Korea	47%	29.4
Koponen	2007	Group 1 N= 175 Placebo Group 2 N= 168 Duloxetine 60mg Group 3 N= 170 Duloxetine 120mg	43.8	99% Caucasian	68%	25.3
Lader	1998	Group 1 N= 81 Placebo Group 2 N= 81 Hydroxyzine 50mg Group 3 N= 82 Buspirone 20mg	41.0	Europe	69%	26.5

Appendix 3 Description of included studies

Author	Year	Arms	Mean Age	Majority Race/ Country	% Female	Mean HAM-A
Lenox-Smith	2003	Group 1 N= 122 Placebo Group 2 N= 122 Venlafaxine 75-150mg	47.0	Europe	59%	28.0
Lenze	2005	Group 1 N= 17 Placebo Group 2 N= 17 Citalopram 30mg	69.4	94% Caucasian	62%	22.3
Lenze	2009	Group 1 N= 92 Placebo Group 2 N= 85 Escitalopram 10-20mg	71.7	82% Caucasian	68%	23.0
Li	2005	Group 1 N= 30 Alprazolam Group 2 N= 30 Mirtazepine	37.1	China	53%	26.9
Li	2011	Group 1 N= 30 Fluoxetine Group 2 N= 30 Escitalopram	39.3	China	55%	25.0
Liu	2004	Group 1 N= 56 Fluoxetine Group 2 N= 56 Diazepam	36.2	China	41%	32.2
LiuX	2005	Group 1 N= 30 Buspirone Group 2 N= 34 Mirtazepine	38.0	China	55%	32.9
Llorca	2002	Group 1 N= 113 Placebo Group 2 N= 116 Bromazepam 6mg Group 3 N= 105 Hydroxyzine 50mg	43.3	Europe	68%	25.5
Mahableshwarkar	2014	Group 1 N= 150 Placebo Group 2 N= 156 Duloxetine 60mg Group 3 N= 156 Vortioxetine 2.5mg Group 4 N= 156 Vortioxetine 5mg Group 5 N= 156 Vortioxetine 10mg	38.6	75-80% Caucasian	68%	25.0
Mahableshwarkar	2014	Group 1 N= 153 Placebo Group 2 N= 152 Vortioxetine 2.5mg Group 3 N= 152 Vortioxetine 10mg	41.2	70% Caucasian	67%	24.9
Majercsik	2003	Group 1 N= 19 Placebo Group 2 N= 33 Buspirone 30mg	81.1	Europe	0%	20.7
Meredith	2012	Group 1 N= 215 Placebo Group 2 N= 213 Escitalopram 10 mg Group 3 N= 219 Quetiapine XR 150mg Group 4 N= 207 Quetiapine XR 300mg	38.5	US	65%	25.0
Mezhebovsky	2013	Group 1 N= 227 Placebo Group 2 N= 223 Quetiapine XR 50-300mg	70.5	US & Europe	70%	25.1
Michelson	2013	Group 1 N= 71 Placebo Group 2 N= 69 Lorazepam 1-6mg	38.9	Europe	78%	24.1

Appendix 3 Description of included studies

Author	Year	Arms	Mean Age	Majority Race/ Country	% Female	Mean HAM-A
Mokhber	2010	Group 1 N= 25 Buspirone 10-15 mg/day Group 2 N= 21 Sertraline 50-100 mg/day	66.5	Iran	57%	28.7
Moller	2001	Group 1 N= 100 Placebo Group 2 N= 100 Alprazolam Group 3 N= 100 Opipramol	48.0		67%	28.3
Montgomery	2006	Group 1 N= 101 Placebo Group 2 N= 113 Venlafaxine ER 75mg Group 3 N= 97 Pregabalin 400mg Group 4 N= 110 Pregabalin 600mg	44.0	99% Caucasian	62%	26.5
Montgomery	2008	Group 1 N= 96 Placebo Group 2 N= 177 Pregabalin 150-600mg	72.3	98% Caucasian	78%	26.6
Nicolini	2009	Group 1 N= 170 Placebo Group 2 N= 169 Venlafaxine ER 75-225 mg Group 3 N= 84 Duloxetine 20mg Group 4 N= 158 Duloxetine 60-120 mg	41.4	Australia, Argentina, Belgium, Canada, Mexico, Russia, Taiwan and the UK	63%	24.3
Nimatoudis	2004	Group 1 N= 22 Placebo Group 2 N= 24 Venlafaxine ER 75-150mg	42.8	67% Caucasian	57%	27.5
Niu	2004	Group 1 N= 36 Fluoxetine Group 2 N= 37 Mirtazepine	43.5	China	69%	22.5
Pande	2003	Group 1 N= 69 Placebo Group 2 N= 68 Lorazepam 6mg Group 3 N= 69 Pregabalin 150mg Group 4 N= 70 Pregabalin 600mg	35.8	84% Caucasian	59%	23.3
Peng	2012	Group 1 N= 31 Fluoxetine Group 2 N= 29 Alprazolam	37.5	China	58%	28.4
Pfizer 1008-025	Unpublished	Group 1 N=64 Placebo Group 2 N= 62 Lorazepam 6 mg Group 3 N= 68 Pregabalin 150 mg Group 4 N= 68 Pregabalin 600 mg			0%	24.5
Pfizer A0081092	Unpublished	Group 1 N= 51 Placebo Group 2 N= 57 Pregabalin 75 - 300mg	41.7	81% Caucasian	70%	
Pfizer A0081147	Unpublished	Group 1 N= 203 Lorazepam 3=4 mg Group 2 N= 206 Pregabalin 150-300 mg Group 3 N= 206 Pregabalin 400-600 mg	41.9	84% Caucasian	61%	24.9

Appendix 3 Description of included studies

Author	Year	Arms	Mean Age	Majority Race/ Country	% Female	Mean HAM-A
Pohl	2005	Group 1 N= 86 Placebo Group 2 N= 78 Pregabalin 200mg Group 3 N= 89 Pregabalin 400mg Group 4 N= 88 Pregabalin 450mg		> 50% Caucasian		25.5
Pollack	2001	Group 1 N= 163 Placebo Group 2 N= 161 Paroxetine 20-50mg	40.5	84% caucasian	63%	24.1
Pollack	2005	Group 1 N= 132 Placebo Group 2 N= 138 Tiagabine 4-16mg	37.3		56%	25.9
Pollack S1	2008	Group 1 N= 230 Placebo Group 2 N= 226 Tiagabine 4mg Group 3 N= 227 Tiagabine 8mg Group 4 N= 227 Tiagabine 12mg	38.4		48%	26.8
Pollack S2	2008	Group 1 N= 237 Placebo Group 2 N= 231 Tiagabine 4-16mg	38.9		64%	26.7
Pollack S3	2008	Group 1 N= 229 Placebo Group 2 N= 223 Tiagabine 4-16mg	40.1		59%	27.0
Rickles	2000	Group 1 N= 97 Placebo Group 2 N= 92 Venlafaxine ER 75mg Group 3 N= 91 Venlafaxine ER dose 150mg Group 4 N= 90 Venlafaxine ER 225mg	40.8	86% Caucasian	56%	24.2
Rickles	2003	Group 1 N= 180 Placebo Group 2 N= 188 Paroxetine 20mg	40.5	85% Caucasian	55%	24.1
Rickles	2005	Group 1 N= 91 Placebo Group 2 N= 93 Alprazolam 1.5mg	39.2	78% Caucasian	64%	24.9
Rocca	1997	Group 1 N= 30 Paroxetine Group 2 N= 26 Imipramine	36.4	Italy	84%	25.8
Rosenthal	2003	Group 1 N= 20 Paroxetine 20-60 mg Group 2 N= 20 Tiagabine 4-16mg	35.0		58%	23.4
Rothschild	2012	Group 1 N= 152 Placebo Group 2 N= 152 Vortioxetine 5mg	41.2	83% Caucasian	66%	24.7
Rynn	2008	Group 1 N= 159 Placebo Group 2 N= 168 Duloxetine 60mg-120mg	41.6	79% Caucasian	62%	23.0
SCTMD05	Unpublished	Group 1 N= 128 Placebo Group 2 N= 124 Escitalopram 10 -20mg	40.3	79% Caucasian	61%	22.4
SCTMD06	Unpublished	Group 1 N= 138 Placebo Group 2 N= 143 Escitalopram 10 -20mg	37.7	79% Caucasian	55%	22.6

