COMPARATIVE EFFICACY AND ACCEPTABILITY OF ANTIDEPRESSANTS IN THE LONG-TERM TREATMENT OF MAJOR DEPRESSION: PROTOCOL FOR A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Supplementary Appendix
Appendix 1: Search Strategies

A. *Ovid MEDLINE(R) and In-Process & Other Non-Indexed Citations*

1 depressive disorder/ or depressive disorder, major/ or dysthymic disorder/ or Adjustment Disorders/ or Mood Disorders/ or Affective Symptoms/
2 (depress* or dysthymi* or adjustment disorder* or mood disorder* or "affective disorder" or "affective symptoms").tw,kw,kf.
3 or/1-2
4 Amitriptyline/ or Bupropion/ or Citalopram/ or CLOMIPRAMINE/ or Desvenlafaxine Succinate/ or Duloxetine Hydrochloride/ or Citalopram/ or FLUOXETINE/ or Fluvoxamine/ or PAROXETINE/ or SERTRALINE/ or TRAZODONE/ or Venlafaxine Hydrochloride/ or Vilazodone Hydrochloride/
5 (agomelatine or amitriptyline or bupropion or citalopram or clomipramine or desvenlafaxine or duloxetine or escitalopram or fluoxetine or fluvoxamine or levomilnacipran or milnacipran or mirtazapine or nefazodone or paroxetine or reboxetine or sertraline or trazodone or venlafaxine or vilazodone or vortioxetine).tw,kw,kf.
6 or/4-5
7 exp clinical trial/
8 exp randomized controlled trials/
9 exp double-blind method/
10 exp single-blind method/
11 exp cross-over studies/
12 randomized controlled trial.pt.
13 clinical trial.pt.
14 controlled clinical trial.pt.
15 (clinical adj2 trial).mp.
16 (random* adj5 control* adj5 trial*).mp.
17 (crossover or cross-over).mp.
18 ((singl* or double* or trebl* or tripl*) adj (blind* or mask*)).mp.
19 randomi*.mp.
20 (random* adj5 (assign* or allocat* or assort* or reciev*)).mp.
21 or/7-20
22 3 and 6 and 21
23 animals/ not humans/
24 22 not 23

B. *Embase*

1 major depression/ or dysthymia/ or mood disorder/ (94960)
2 (depress* or dysthymi* or adjustment disorder* or mood disorder* or "affective disorder" or "affective symptoms").tw,kw.
3 or/1-2
4 agomelatine/ or amitriptyline/ or amfebutamone/ or citalopram/ or clomipramine/ or desvenlafaxine/ or duloxetine/ or escitalopram/ or fluoxetine/ or fluvoxamine/ or milnacipran/ or mirtazapine/ or nefazodone/ or paroxetine/ or reboxetine/ or sertraline/ or trazodone/ or venlafaxine/ or vilazodone/ or vortioxetine/ (140923)
5 (agomelatine or amitriptyline or bupropion or citalopram or clomipramine or desvenlafaxine or duloxetine or escitalopram or fluoxetine or fluvoxamine or levomilnacipran or milnacipran or mirtazapine or nefazodone or paroxetine or reboxetine or sertraline or trazodone or venlafaxine or vilazodone or vortioxetine).tw,kw.
6 or/4-5
7 (clinical adj2 trial).mp.
8 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).mp.
9 (random* adj5 (assign* or allocat*)).mp.
10 randomi*.mp.
11 crossover.mp.
C. **Cochrane Library**

1. MeSH descriptor: [Depressive Disorder] this term only
2. MeSH descriptor: [Depressive Disorder, Major] this term only
3. MeSH descriptor: [Dysthymic Disorder] explode all trees
4. MeSH descriptor: [Adjustment Disorders] this term only
5. MeSH descriptor: [Mood Disorders] this term only
6. MeSH descriptor: [Affective Symptoms] this term only
7. ((depress* or dysthymi* or "adjustment disorder" or "adjustment disorders" or "mood disorder" or "mood disorders" or "affective disorder" or "affective symptoms"):ti,ab,kw (Word variations have been searched))
8. #1 or #2 or #3 or #4 or #5 or #6 or #7
9. MeSH descriptor: [Amitriptyline] this term only
10. MeSH descriptor: [Bupropion] this term only
11. MeSH descriptor: [Citalopram] this term only
12. MeSH descriptor: [Clomipramine] this term only
13. MeSH descriptor: [Desvenlafaxine Succinate] this term only
14. MeSH descriptor: [Duloxetine Hydrochloride] this term only
15. MeSH descriptor: [Citalopram] this term only
16. MeSH descriptor: [Fluoxetine] this term only
17. MeSH descriptor: [Fluvoxamine] this term only
18. MeSH descriptor: [Paroxetine] this term only
19. MeSH descriptor: [Sertraline] this term only
20. MeSH descriptor: [Trazodone] this term only
21. MeSH descriptor: [Venlafaxine Hydrochloride] this term only
22. MeSH descriptor: [Vilazodone Hydrochloride] this term only
23. ((agomelatine or amitriptyline or bupropion or citalopram or clomipramine or desvenlafaxine or duloxetine or escitalopram or fluoxetine or fluvoxamine or levomilnacipran or milnacipran or mirtazapine or nefazodone or paroxetine or reboxetine or sertraline or trazodone or venlafaxine or vilazodone or vortioxetine):ti,ab,kw (Word variations have been searched))
24. #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23
25. #8 and #24 in Trials

