Supplemental Table S3.1. Individual comparative meta-analyses of newer antidepressants since 2009, with summary of efficacy and tolerability differences.

Antidepressant (Reference)	No. included trials (No. participants)	More effective than:	Less effective than:	More tolerable than:	Less tolerable than:
Agomelatine (Taylor et al., 2014)[1]	20 (7460)	• Sertraline	• None	• Comparators (dropouts – adverse events)	• None
Citalopram (Cipriani et al., 2009)[2]*	37 (3803)	• Paroxetine • Reboxetine	• Escitalopram	• Reboxetine • Venlafaxine	• None
Duloxetine (Cipriani et al., 2012)[3]*	16 (5735)	• None	• None	• None	• Escitalopram • Venlafaxine
Escitalopram (Cipriani et al., 2009)[2]*	22 (approx 4000)	• Citalopram	• None	• Duloxetine • Venlafaxine	• None
Fluoxetine (Magni et al., 2013; Purgato et al., 2014) [4,5]*	171 (24868)	• Milnacipran	• Mirtazapine • Sertraline • Venlafaxine	• Reboxetine	• None
Fluvoxamine (Omori et al., 2009; Omori et al., 2010)[6,7]*	54 (5122)	• None	• None	• Comparators (GI)	• None

Antidepressant (Reference)	**No. included trials (No. participants)**	**More effective than:**	**Less effective than:**	**More tolerable than:**	**Less tolerable than:**
Milnacipran (Nakagawa et al., 2009)[8]	16 (2277)	• None	• None	• None	• None
Mirtazapine (Watanabe et al., 2011)[9]*	29 (4974)	• SSRIs • Venlafaxine	• None	• SSRIs (GI, sex dysfx)	• SSRIs (wt gain, somnolence)
Paroxetine (Purgato et al., 2014*; Wang et al., 2014)[10,11]	115 (26134)	• Fluoxetine	• None	• None	• Agomelatine
Sertraline (Cipriani et al., 2010)[12]*	59 (9303)	• Fluoxetine	• Mirtazapine	• Paroxetine • Mirtazapine;	• Bupropion
Vortioxetine (Pae et al., 2015)[13]	12 (4947)	• None	• SNRIs	• Paroxetine • Mirtazapine;	• Bupropion

* indicates Meta-analyses of New Generation Antidepressants (MANGA) Cochrane Group.

Supplemental eTable S3.2. Network meta-analyses of newer antidepressants since 2009, with summary of efficacy and tolerability differences.

Reference	Antidepressants studied	No. studies (total participants)	Main findings on efficacy	Main findings on tolerability
(Khoo et al., 2015)[14] Search to Jun 2015.	10 antidepressants: Ago, Dlx, Esc, Flv, Flx, Mir, Par, Ser, Trz, Ven.	76 (16389) head-to-head trials	Response: **Ago, Esc, Mir, Ven** superior to Flx. **Mir, Ven** superior to Dlx, Par, Ser. **Ago** superior to Ser.	Withdrawals for adverse events: **Ago** fewer than other agents except Ser. **Esc, Ser** fewer than Par, Ven.
(Gartlehner et al., 2011)[15] Search to Aug 2011.	13 antidepressants: Bup, Cit, Des, Dlx, Esc, Flx, Flv, Mir, Nef, Par, Ser, Trz, Ven.	234 (93 direct studies with >20000; 64 indirect studies)	Response: **Esc** superior to Cit, Dlx, Flx. **Ser** superior to Flx. **Ven** superior to Flx.	Rates of adverse events: Mir: Greater weight gain. Ser: Higher incidence of diarrhea. Ven: Higher incidence of nausea and vomiting.
(Cipriani et al., 2009)[16] Search to Nov 2007.	12 antidepressants: Bup, Cit, Dlx, Esc, Flx, Flv, Mil, Mir, Par, Reb, Ser, Ven.	117 (25928)	Response: **Esc, Mir, Ser, Ven** superior to Dlx, Flx, Flv, Par, Reb.	Acceptability: **Bup, Cit, Esc, Ser** superior to Dlx, Flx, Mir, Ven.
(Linde et al., 2015)[17] Search to Dec 2013.	Antidepressants: Cit, Esc, Flx, Flv, Mir, Moc, Par, Reb, Ser, Trz, Ven, TCAs.	66 (15161) in primary care. Only antidepressant classes (SSRIs, SNRIs, TCAs, NaSSAs) were compared.	Response: **TCAs** superior to NaSSAs, Moc. **SSRIs** superior to NaSSAs, Moc.	Withdrawals for adverse events: **Moc** fewer than other classes.

Reference	Antidepressants studied	No. studies (total participants)	Main findings on efficacy	Main findings on tolerability
(Ramsberg et al., 2012)[18] Search to Jan 2010.	10 antidepressants: Cit, Dlx, Esc, Flx, Flv Mir, Par, Reb, Ser, Ven.	87 (~20000) in primary care.	Remission: **Esc** superior to Flx, Flv, Par, Ser. **Ven** superior to Cit, Flx.	Not reported.