Appendix 3 Description of included studies

Author	Year	Arms	Mean Age	Majority Race/ Country	% Female	Mean HAM-A
Silverstone	2001	Group 1 N= 25 Placebo Group 2 N= 32 Venlafaxine ER 75mg Group 3 N= 33 Fluoxetine 20mg	43.5		67%	27.3
Song	2007	Group 1 N= 33 Alprazolam Group 2 N= 33 Mirtazepine	41.0	China	41%	34.4
Stein	2008	Group 1 N= 58 Placebo Group 2 N= 63 Agomelatine 25-50mg	41.7	Finland and South Africa	69%	28.8
Stein	2014	Group 1 N= 131 Placebo Group 2 N= 142 Escitalopram 10 -20mg Group 2 N= 139 Agomelatine 25-50mg	42.6	Finland, Russia, Poland, Czech Republic, Slovakia, Argentina and South Korea	72%	28.5
Tang	2012	Group 1 N= 30 Fluoxetine Group 2 N= 30 Duloxetine	29.8	China	32%	24.5
Wang	2009	Group 1 N= 30 Paroxetine Group 2 N= 29 Mirtazepine	30.0	China	68%	28.2
Wu	2011	Group 1 N= 102 Placebo Group 2 N= 108 Duloxetine60 mg	37.6	China	50%	24.4
Wu	2012	Group 1 N= 102 Placebo Group 2 N= 108 Duloxetine 60mg		China	0%	
Yang	2005	Group 1 N= 30 Maprotiline Group 2 N= 30 Mirtazepine	37.9	China	52%	23.0

Appendix 4 Risk of bias assessments

Author	Year	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
Alaka	2014	Low	Low	Low	Low	Low	Low	Low
Allgulander	2001	Low	Low	Low	Low	High	Unclear	Low
Allgulander	2004	Unclear	Unclear	Low	Low	High	Unclear	Unclear
Baldwin	2006	Low	Low	Low	Low	High	Unclear	Low
Ball	2005	Unclear	Unclear	Low	Low	High	Unclear	Unclear
Bandelow	2010	Low	Low	Low	Low	High	Unclear	Low
Beyazyuz	2013	Unclear	Unclear	High	High	High	Unclear	Unclear
Bidzan	2012	Low	Low	Low	Low	High	Unclear	Low
Bielski	2005	Unclear	Unclear	Low	Low	High	Low	Unclear
Boerner	2003	Low	Low	Low	Low	High	Unclear	Unclear
Bose	2008	Low	Low	Low	Low	High	Unclear	Low
Brawman-Mintzer	2006	Low	Low	Low	Low	High	Unclear	Unclear
Bystritsky	2008	Low	Low	Low	Low	High	Unclear	Unclear
Coric	2010	Low	Low	Low	Low	High	Unclear	Low
Cvjetkovic-Bosnjak	2015	Unclear	Unclear	High	High	Low	Unclear	Unclear
Czobor	2010	Unclear	Unclear	Low	Low	High	Unclear	Unclear
Davidson	1999	Unclear	Unclear	Low	Low	High	Unclear	Low
Davidson	2004	Unclear	Unclear	Low	Low	High	Unclear	Low
Durgam	2016	Low	Low	Low	Low	High	Unclear	Low
Feltner	2003	Unclear	Unclear	Low	Low	High	Unclear	Unclear
Fresquet	2000	Unclear	Unclear	Low	Low	Low	Unclear	Unclear
Gao	2009	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Gelenberg	2000	Low	Low	Low	Low	High	Unclear	Low
Gommoll	2015	Low	Low	Low	Low	High	Unclear	Low
Gommoll	2015	Low	Low	Low	Low	High	Unclear	Low
GSK 637	Unpublished	Unclear	Unclear	Low	Low	High	Unclear	Low
GSK 791	Unpublished	Unclear	Unclear	Low	Low	High	Unclear	Low
GSK 856	Unpublished	Unclear	Unclear	Low	Low	High	Unclear	Low
Hackett	2003	Unclear	Unclear	Low	Low	High	Unclear	Low
Hartford	2007	Unclear	Unclear	Low	Low	High	Low	Low
Huang	2005	High	High	High	High	Low	Unclear	Unclear
Guo (2)	2009	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear

Appendix 4 Risk of bias assessments

Author	Year	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
Jia	2009	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Kasper	2009	Low	Low	Low	Low	High	Unclear	Low
Kasper	2014	Low	Low	Low	Low	High	Unclear	Unclear
Khan	2011	Low	Low	Low	Low	High	Low	Low
Kim	2006	Unclear	Unclear	High	High	High	Unclear	Unclear
Koponen	2007	Low	Low	Low	Low	High	Low	Low
Lader	1998	Low	Low	Low	Low	High	Unclear	Unclear
Lenox-Smith	2003	Low	Low	Low	Low	High	Unclear	Unclear
Lenze	2005	Low	Low	Low	Low	High	Unclear	Unclear
Lenze	2009	Low	Low	Low	Low	High	Unclear	Unclear
Li	2005	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Li	2011	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Liu	2004	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
LiuX	2005	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Llorca	2002	Unclear	Unclear	Low	Low	High	Unclear	Unclear
Mahableshwarkar	2014	Low	Low	Low	Low	High	Unclear	Low
Mahableshwarkar	2014	Low	Low	Low	Low	High	Unclear	Low
Majercsik	2003	Unclear	Unclear	Low	Low	Low	Unclear	Unclear
Meredith	2012	Low	Low	Low	Low	High	Unclear	Low
Mezhebovsky	2013	Low	Low	Low	Low	High	Unclear	Low
Michelson	2013	Low	Low	Low	Low	High	Unclear	Unclear
Mokhber	2010	Unclear	Unclear	Low	High	Low	Unclear	Unclear
Moller	2001	Low	Low	Low	Low	High	Unclear	Unclear
Montgomery	2006	Unclear	Unclear	Low	Low	High	Unclear	Low
Montgomery	2008	Unclear	Unclear	Low	Low	High	Unclear	Low
Nicolini	2009	Low	Low	Low	Low	High	Low	Low
Nimatoudis	2004	Unclear	Unclear	Low	Low	High	Unclear	Unclear
Niu	2004	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Pande	2003	Unclear	Unclear	Low	Low	High	Unclear	Low
Peng	2012	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Pfizer 1008-025	Unpublished	Unclear	Unclear	Low	Low	High	Unclear	High
Pfizer A0081092	Unpublished	Low	Low	Low	Low	High	Unclear	Low

Appendix 4 Risk of bias assessments

Author	Year	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
Pfizer A0081147	Unpublished	Unclear	Unclear	Low	Low	High	Unclear	Low
Pohl	2005	Unclear	Unclear	Low	Low	High	Unclear	Low
Pollack	2001	Unclear	Unclear	Low	Low	High	Low	Low
Pollack	2005	Unclear	Unclear	Low	Low	High	Unclear	Low
Pollack S1	2008	Low	Low	Low	Low	High	Unclear	Low
Pollack S2	2008	Low	Low	Low	Low	High	Unclear	Low
Pollack S3	2008	Low	Low	Low	Low	High	Unclear	Low
Rickles	2000	Unclear	Unclear	Low	Low	High	Unclear	Low
Rickles	2003	Unclear	Unclear	Low	Low	High	Unclear	Low
Rickles	2005	Low	Low	Low	Low	High	Unclear	Low
Rocca	1997	Unclear	Unclear	High	High	High	Unclear	Unclear
Rosenthal	2003	Unclear	Unclear	High	High	High	Unclear	Low
Rothschild	2012	Low	Low	Low	Low	High	Unclear	Low
Rynn	2008	Unclear	Unclear	Low	Low	High	Low	Low
SCTMD05	Unpublished	Unclear	Unclear	Low	Low	High	Low	Low
SCTMD06	Unpublished	Unclear	Unclear	Low	Low	High	Low	Low
Silverstone	2001	Unclear	Unclear	Low	Low	High	Unclear	Unclear
Song	2007	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Stein	2008	Low	Low	Low	Low	Low	Unclear	Low
Stein	2014	Low	Low	Low	Low	High	Unclear	Low
Tang	2012	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Wang	2009	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear
Wu	2011	Low	Unclear	Low	Low	Unclear	Low	
Wu	2012	Low	Low	Low	Low	Low	Low	Unclear
Yang	2005	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear

Appendix 5 Efficacy Subgroups

Drug	Main	Anxiety		Depression	
		HAM-A ≤ 25	HAM-A > 25	ES ≤ 4.05	ES > 4.05
Agomelatine	-3.55 (-5.83, -1.26)		-3.82 (-6.56, -1.12)		-3.63 (-7.20, -0.10)
Benzodiazepine	-2.29 (-3.19, -1.39)	-2.01 (-3.02, -1.07)	-1.97 (-3.93, 0.02)	-2.26 (-3.34, -1.14)	-2.69 (-7.82, 2.42)
Bupropion	-5.30 (-8.62, -2.00)		-8.89 (-14.19, -3.57)	-7.96 (-11.87, -4.08)	-1.64 (-6.80, 3.49)
Buspirone	-2.37 (-3.83, -0.91)	-3.61 (-5.34, -1.87)	-1.13 (-3.95, 1.67)		
Citalopram	-2.22 (-4.28, -0.19)	-3.62 (-6.74, -0.45)	-2.13 (-5.37, 1.07)	-3.61 (-6.45, -0.82)	-1.17 (-5.75, 3.42)
Duloxetine	-3.13 (-4.13, -2.13)	-2.88 (-4.03, -1.74)	-3.10 (-5.00, -1.21)	-3.11 (-3.90, -2.32)	
Escitalopram	-2.45 (-3.27, -1.63)	-2.15 (-2.98, -1.37)	-3.15 (-5.12, -1.23)	-2.37 (-3.23, -1.51)	-2.66 (-5.43, 0.07)
Fluoxetine	-2.43 (-3.74, -1.16)	-1.57 (-3.27, 0.09)	-2.81 (-5.05, -0.63)		-1.17 (-5.73, 3.39)
Hydroxyzine	-3.00 (-5.03, -0.96)		-2.62 (-5.14, -0.09)		-3.63 (-8.79, 1.48)
Imipramine	-0.59 (-3.85, 2.70)		-1.10 (-5.11, 2.93)		-0.73 (-6.41, 5.00)
Maprotiline	0.38 (-3.25, 4.02)	0.24 (-3.09, 3.60)			
Mirtazapine	-3.12 (-4.43, -1.80)	-3.22 (-4.73, -1.76)	-2.15 (-4.72, 0.42)		
Ocinaplon	-7.90 (-14.68, -1.06)		-7.86 (-14.91, -0.70)		-7.91 (-15.78, -0.07)
Opipramol	-1.92 (-3.99, 0.15)	;-4.30 (-8.28, -0.22)	-1.37 (-4.47, 1.74)	-1.55 (-3.14, 0.07)	
Paroxetine	-2.29 (-3.11, -1.47)	-2.19 (-3.27, -1.12)	-2.80 (-4.23, -1.36)	-1.44 (-2.68, -0.12)	-2.45 (-5.16, 0.25)
Pregabalin	-2.79 (-3.69, -1.91)	-2.34 (-3.37, -1.36)	-3.07 (-4.82, -1.33)	-2.84 (-3.85, -1.85)	-2.78 (-7.98, 2.48)
Quetiapine	-3.60 (-4.83, -2.39)	-2.32 (-3.63, -1.01)	-5.00 (-7.20, -2.80)	-2.31 (-3.78, -0.79)	-4.99 (-8.22, -1.82)
Sertraline	-2.88 (-4.17, -1.59)	-2.49 (-3.81, -1.19)	-3.47 (-6.37, -0.60)	-3.69 (-5.60, -1.77)	-2.16 (-5.64, 1.26)
Tiagabine	-0.77 (-2.18, 0.62)	-0.97 (-5.95, 4.07)	-0.77 (-2.56, 1.01)		-1.49 (-5.65, 2.67)
Venlafaxine	-2.69 (-3.50, -1.89)	-3.05 (-4.23, -1.87)	-2.71 (-3.94, -1.54)	-3.06 (-4.03, -2.09)	-0.49 (-5.68, 4.76)
Vilazodone	-1.45 (-3.02, 0.12)	-1.52 (-3.04, -0.02)	-1.25 (-4.67, 2.17)		-1.10 (-4.48, 2.22)
Vortioxetine	-1.12 (-2.47, 0.24)	-0.43 (-1.63, 0.79)	-3.83 (-7.46, -0.18)	-0.40 (-1.53, 0.80)	-3.85 (-8.81, 1.16)

Appendix 5 Efficacy Subgroups

Drug	Main	Age ≤ 40.3 Years	Age > 40.3 Years	% Female ≤ 61.8%	% Female > 61.8%	Excluding China
Agomelatine	-3.55 (-5.83, -1.26)		-3.71 (-6.53, -0.93)		-3.53 (-5.90, -1.16)	-3.57 (-5.89, -1.25)
Benzodiazepine	-2.29 (-3.19, -1.39)	-2.26 (-3.21, -1.27)	-3.21 (-5.32, -1.19)	-2.04 (-3.29, -0.82)	-2.65 (-4.21, -1.13)	-2.61 (-3.63, -1.61)
Bupropion	-5.30 (-8.62, -2.00)	-7.88 (-11.86, -3.75)		-2.87 (-7.98, 2.19)	-8.05 (-12.75, -3.37)	-8.20 (-12.81, -3.57)
Buspirone	-2.37 (-3.83, -0.91)	-1.99 (-3.97, -0.04)	-2.94 (-5.31, -0.49)	-2.87 (-4.70, -0.97)	-1.16 (-3.81, 1.51)	-2.38 (-3.92, -0.82)
Citalopram	-2.22 (-4.28, -0.19)	-1.20 (-3.29, 0.73)	-3.60 (-7.79, 0.58)	-3.60 (-7.28, 0.03)	-1.19 (-3.92, 1.54)	-2.06 (-4.19, 0.05)
Duloxetine	-3.13 (-4.13, -2.13)	-2.87 (-4.26, -1.49)	-3.12 (-4.69, -1.55)	-2.92 (-4.53, -1.33)	-3.45 (-4.88, -2.03)	-3.10 (-4.25, -1.95)
Escitalopram	-2.45 (-3.27, -1.63)	-2.13 (-2.89, -1.43)	-2.9 (-4.87, -0.98)	-2.81 (-4.18, -1.47)	-2.36 (-3.52, -1.23)	-2.49 (-3.35, -1.64)
Fluoxetine	-2.43 (-3.74, -1.16)	-2.00 (-3.28, -0.74)	-1.40 (-4.73, 1.89)	-2.86 (-4.90, -0.89)	-1.25 (-3.38, 0.82)	-1.72 (-3.92, 0.44)
Hydroxyzine	-3.00 (-5.03, -0.96)		-3.31 (-5.85, -0.81)		-2.78 (-4.96, -0.58)	-3.07 (-5.14, -0.98)
Imipramine	-0.59 (-3.85, 2.70)	-0.32 (-3.04, 2.31)			-0.53 (-3.96, 2.94)	-0.40 (-3.76, 2.94)
Maprotiline	0.38 (-3.25, 4.02)	0.46 (-2.63, 3.50)		0.50 (-3.45, 4.41)		
Mirtazapine	-3.12 (-4.43, -1.80)	-3.08 (-4.47, -1.65)	-2.61 (-5.46, 0.20)	-3.00 (-4.73, -1.27)	-2.40 (-5.12, 0.25)	
Ocinaplon	-7.90 (-14.68, -1.06)		-7.90 (-14.93, -0.76)		-7.88 (-14.73, -1.03)	-7.84 (-14.66, -0.96)
Opipramol	-1.92 (-3.99, 0.15)		-2.02 (-5.22, 1.19)		-1.75 (-4.08, 0.58)	-2.04 (-4.21, 0.09)
Paroxetine	-2.29 (-3.11, -1.47)	-2.07 (-3.08, -1.13)	-2.33 (-3.68, -0.99)	-2.15 (-3.55, -0.74)	-2.22 (-3.32, -1.12)	-2.10 (-2.98, -1.23)
Pregabalin	-2.79 (-3.69, -1.91)	-2.45 (-3.58, -1.36)	-3.24 (-5.01, -1.55)	-2.52 (-3.68, -1.38)	-3.08 (-4.79, -1.39)	-2.90 (-3.83, -1.98)
Quetiapine	-3.60 (-4.83, -2.39)	-2.32 (-3.41, -1.22)	-4.86 (-7.16, -2.58)	-1.81 (-4.55, 0.92)	-4.07 (-5.55, -2.61)	-3.59 (-4.84, -2.34)
Sertraline	-2.88 (-4.17, -1.59)	-2.47 (-3.95, -1.00)	-3.12 (-5.48, -0.80)	-3.01 (-5.01, -1.07)	-2.60 (-4.62, -0.61)	-2.81 (-4.13, -1.48)
Tiagabine	-0.77 (-2.18, 0.62)	-0.68 (-1.72, 0.30)		-0.92 (-2.60, 0.75)	-0.30 (-3.31, 2.68)	-0.77 (-2.21, 0.66)
Venlafaxine	-2.69 (-3.50, -1.89)	-2.96 (-4.20, -1.76)	-2.61 (-3.79, -1.46)	-2.28 (-3.32, -1.23)	-3.42 (-4.91, -2.02)	-2.67 (-3.51, -1.86)
Vilazodone	-1.45 (-3.02, 0.12)	-1.43 (-2.49, -0.39)			-1.45 (-3.10, 0.18)	-1.45 (-3.06, 0.14)
Vortioxetine	-1.12 (-2.47, 0.24)	-0.69 (-2.32, 0.95)	-1.31 (-3.43, 0.79)		-1.18 (-2.61, 0.24)	-1.13 (-2.51, 0.26)