Bup, bupropion; Cit, citalopram; Des, desvenlafaxine; Dlx, duloxetine; Esc, escitalopram; Flx, fluoxetine; Flv, fluvoxamine; Mil, milnacipran; Mir, mirtazapine; Moc, moclobemide; Nef, nefazodone; Par, paroxetine; Reb, reboxetine; Ser, sertraline; TCAs, tricyclic antidepressants; Trz, trazodone; Ven, venlafaxine.

References for Table S3.1 and S3.2.

1. Taylor D, Sparshatt A, Varma S, et al. Antidepressant efficacy of agomelatine: meta-analysis of published and unpublished studies. BMJ. 2014;348:g1888.

2. Cipriani A, Santilli C, Furukawa TA, et al. Escitalopram versus other antidepressive agents for depression. Cochrane Database Syst Rev. 2009;2:CD006532.

3. Cipriani A, Koesters M, Furukawa TA, et al. Duloxetine versus other anti-depressive agents for depression. Cochrane Database Syst Rev. 2012;10:CD006533.

4. Magni LR, Purgato M, Gastaldon C,et al. Fluoxetine versus other types of pharmacotherapy for depression. Cochrane Database Syst Rev. 2013;7:CD004185.

5. Purgato M, Gastaldon C, Papola D, et al. Drug dose as mediator of treatment effect in antidepressant drug trials: the case of fluoxetine. Acta Psychiatr Scand. 2015;131:408-16.

6. Omori IM, Watanabe N, Nakagawa A, et al. Efficacy, tolerability and side-effect profile of fluvoxamine for major depression: meta-analysis. J Psychopharmacol. 2009;23:539-50.

7. Omori IM, Watanabe N, Nakagawa A, et al. Fluvoxamine versus other anti-depressive agents for depression. Cochrane Database Syst Rev. 2010;3:CD006114.
8. Nakagawa A, Watanabe N, Omori IM, et al. Milnacipran versus other antidepressive agents for depression. Cochrane Database Syst Rev. 2009;3:CD006529.

9. Watanabe N, Omori IM, Nakagawa A, et al. Mirtazapine versus other antidepressive agents for depression. Cochrane Database Syst Rev. 2011;12:CD006528.

10. Purgato M, Papola D, Gastaldon C, et al. Paroxetine versus other anti-depressive agents for depression. Cochrane Database Syst Rev. 2014;4:CD006531.

11. Wang Y, Yu L, Xie J, et al. Comparative efficacies of fluoxetine and paroxetine in major depression across varying acute-phase treatment periods: a meta-analysis. Asia Pac Psychiatry. 2014;6:353-62.

12. Cipriani A, La Ferla T, Furukawa TA, et al. Sertraline versus other antidepressive agents for depression. Cochrane Database Syst Rev. 2010;4:CD006117.

13. Pae CU, Wang SM, Han C, et al. Vortioxetine: a meta-analysis of 12 short-term, randomized, placebo-controlled clinical trials for the treatment of major depressive disorder. J Psychiatry Neurosci. 2015;40:174-86.

14. Khoo AL, Zhou HJ, Teng M, et al. Network meta-analysis and cost-effectiveness analysis of new generation antidepressants. CNS Drugs. 2015;29:695-712.

15. Gartlehner G, Hansen RA, Morgan LC, et al. Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: an updated meta-analysis. Ann Intern Med. 2011;155:772-85.

16. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. Lancet. 2009;373:746-58.

17. Linde K, Kriston L, Rücker G, et al. Efficacy and acceptability of pharmacological treatments for depressive disorders in primary care: systematic review and network meta-analysis. Ann Fam Med. 2015;13:69-79.

18. Ramsberg J, Asseburg C, Henriksson M. Effectiveness and cost-effectiveness of antidepressants in primary care: a multiple treatment comparison meta-analysis and cost-effectiveness model. PLoS One. 2012;7:e42003.

Supplemental Table S3.3. References for Table 3.7, Prevalence of adverse events among newer antidepressants.

Name	PM or ref no.	Corporation	HC Control No.	Last updated
Agomelatine	WC500046227	Servier	n/a	19Feb2014
Bupropion SR	PM00032724	Valeant	187467	20Nov2015
Bupropion XL	PM00032785	Valeant	187468	20Nov2015
Citalopram	PM00025492	Sivem	174639	16June2014
Desvenlafaxine	PM00028540	Pfizer	170902	3Dec2014
Duloxetine	PM00032079	Eli Lilly	181021	17Sep2015
Escitalopram	PM00026539	Sanis	177101	20Aug2014
Fluoxetine	PM00031185	Sanis	184260	26May2015
Fluvoxamine	PM00027404	Pro Doc	177878	2Oct2014
Levomilnacipran	PM00030443	Actavis	167319	7May2015
Milnacipran	1B8D8975	Actavis	n/a	Jan2015
Mirtazapine	PM00032730	Merck	186836	18Sep2015
Moclobemide	PM00032713	Valeant	187463	18Nov2015
Paroxetine	PM00031020	Sanis	185042	29June2015
Sertraline	PM00032456	Sanis	188255	19Oct2015

Name	PM or ref no.	Corporation	HC Control No.	Last updated
Venlafaxine	PM00030415	Pfizer	182858	7May2015
Vilazodone	C588A5E5	Actavis	n/a	Mar2015
Vortioxetine	PM00027837	Lundbeck	159019	17Oct2014

PM, Product Monograph; HC, Health Canada.