Appendix 6 Acceptability Subgroups

	Main	Anxiety		Depression	
		HAM-A ≤ 25	HAM-A > 25	ES ≤ 4.05	ES > 4.05
Agomelatine	0.67 (0.37, 1.18)		0.66 (0.36, 1.17)		0.67 (0.36, 1.23)
Benzodiazepine	1.43 (1.12, 1.86)	1.73 (1.25, 2.43)	0.68 (0.36, 1.26)	1.32 (0.82, 2.11)	2.44 (1.09, 5.60)
Bupropion	0.96 (0.10, 10.5)		1.09 (0.08, 13.51)	1.24 (0.12, 11.75)	
Buspirone	0.76 (0.47, 1.25)	0.73 (0.39, 1.37)	0.82 (0.33, 2.00)		0.90 (0.33, 2.41)
Citalopram	3.62 (0.74, 20.27)	1.69 (0.23, 19.5)	8.26 (0.50, 248.7)	1.54 (0.22, 13.54)	6.42 (0.53, 115.70)
Duloxetine	1.09 (0.89, 1.32)	1.25 (0.93, 1.70)	0.93 (0.69, 1.24)	1.11 (0.88, 1.40)	
Escitalopram	0.96 (0.79, 1.16)	0.99 (0.78, 1.26)	0.91 (0.60, 1.37)	1.01 (0.73, 1.41)	1.00 (0.66, 1.53)
Fluoxetine	1.36 (0.57, 3.15)	1.91 (0.15, 36.68)	1.19 (0.45, 3.08)		0.07 (0.01, 5.40)
Hydroxyzine	0.97 (0.55, 1.68)		0.81 (0.45, 1.46)		0.90 (0.34, 2.45)
Imipramine	2.83 (0.74, 12.10)		2.87 (0.75, 12.21)		2.71 (0.67, 11.64)
Maprotiline	2.32 (0.21, 26.74)	0.08 (0.01, 473.50)			
Mirtazapine	3.36 (0.67, 19.07)	0.12 (0.01, 710.10)	1.72 (0.26, 12.54)		
Ocinaplon	0.74 (0.24, 2.22)		0.72 (0.23, 2.20)		0.74 (0.24, 2.28)
Opipramol	0.31 (0.07, 1.17)	0.12 (0.01, 1.15)	0.32 (0.04, 1.40)	0.40 (0.06, 1.73)	
Paroxetine	1.24 (1.03, 1.50)	1.22 (0.89, 1.64)	1.30 (0.96, 1.77)	1.32 (0.85, 2.07)	1.23 (0.79, 1.91)
Pregabalin	0.80 (0.66, 0.98)	0.87 (0.62, 1.22)	0.85 (0.64, 1.17)	0.78 (0.56, 1.09)	1.00 (0.52, 1.95)
Quetiapine	1.44 (1.16, 1.80)	1.50 (1.09, 2.10)	1.41 (0.99, 1.99)	1.58 (0.93, 2.64)	1.45 (1.00, 2.12)
Sertraline	0.94 (0.65, 1.35)	0.95 (0.65, 1.40)	0.01 (0.01, 2.80)	0.76 (0.42, 1.36)	1.14 (0.64, 2.04)
Tiagabine	1.37 (1.08, 1.74)	2.17 (0.43, 10.92)	1.36 (1.06, 1.74)		1.33 (0.74, 2.41)
Venlafaxine	0.98 (0.83, 1.16)	1.14 (0.84, 1.54)	0.89 (0.72, 1.10)	0.99 (0.74, 1.33)	1.30 (0.68, 2.48)
Vilazodone	1.59 (1.20, 2.13)	1.60 (1.09, 2.33)	1.61 (0.93, 2.81)		1.56 (1.06, 2.33)
Vortioxetine	0.88 (0.67, 1.15)	0.91 (0.66, 1.24)	0.86 (0.43, 1.73)	0.86 (0.58, 1.29)	0.86 (0.42, 1.76)

Appendix 6 Acceptability Subgroups

	Main	Age		% Female		Excluding China
		≤ 40.3 Years	> 40.3 Years	≤ 61.8%	> 61.8%	
Agomelatine	0.67 (0.37, 1.18)		0.65 (0.34, 1.21)		0.68 (0.39, 1.14)	0.67 (0.37, 1.19)
Benzodiazepine	**1.43 (1.12, 1.86)**	**1.54 (1.06, 2.25)**	0.84 (0.50, 1.35)	**1.92 (1.26, 2.96)**	1.09 (0.76, 1.57)	**1.45 (1.12, 1.88)**
Bupropion	0.96 (0.10, 10.5)	1.18 (0.10, 15.26)			1.02 (0.12, 10.44)	1.17 (0.10, 15.08)
Buspirone	0.76 (0.47, 1.25)	0.65 (0.35, 1.17)	0.85 (0.33, 2.13)	0.70 (0.34, 1.49)	0.94 (0.41, 2.12)	0.75 (0.46, 1.21)
Citalopram	3.62 (0.74, 20.27)	9.59 (0.60, 186.4)	1.66 (0.21, 15.88)	1.73 (0.22, 17.63)	7.11 (0.66, 103.8)	3.73 (0.75, 21.66)
Duloxetine	1.09 (0.89, 1.32)	1.21 (0.78, 1.85)	1.06 (0.82, 1.37)	1.01 (0.68, 1.49)	1.14 (0.89, 1.45)	1.11 (0.90, 1.37)
Escitalopram	0.96 (0.79, 1.16)	0.97 (0.76, 1.23)	0.90 (0.61, 1.35)	0.92 (0.63, 1.32)	0.97 (0.76, 1.25)	0.96 (0.79, 1.17)
Fluoxetine	1.36 (0.57, 3.15)	0.68 (0.09, 5.14)	1.35 (0.48, 3.76)	1.39 (0.12, 20.02)	1.28 (0.51, 3.31)	1.23 (0.46, 3.16)
Hydroxyzine	0.97 (0.55, 1.68)		0.86 (0.47, 1.57)		0.94 (0.53, 1.63)	0.98 (0.55, 1.68)
Imipramine	2.83 (0.74, 12.10)	2.86 (0.77, 11.11)			2.85 (0.79, 11.06)	2.80 (0.72, 12.22)
Maprotiline	2.32 (0.21, 26.74)	1.53 (0.16, 13.63)		2.92 (0.23, 41.58)		
Mirtazapine	3.36 (0.67, 19.07)	2.13 (0.49, 9.57)	0.01 (0.01, 2.71)	4.18 (0.75, 31.00)	0.04 (0.01, 7.48)	
Ocinaplon	0.74 (0.24, 2.22)		0.72 (0.23, 2.21)		0.74 (0.27, 2.15)	0.71 (0.24, 2.14)
Opipramol	0.31 (0.07, 1.17)		0.35 (0.05, 1.48)		**0.29 (0.07, 0.93)**	0.29 (0.06, 1.09)
Paroxetine	**1.24 (1.03, 1.50)**	1.25 (0.90, 1.78)	**1.29 (1.00, 1.67)**	1.09 (0.72, 1.63)	**1.28 (1.02, 1.61)**	**1.24 (1.02, 1.51)**
Pregabalin	**0.80 (0.66, 0.98)**	0.70 (0.48, 1.02)	0.77 (0.56, 1.07)	0.93 (0.69, 1.27)	**0.67 (0.48, 0.95)**	**0.81 (0.66, 0.99)**
Quetiapine	**1.44 (1.16, 1.80)**	**1.46 (1.09, 1.96)**	**1.40 (0.94, 2.04)**	1.36 (0.76, 2.44)	**1.48 (1.17, 1.89)**	**1.44 (1.15, 1.80)**
Sertraline	0.94 (0.65, 1.35)	0.93 (0.18, 3.59)	0.95 (0.62, 1.44)	0.94 (0.58, 1.52)	0.80 (0.22, 3.00)	0.94 (0.65, 1.35)
Tiagabine	**1.37 (1.08, 1.74)**	**1.37 (1.08, 1.74)**		1.29 (0.90, 1.85)	**1.63 (1.07, 2.50)**	**1.37 (1.08, 1.73)**
Venlafaxine	0.98 (0.83, 1.16)	0.99 (0.71, 1.36)	0.97 (0.79, 1.21)	0.97 (0.76, 1.25)	1.01 (0.76, 1.35)	0.98 (0.83, 1.16)
Vilazodone	**1.59 (1.20, 2.13)**	**1.60 (1.19, 2.14)**			**1.58 (1.21, 2.09)**	**1.60 (1.19, 2.15)**
Vortioxetine	0.88 (0.67, 1.15)	1.01 (0.64, 1.60)	0.82 (0.56, 1.19)		0.89 (0.69, 1.14)	0.89 (0.68, 1.16)

Appendix 7 Results of meta analysis of direct comparisons

Change in HAM-A				Change in HAM-A Pairwise mean dif (95% CI)		Hetero-		Study Discontinuation Pairwise OR (95% CI)		Hetero-	
Tx1	Tx2	Studies	Patients	Fixed effects	Random effects	geneity	P-val	Fixed effects	Random effects	geneity	P-val
Benzodiazepine	Fluoxetine	2	172	0.28 (-0.02, 0.58)	0.28 (-0.02, 0.58)	0.0%	0.552	0.97 (0.06, 15.75)	0.97 (0.06, 15.75)	0.0%	0.982
Benzodiazepine	Hydroxyzine	1	221	-0.10 (-0.37, 0.17)	NA	NA	NA	1.12 (0.54, 2.34)	NA	NA	NA
Benzodiazepine	Mirtazapine	4	240	0.16 (-0.13, 0.46)	0.16 (-0.10, 0.42)	22.8%	0.292	1.92 (0.49, 7.63)	1.92 (0.49, 7.63)	0.0%	0.919
Benzodiazepine	Opipramol	1	206	-0.14 (-0.42, 0.13)	NA	NA	NA	0.51 (0.09, 2.85)	NA	NA	NA
Benzodiazepine	Pregabalin	5	1587	0.03 (-0.09, 0.14)	0.03 (-0.16, 0.21)	61.7%	0.046	0.54 (0.43, 0.69)	0.50 (0.23, 1.05)	58.9%	0.039
Bupropion	Escitalopram	1	24	-1.14 (-2.00, -0.27)	NA	NA	NA	0.82 (0.10, 7.02)	NA	NA	NA
Bupropion	Fluoxetine	1	59	0.00 (-0.51, 0.51)	NA	NA	NA	1.03 (0.02, 53.83)	NA	NA	NA
Buspirone	Hydroxyzine	1	164	0.26 (-0.05, 0.57)	NA	NA	NA	1.00 (0.39, 2.55)	NA	NA	NA
Buspirone	Mirtazapine	1	64	0.08 (-0.34, 0.51)	NA	NA	NA	0.88 (0.02, 45.92)	NA	NA	NA
Buspirone	Opipramol	1	86	0.08 (-0.34, 0.51)	NA	NA	NA	0.23 (0.02, 2.17)	NA	NA	NA
Buspirone	Sertraline	1	46	0.33 (-0.25, 0.92)	NA	NA	NA	1.19 (0.02, 62.32)	NA	NA	NA
Buspirone	Venlafaxine	1	301	0.09 (-0.16, 0.34)	NA	NA	NA	1.68 (1.00, 2.81)	NA	NA	NA
Citalopram	Escitalopram	1	40	0.10 (-0.52, 0.72)	NA	NA	NA	0.47 (0.04, 5.69)	NA	NA	NA
Citalopram	Fluoxetine	1	40	0.00 (-0.62, 0.62)	NA	NA	NA	0.18 (0.01, 4.01)	NA	NA	NA
Citalopram	Paroxetine	1	40	0.67 (0.04, 1.31)	NA	NA	NA	0.18 (0.01, 4.01)	NA	NA	NA
Citalopram	Sertraline	1	40	0.40 (-0.22, 1.03)	NA	NA	NA	0.18 (0.01, 4.01)	NA	NA	NA
Duloxetine	Fluoxetine	1	60	-0.36 (-0.87, 0.15)	NA	NA	NA	1.00 (0.02, 52.04)	NA	NA	NA
Duloxetine	Venlafaxine	2	737	0.06 (-0.09, 0.21)	0.06 (-0.09, 0.21)	0.0%	0.873	0.83 (0.61, 1.13)	0.83 (0.61, 1.13)	0.0%	0.395
Duloxetine	Vortioxetine	1	624	-0.27 (-0.46, -0.09)	NA	NA	NA	0.73 (0.49, 1.09)	NA	NA	NA
Escitalopram	Agomelatine	1	281	0.00 (-0.24, 0.24)	NA	NA	NA	0.88 (0.48, 1.64)	NA	NA	NA
Escitalopram	Fluoxetine	2	100	-0.04 (-0.43, 0.35)	-0.04 (-0.43, 0.35)	0.0%	0.798	1.05 (0.15, 7.47)	1.05 (0.15, 7.47)	0.0%	0.368
Escitalopram	Paroxetine	3	706	-0.15 (-0.32, 0.01)	-0.02 (-0.50, 0.46)	80.6%	0.038	1.45 (0.96, 2.18)	1.45 (0.96, 2.18)	0.0%	0.646
Escitalopram	Quetiapine	1	639	0.12 (-0.05, 0.29)	NA	NA	NA	1.33 (0.93, 1.91)	NA	NA	NA
Escitalopram	Sertraline	1	40	0.34 (-0.29, 0.96)	NA	NA	NA	0.32 (0.01, 8.26)	NA	NA	NA
Escitalopram	Venlafaxine	1	264	0.06 (-0.18, 0.31)	NA	NA	NA	1.36 (0.77, 2.37)	NA	NA	NA
Fluoxetine	Mirtazapine	1	70	0.49 (0.02, 0.97)	NA	NA	NA	1.00 (0.02, 51.8)	NA	NA	NA
Fluoxetine	Paroxetine	1	40	0.69 (0.05, 1.33)	NA	NA	NA	1.00 (0.02, 52.85)	NA	NA	NA
Fluoxetine	Sertraline	1	40	0.41 (-0.22, 1.04)	NA	NA	NA	1.00 (0.02, 52.85)	NA	NA	NA
Fluoxetine	Venlafaxine	1	67	0.23 (-0.26, 0.72)	NA	NA	NA	0.73 (0.26, 2.03)	NA	NA	NA
Imipramine	Paroxetine	1	56	0.47 (-0.15, 1.08)	NA	NA	NA	0.45 (0.13, 1.60)	NA	NA	NA
Maprotiline	Mirtazapine	1	60	0.74 (0.19, 1.30)	NA	NA	NA	1.38 (0.28, 6.80)	NA	NA	NA
Mirtazapine	Paroxetine	3	197	-0.05 (-0.33, 0.23)	-0.05 (-0.33, 0.23)	0.0%	0.356	1.01 (0.1, 9.88)	1.01 (0.1, 9.88)	0.0%	0.999
Paroxetine	Quetiapine	1	656	0.06 (-0.10, 0.23)	NA	NA	NA	1.35 (0.91, 2.00)	NA	NA	NA
Paroxetine	Sertraline	2	93	-0.12 (-0.53, 0.29)	-0.12 (-0.53, 0.29)	0.0%	0.491	0.88 (0.24, 3.24)	0.88 (0.24, 3.24)	0.0%	0.948
Paroxetine	Tiagabine	1	40	-0.16 (-0.78, 0.46)	NA	NA	NA	1.71 (0.40, 7.34)	NA	NA	NA
Paroxetine	Venlafaxine	1	60	-0.19 (-0.77, 0.39)	NA	NA	NA	2.14 (0.62, 7.39)	NA	NA	NA
Placebo	Agomelatine	2	391	0.48 (0.28, 0.68)	0.48 (0.28, 0.68)	0.0%	0.469	0.58 (0.33, 1.01)	0.58 (0.33, 1.01)	0.0%	0.558

Appendix 7 Results of meta analysis of direct comparisons

Change in HAM-A				Change in HAM-A Pairwise mean dif (95% CI)		Hetero-		Study Discontinuation Pairwise OR (95% CI)		Hetero-	
Tx1	Tx2	Studies	Patients	Fixed effects	Random effects	geneity	P-val	Fixed effects	Random effects	geneity	P-val
Placebo	Benzodiazepine	8	1213	0.39 (0.27, 0.51)	0.40 (0.23, 0.56)	48.0%	0.063	1.54 (1.17, 2.04)	1.48 (0.46, 4.17)	63.3%	0.008
Placebo	Buspirone	3	418	0.34 (0.14, 0.54)	0.63 (-0.24, 1.51)	94.0%	0.000	0.82 (0.5, 1.34)	0.82 (0.5, 1.34)	0.0%	0.963
Placebo	Citalopram	1	34	0.88 (0.17, 1.58)	NA	NA	NA	1.61 (0.23, 11.09)	NA	NA	NA
Placebo	Duloxetine	7	2389	0.38 (0.30, 0.47)	0.38 (0.30, 0.47)	0.0%	0.540	1.06 (0.89, 1.27)	1.07 (0.54, 2.12)	63.3%	0.011
Placebo	Escitalopram	9	2706	0.33 (0.25, 0.40)	0.33 (0.24, 0.42)	21.9%	0.286	1.01 (0.78, 1.31)	1.01 (0.83, 1.23)	7.5%	0.501
Placebo	Fluoxetine	1	58	0.57 (0.04, 1.10)	NA	NA	NA	1.47 (0.48, 4.53)	NA	NA	NA
Placebo	Hydroxyzine	2	382	0.39 (0.18, 0.59)	0.39 (0.18, 0.59)	0.0%	0.487	0.83 (0.48, 1.45)	0.83 (0.48, 1.45)	0.0%	0.845
Placebo	Ocinaplon	1	60	0.64 (0.10, 1.18)	NA	NA	NA	0.73 (0.26, 2.08)	NA	NA	NA
Placebo	Opipramol	1	208	0.29 (0.01, 0.56)	NA	NA	NA	0.34 (0.070, 1.73)	NA	NA	NA
Placebo	Paroxetine	8	2948	0.20 (0.13, 0.28)	0.20 (0.13, 0.28)	6.6%	0.457	1.29 (1.07, 1.55)	1.29 (1.07, 1.55)	0.0%	0.742
Placebo	Pregabalin	9	2251	0.36 (0.27, 0.46)	0.36 (0.27, 0.46)	0.0%	0.843	0.85 (0.69, 1.04)	0.85 (0.69, 1.04)	0.0%	0.610
Placebo	Quetiapine	4	2698	0.45 (0.37, 0.53)	0.51 (0.11, 0.92)	95.6%	0.000	1.46 (1.21, 1.76)	1.46 (1.21, 1.76)	0.0%	0.438
Placebo	Sertraline	2	716	0.34 (0.19, 0.49)	0.34 (0.10, 0.57)	58.5%	0.121	0.95 (0.68, 1.32)	0.95 (0.54, 1.67)	38.9%	0.201
Placebo	Tiagabine	4	2102	0.07 (-0.02, 0.17)	0.07 (-0.02, 0.17)	0.0%	0.551	1.35 (1.11, 1.64)	1.35 (1.11, 1.64)	0.0%	0.729
Placebo	Venlafaxine	13	3668	0.31 (0.23, 0.38)	0.38 (0.19, 0.48)	74.4%	<0.001	0.93 (0.80, 1.09)	0.95 (0.43, 2.09)	64.1%	0.001
Placebo	Vilazodone	3	1497	0.18 (0.08, 0.29)	0.18 (0.08, 0.29)	0.0%	0.485	1.59 (1.24, 2.04)	1.59 (1.24, 2.04)	0.0%	0.977
Placebo	Vortioxetine	4	1687	0.13 (0.03, 0.24)	0.14 (-0.07, 0.35)	74.2%	0.014	0.92 (0.72, 1.18)	0.92 (0.72, 1.18)	0.0%	0.440
Pregabalin	Sertraline	1	107	0.00 (-0.38, 0.38)	NA	NA	NA	0.79 (0.02, 40.30)	NA	NA	NA
Pregabalin	Venlafaxine	2	566	-0.12 (-0.30, 0.05)	-0.13 (-0.32, 0.06)	20.0%	0.264	1.43 (0.98, 2.08)	1.43 (0.98, 2.08)	0.0%	0.651

Appendix 8. WINBUGS code

Continuous model – change in HAM – A

```
model{

for(i in 1:ns){
            w[i,1] <- 0
            delta[i,1] <- 0                  # treatment effect is zero for control arm
            mu[i] ~ dnorm(0,.0001)           # vague priors for all trial baselines
             for (k in 1:na[i]) {
                    var[i,k] <- pow(se[i,k],2)
                    prec[i,k] <- 1/var[i,k]
                    y[i,k] ~ dnorm(theta[i,k],prec[i,k])    # binomial likelihood
                    theta[i,k] <- mu[i] + delta[i,k]        # model for linear predictor
                    dev[i,k] <- (y[i,k]-theta[i,k])*(y[i,k]-theta[i,k])*prec[i,k]
          }
  resdev[i] <- sum(dev[i,1:na[i]])

  for (k in 2:na[i]) {
            delta[i,k] ~ dnorm(md[i,k],taud[i,k])
            md[i,k] <- d[t[i,k]] - d[t[i,1]] + sw[i,k]
            taud[i,k] <- tau *2*(k-1)/k
            w[i,k] <- (delta[i,k] - d[t[i,k]] + d[t[i,1]])
            sw[i,k] <- sum(w[i,1:k-1])/(k-1)
            }
        }
totresdev <- sum(resdev[])
d[1]<-0
for (k in 2:nt){ d[k] ~ dnorm(0,.0001) }      # vague priors for treatment effects
sd ~ dunif(0,50)                              # vague prior for between-trial SD
tau <- pow(sd,-2)                             # between-trial precision

for (c in 1:(nt)) { for (k in 1:nt) { diff[c,k] <- (d[c] - d[k] )}}      # pairwise differences
}
```

Binary model – trial discontinuation

```
model{
for(i in 1:N)  {  logit(p[i])<-mu[s[i]]+ delta[i]  * (1-equals(t[i],b[i]))        #  model
                  r[i]~dbin(p[i],n[i])                                             #  binomial likelihood
                  delta[i] ~ dnorm(md[i],invtausq)                                 # random effects: trial-specific LORs
                  md[i] <- d[t[i]] - d[b[i]]   }                                   # means of trials-specific LORS


for(j in 1:NS){ mu[j]~dnorm(0,.005) }                                             # vague priors for basic parameters
d[1]<-0
for (k in 2:NT)  {d[k] ~ dnorm(0,.005) }
  invtausq<-1/tausq
  tausq ~ dlnorm(-3.93,0.44)   # Log-normal prior with mean -3.93, precision 0.44=1/(1.512) for heterogeneity var. param. Tausq
                               # See Turner International Journal of Epidemiology 2012;41:818–827
mA ~ dnorm(-0.632960547, 6.424869024)        # Absolute log odds(success)
for (k in 1:NT)   { logit(T[k])<- mA  +d[k] }        # Absolute pr(success)
for (c in 1:(NT))                                     # pairwise ORs
      { for (k in 1:NT)
          { lor[c,k] <- d[k] - d[c]
            log(or[c,k]) <- lor[c,k]
          }
      }
}
```

Appendix 9. Electronic Search Criteria

MEDLINE search code

1. exp Anxiety Disorders/ or exp Anxiety/
2. anxiet$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
3. 1 or 2
4. (anxiety or anxiety disorders).sh.
5. (anxiet$ or anxious$ or ((chronic$ or excessiv$ or intens$ or (long$ adj2 last$) or neuros$ or neurotic$ or ongoing or persist$ or serious$ or sever$ or uncontrol$ or un control$ or unrelent$ or un relent$) adj2 worry)).ti,ab.
6. 4 or 5
7. exp Randomized Controlled Trial/
8. random$.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
9. 7 or 8
10. 6 and 9
11. limit 10 to yr="1994 -Current"

Appendix 10. Study Data

Author	SE Method	Year	Drug Name	Number Randomised	Number Discont'd	Number w/ HAM-A Change	Mean HAM-A Change	SE HAM-A Change
Alaka	Chg SE/SD	2014	Duloxetine	151	36	151	-15.90	0.60
Alaka		2014	Placebo	140	35	140	-11.70	0.70
Allgulander	Diff CI	2001	Placebo	130	45	130	-11.00	0.83
Allgulander		2001	Venlafaxine	411	102	399	-15.21	0.48
Allgulander	Chg SE/SD	2004	Placebo	190	51	188	-8.00	0.60
Allgulander		2004	Sertraline	188	41	182	-11.70	0.60
Baldwin		2006	Escitalopram	403	57	400	-16.20	0.39
Baldwin	Chg SE/SD	2006	Paroxetine	140	27	136	-14.71	0.67
Baldwin		2006	Placebo	139	15	138	-14.20	0.66
Ball	F-statistic	2005	Paroxetine	25	5	25	-11.92	1.21
Ball		2005	Sertraline	28	5	28	-11.96	1.14
Bandelow		2010	Paroxetine	217	44	214	-14.45	0.53
Bandelow	Diff CI	2010	Placebo	217	41	217	-12.30	0.53
Bandelow		2010	Quetiapine	439	112	435	-14.95	0.37
Beyazyuz		2013	Citalopram	20	2	20	-14.40	0.73
Beyazyuz		2013	Escitalopram	20	1	20	-14.70	0.61
Beyazyuz	BL, EP SD, r=0.314	2013	Fluoxetine	20	0	20	-14.40	0.70
Beyazyuz		2013	Paroxetine	20	0	20	-16.60	0.70
Beyazyuz		2013	Sertraline	20	0	20	-15.70	0.69
Bidzan	Chg SE/SD	2012	Placebo	151	25	148	-9.59	0.71
Bidzan		2012	Vortioxetine	150	22	149	-13.43	0.70
Bielski	Chg SE/SD	2005	Escitalopram	61	22	60	-15.30	0.80
Bielski		2005	Paroxetine	62	29	61	-13.30	1.00
Boerner	Diff CI	2003	Buspirone	43	4	42	-15.55	1.18
Boerner		2003	Opipramol	43	1	42	-16.19	1.18
Bose		2008	Escitalopram	131	29	125	-10.94	0.67
Bose	Chg SE/SD	2008	Placebo	140	36	135	-9.21	0.67
Bose		2008	Venlafaxine	133	37	125	-11.42	0.66
Brawman-Mintzer	Chg SE/SD	2006	Placebo	170	46	162	-11.15	0.58
Brawman-Mintzer		2006	Sertraline	168	51	164	-12.71	0.56
Bystritsky	F-statistic	2008	Bupropion	11	2	11	-20.45	1.45
Bystritsky		2008	Escitalopram	13	2	13	-14.77	1.33

Appendix 10. Study Data

Author	SE Method	Year	Drug Name	Number Randomised	Number Discont'd	Number w/ HAM-A Change	Mean HAM-A Change	SE HAM-A Change
Coric	Diff CI	2010	Escitalopram	53	11	47	-12.50	1.06
Coric		2010	Placebo	104	24	98	-9.40	0.73
Cvjetkovic-Bosnjak	BL, EP SD,	2015	Pregabalin	47	0	47	-9.60	0.91
Cvjetkovic-Bosnjak	r=0.314	2015	Sertraline	60	0	60	-9.60	0.42
Czobor	Chg SE/SD	2010	Ocinaplon	31	18	28	-14.20	2.60
Czobor		2010	Placebo	29	19	27	-6.30	2.00
Davidson		1999	Buspirone	98	29	93	-9.50	0.76
Davidson	Chg SE/SD	1999	Placebo	104	36	98	-8.00	0.73
Davidson		1999	Venlafaxine	203	84	174	-10.20	0.59
Davidson	Chg SE/SD	2004	Escitalopram	158	39	154	-11.30	0.60
Davidson		2004	Placebo	157	34	153	-7.40	0.60
Durgam	Chg SE/SD	2016	Placebo	207	44	200	-10.19	0.54
Durgam		2016	Vilazodone	208	64	200	-12.39	0.56
Feltner		2003	Benzodiazepine	68	32	64	-11.62	0.86
Feltner	Chg SE/SD	2003	Placebo	67	19	66	-9.27	0.84
Feltner		2003	Pregabalin	136	37	130	-11.96	0.60
Fresquet	Chg CI	2000	Benzodiazepine	30	1	30	-6.10	0.77
Fresquet		2000	Placebo	20	2	20	-3.40	0.71
Gao	BL, EP SD,	2009	Benzodiazepine	27	0	27	-17.74	1.65
Gao	r=0.314	2009	Mirtazapine	27	0	27	-18.98	1.44
Gelenberg	Chg SE/SD	2000	Placebo	127	83	123	-8.70	0.70
Gelenberg		2000	Venlafaxine	124	64	115	-13.40	0.79
Gommoll	Chg SE/SD	2015	Placebo	223	43	221	-10.83	0.52
Gommoll		2015	Vilazodone	457	123	446	-11.81	0.36
Gommoll (2)	Chg SE/SD	2015	Placebo	201	40	197	-9.94	0.53
Gommoll (2)		2015	Vilazodone	201	57	198	-11.17	0.52
GSK 637	Chg SE/SD	Unpublished	Paroxetine	188	35	181	-12.40	0.80
GSK 637		Unpublished	Placebo	186	23	183	-11.30	0.80
GSK 791	Chg SE/SD	Unpublished	Paroxetine	168	44	164	-11.93	0.58
GSK 791		Unpublished	Placebo	167	41	162	-10.71	0.58
GSK 856	Chg SE/SD	Unpublished	Paroxetine	179	30	177	-10.30	0.58
GSK 856		Unpublished	Placebo	182	28	181	-9.50	0.57

Appendix 10. Study Data

Author	SE Method	Year	Drug Name	Number Randomised	Number Discont'd	Number w/ HAM-A Change	Mean HAM-A Change	SE HAM-A Change
Hackett	P-val Kelsey	2003	Placebo	97	16	97	-11.70	0.75
Hackett	2000	2003	Venlafaxine	370	77	354	-13.42	0.39
Hartford		2007	Duloxetine	162	74	149	-11.80	0.69
Hartford	Chg SE/SD	2007	Placebo	161	62	158	-9.19	0.67
Hartford		2007	Venlafaxine	164	62	159	-12.40	0.67
Huang	BL, EP SD,	2005	Benzodiazepine	30	0	30	-13.22	0.86
Huang	r=0.314	2005	Mirtazapine	30	0	30	-15.65	0.85
Guo (2)	t-statistic	2009	Mirtazapine	32	0	32	-16.32	0.51
Guo (2)		2009	Paroxetine	30	0	30	-15.35	0.53
Jia	t-statistic	2009	Mirtazapine	38	0	38	-12.50	0.58
Jia		2009	Paroxetine	38	0	38	-12.50	0.62
Kasper		2009	Placebo	128	35	128	-11.70	0.90
Kasper	Chg SE/SD	2009	Pregabalin	121	33	121	-14.50	0.90
Kasper		2009	Venlafaxine	125	41	125	-12.20	0.90
Kasper	Chg SE/SD	2014	Paroxetine	137	29	132	-11.30	0.70
Kasper		2014	Placebo	136	18	135	-9.50	0.77
Khan	p-values	2011	Placebo	235	70	225	-11.10	0.48
Khan		2011	Quetiapine	716	261	669	-12.91	0.28
Kim	F-statistic	2006	Paroxetine	30	5	25	-20.10	0.83
Kim		2006	Venlafaxine	30	9	21	-19.30	0.90
Koponen	Chg SE/SD	2007	Duloxetine	338	79	334	-12.65	0.48
Koponen		2007	Placebo	175	45	173	-8.38	0.67
Lader		1998	Buspirone	82	10	82	-8.80	0.86
Lader	Chg SE/SD	1998	Hydroxyzine	82	10	81	-10.80	0.83
Lader		1998	Placebo	82	11	81	-7.20	0.86
Lenox-Smith	Fig 2, Diff CI	2003	Placebo	122	25	122	-16.00	0.76
Lenox-Smith		2003	Venlafaxine	122	15	122	-13.90	0.76
Lenze	Cohen's d	2005	Citalopram	17	3	17	-10.80	0.97
Lenze		2005	Placebo	17	2	17	-7.20	0.97
Lenze	Cohen's d	2009	Escitalopram	86	17	85	-5.16	0.48
Lenze		2009	Placebo	93	18	92	-3.84	0.48

Appendix 10. Study Data

Author	SE Method	Year	Drug Name	Number Randomised	Number Discont'd	Number w/ HAM-A Change	Mean HAM-A Change	SE HAM-A Change
Li	BL, EP SD,	2005	Benzodiazepine	30	2	28	-16.00	0.97
Li	r=0.314	2005	Mirtazapine	30	5	25	-17.40	1.64
Li	BL, EP SD,	2011	Escitalopram	30	1	30	-16.73	0.87
Li	r=0.314	2011	Fluoxetine	30	2	30	-16.75	0.84
Liu	BL, EP SD,	2004	Benzodiazepine	56	0	56	-21.80	1.34
Liu	r=0.314	2004	Fluoxetine	56	0	56	-25.20	1.23
LiuX	BL, EP SD,	2005	Buspirone	30	0	30	-24.45	1.69
LiuX	r=0.314	2005	Mirtazapine	34	0	34	-25.20	1.68
Llorca		2002	Benzodiazepine	116	17	114	-13.20	1.15
Llorca	Fig 2, Diff CI	2002	Hydroxyzine	105	17	102	-12.16	0.77
Llorca		2002	Placebo	113	22	108	-9.64	0.74
Mahableshwarkar		2014	Duloxetine	156	50	149	-13.87	0.64
Mahableshwarkar	Chg SE/SD	2014	Placebo	157	36	154	-11.27	0.59
Mahableshwarkar		2014	Vortioxetine	468	120	456	-11.82	0.35
Mahableshwarkar (2)	Chg SE/SD	2014	Placebo	153	42	148	-9.87	0.58
Mahableshwarkar (2)		2014	Vortioxetine	304	79	290	-10.71	0.41
Majercsik	F-statistic	2003	Buspirone	33	0	33	-6.71	0.61
Majercsik		2003	Placebo	19	0	19	-0.95	0.81
Meredith		2012	Escitalopram	213	59	203	-12.27	0.51
Meredith	Diff CI	2012	Placebo	215	46	212	-10.72	0.50
Meredith		2012	Quetiapine	426	144	413	-13.14	0.36
Mezhebovsky	Diff CI	2013	Placebo	227	49	226	-7.21	0.45
Mezhebovsky		2013	Quetiapine	223	55	222	-14.97	0.46
Michelson	Chg SE/SD	2013	Benzodiazepine	69	30	62	-11.10	0.89
Michelson		2013	Placebo	71	17	67	-8.40	0.82
Mokhber	Chg SE/SD	2010	Buspirone	25	0	25	-13.14	1.50
Mokhber		2010	Sertraline	21	0	21	-15.68	1.63
Moller		2001	Benzodiazepine	105	4	102	-15.30	0.40
Moller	p-values	2001	Opipramol	101	2	100	-14.60	0.55
Moller		2001	Placebo	107	6	105	-13.10	0.47
Montgomery		2006	Placebo	101	20	100	-11.60	0.80
Montgomery	Chg SE/SD	2006	Pregabalin	207	45	198	-14.38	0.57
Montgomery		2006	Venlafaxine	113	34	110	-14.10	0.80

Appendix 10. Study Data

Author	SE Method	Year	Drug Name	Number Randomised	Number Discont'd	Number w/ HAM-A Change	Mean HAM-A Change	SE HAM-A Change
Montgomery	Chg SE/SD	2008	Placebo	96	27	96	-10.70	0.90
Montgomery		2008	Pregabalin	177	44	177	-12.80	0.70
Nicolini		2009	Duloxetine	242	70	234	-15.09	0.58
Nicolini	Chg SE/SD	2009	Placebo	170	68	163	-11.60	0.70
Nicolini		2009	Venlafaxine	169	47	158	-15.50	0.70
Nimatoudis	Chg SE/SD	2004	Placebo	22	11	22	-10.80	1.73
Nimatoudis		2004	Venlafaxine	24	5	24	-19.20	1.04
Niu	Chg SE/SD	2004	Fluoxetine	35	0	35	-14.00	0.68
Niu		2004	Mirtazapine	35	0	35	-16.00	0.68
Pande		2003	Benzodiazepine	68	28	62	-11.96	0.81
Pande	t-statistic	2003	Placebo	69	19	64	-6.82	0.80
Pande		2003	Pregabalin	139	27	136	-9.75	0.55
Peng	t-statistic	2012	Benzodiazepine	29	0	29	-16.50	1.03
Peng		2012	Fluoxetine	31	0	31	-17.40	0.99
Pfizer 1008-025		Unpublished	Benzodiazepine	64	35	62	-7.63	0.41
Pfizer 1008-025	p-values	Unpublished	Placebo	67	16	64	-7.86	0.44
Pfizer 1008-025		Unpublished	Pregabalin	135	37	136	-9.22	0.50
Pfizer A0081092	Chg SE/SD	Unpublished	Placebo	51	32	41	2.77	1.36
Pfizer A0081092		Unpublished	Pregabalin	57	27	46	-2.01	1.13
Pfizer A0081147	Chg SE/SD	Unpublished	Benzodiazepine	203	59	185	-16.70	0.58
Pfizer A0081147		Unpublished	Pregabalin	412	102	374	-16.73	0.39
Pohl	Chg SE/SD	2005	Placebo	86	25	86	-9.30	0.80
Pohl		2005	Pregabalin	255	70	255	-12.57	0.46
Pollack	Chg SE/SD	2001	Paroxetine	162	37	161	-11.80	0.70
Pollack		2001	Placebo	164	32	163	-9.50	0.70
Pollack	p-values	2005	Placebo	134	34	130	-10.20	0.88
Pollack		2005	Tiagabine	138	41	130	-11.80	0.88
Pollack S1	Chg SE/SD	2008	Placebo	230	85	213	-11.00	0.55
Pollack S1		2008	Tiagabine	680	288	627	-11.07	0.34
Pollack S2	Chg SE/SD	2008	Placebo	237	71	226	-9.40	0.58
Pollack S2		2008	Tiagabine	231	95	215	-9.70	0.64

Appendix 10. Study Data

Author	SE Method	Year	Drug Name	Number Randomised	Number Discont'd	Number w/ HAM-A Change	Mean HAM-A Change	SE HAM-A Change
Pollack S3	Chg SE/SD	2008	Placebo	229	55	223	-9.40	0.57
Pollack S3		2008	Tiagabine	223	65	215	-10.80	0.63
Rickles	Chg SE/SD	2000	Placebo	96	19	96	-9.50	0.85
Rickles		2000	Venlafaxine	253	83	253	-11.63	0.51
Rickles	Chg SE/SD	2003	Paroxetine	386	100	385	-12.35	0.44
Rickles		2003	Placebo	180	40	180	-9.30	0.65
Rickles		2005	Benzodiazepine	93	25	88	-10.90	0.80
Rickles	Chg SE/SD	2005	Placebo	91	26	85	-8.40	0.80
Rickles		2005	Pregabalin	270	51	261	-11.67	0.46
Rocca	BL, EP SD,	1997	Imipramine	26	8	18	-13.90	0.86
Rocca	r=0.314	1997	Paroxetine	30	5	25	-15.60	0.70
Rosenthal	BL, EP SD,	2003	Paroxetine	20	4	20	-11.80	1.47
Rosenthal	r=0.314	2003	Tiagabine	20	6	20	-10.60	1.82
Rothschild	Chg SE/SD	2012	Placebo	152	38	144	-13.16	0.66
Rothschild		2012	Vortioxetine	152	27	145	-12.57	0.65
Rynn	Chg SE/SD	2008	Duloxetine	168	75	161	-8.12	0.70
Rynn		2008	Placebo	159	50	158	-5.89	0.70
SCTMD05	Chg SE/SD	Unpublished	Escitalopram	126	29	124	-9.60	0.60
SCTMD05		Unpublished	Placebo	128	33	128	-7.70	0.60
SCTMD06	Chg SE/SD	Unpublished	Escitalopram	145	27	143	-9.20	0.50
SCTMD06		Unpublished	Placebo	142	28	138	-7.60	0.50
Silverstone		2001	Fluoxetine	33	12	33	-13.50	1.40
Silverstone	Diff CI	2001	Placebo	25	7	25	-8.80	1.62
Silverstone		2001	Venlafaxine	34	10	32	-15.40	1.44
Song	BL, EP SD,	2007	Benzodiazepine	33	0	33	-26.29	1.67
Song	r=0.314	2007	Mirtazapine	33	0	33	-24.62	1.50
Stein	Chg SE/SD	2008	Agomelatine	63	3	63	-16.60	1.12
Stein		2008	Placebo	58	3	58	-13.20	1.25
Stein		2014	Agomelatine	139	23	139	-15.60	0.80
Stein	Chg SE/SD	2014	Escitalopram	142	26	139	-15.60	0.70
Stein		2014	Placebo	131	35	131	-10.60	0.83

Appendix 10. Study Data

Author	SE Method	Year	Drug Name	Number Randomised	Number Discont'd	Number w/ HAM-A Change	Mean HAM-A Change	SE HAM-A Change
Tang	BL, EP SD,	2012	Duloxetine	30	0	30	-15.40	0.66
Tang	r=0.314	2012	Fluoxetine	30	0	30	-14.00	0.74
Wang	BL, EP SD,	2009	Mirtazapine	29	0	29	-17.57	0.86
Wang	r=0.314	2009	Paroxetine	30	0	30	-18.47	0.89
Wu	Chg SE/SD	2011	Duloxetine	108	26	107	-14.31	0.80
Wu		2011	Placebo	102	28	100	-11.75	0.83
Wu	Chg SE/SD	2012	Bupropion	30	0	30	-8.80	1.40
Wu		2012	Fluoxetine	29	0	29	-8.79	1.43
Yang	BL, EP SD,	2005	Maprotiline	30	3	27	-10.70	0.83
Yang	r=0.314	2005	Mirtazapine	30	4	26	-14.19	0.97