D. **PsycINFO**

1. major depression/ or dysthymic disorder/ or adjustment disorders/ or affective disorders/
2. (depress* or dysthymi* or adjustment disorder* or mood disorder* or "affective disorder" or "affective symptoms").tw.
3. or/1-2
4 AMITRIPTYLINE/ or BUPROPION/ or CITALOPRAM/ or FLUOXETINE/ or FLUVOXAMINE/ or NEFAZODONE/ or PAROXETINE/ or SERTRALINE/ or TRAZODONE/ or VENLAFAXINE/
5 (agomelatine or amitriptyline or bupropion or citalopram or clomipramine or desvenlafaxine or duloxetine or escitalopram or fluoxetine or fluvoxamine or levomilnacipran or milnacipran or mirtazapine or nefazodone or paroxetine or reboxetine or sertraline or trazodone or venlafaxine or vilazodone or vortioxetine).tw.
6 or/4-5
7 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).mp.
8 (random* adj5 (assign* or allocat*)).mp.
9 randomi*.mp.
10 crossover.mp.
11 or/7-10
12 3 and 6 and 11

E. AMED (Allied and Complementary Medicine)
1 affective disorders/ or depressive disorder/ or adjustment disorders/ or affective symptoms/ (1983)
2 (depress* or dysthymi* or adjustment disorder* or mood disorder* or "affective disorder" or "affective symptoms").tw.
3 or/1-2
4 Amitriptyline/
5 (agomelatine or amitriptyline or bupropion or citalopram or clomipramine or desvenlafaxine or duloxetine or escitalopram or fluoxetine or fluvoxamine or levomilnacipran or milnacipran or mirtazapine or nefazodone or paroxetine or reboxetine or sertraline or trazodone or venlafaxine or vilazodone or vortioxetine).tw.
6 or/4-5
7 Randomized controlled trials/
8 ((singl* or doubl* or trebl* or tripl*) adj (blind* or mask*)).mp.
9 (random* adj5 (assign* or allocat*)).mp. (3990)
10 randomi*.mp.
11 crossover.mp.
12 or/7-11
13 3 and 6 and 12

F. CINAHL
S16 S3 AND S6 AND S15
S15 S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14
S14 TI allocat* random* or AB allocat* random*
S13 TI random* allocat* or AB random* allocat*
S12 (MH "Random Assignment")
S11 TI random* control* trial* or AB random* control* trial*
S10 TI ((singl* n1 blind*) or (singl* n1 mask*)) or TI ((doubl* n1 blind*) or (doubl* n1 mask*)) or TI ((tripl* n1 blind*) or (tripl* n1 mask*)) or TI ((trebl* n1 blind*) or (trebl* n1 mask*)) or AB ((singl* n1 blind*) or (singl* n1 mask*)) or AB ((doubl* n1 blind*) or (doubl* n1 mask*)) or AB ((tripl* n1 blind*) or (tripl* n1 mask*)) or AB ((trebl* n1 blind*) or (trebl* n1 mask*))
S9 TI clinic* n1 trial* or AB clinic* n1 trial*
S8 PT Clinical trial
S7 (MH "Clinical Trials+")
S6 S4 OR S5
S5 TI (agomelatine or amitriptyline or bupropion or citalopram or clomipramine or desvenlafaxine or duloxetine or escitalopram or fluoxetine or fluvoxamine or levomilnacipran or milnacipran or mirtazapine or nefazodone or paroxetine or reboxetine or sertraline or trazodone or venlafaxine or vilazodone or vortioxetine) or AB (agomelatine or amitriptyline or bupropion or citalopram or clomipramine or desvenlafaxine or duloxetine or escitalopram or fluoxetine or fluvoxamine or levomilnacipran or milnacipran or mirtazapine or
(MH "Amitriptyline") or (MH "Bupropion") or (MH "Citalopram") or (MH "Clomipramine") or (MH "Desvenlafaxine Succinate") or (MH "Fluoxetine") or (MH "Milnacipran Hydrochloride") or (MH "Mirtazapine") or (MH "Nefazodone") or (MH "Paroxetine") or (MH "Sertraline Hydrochloride") or (MH "Trazodone") or (MH "Venlafaxine")

S3 S1 OR S2

S2 TI (depress* or dysthymi* or "adjustment disorder*" or "mood disorder*" or "affective disorder" or "affective symptoms") or AB (depress* or dysthymi* or "adjustment disorder*" or "mood disorder*" or "affective disorder" or "affective symptoms")

S1 (MH "Depression") or (MH "Dysthymic Disorder") OR (MH "Affective Symptoms") or (MH "Affective Disorders") or (MH "Adjustment Disorders")

G. **LILACS**

(tw:(depress* OR dysthymi* OR "adjustment disorder*" OR "adjustment disorders" OR "mood disorder*" OR "mood disorders" OR "affective disorder" OR "affective disorders" OR "affective symptoms"))) AND (tw:(agomelatine OR amitriptyline OR bupropion OR citalopram OR clomipramine OR desvenlafaxine OR duloxetine OR escitalopram OR fluoxetine OR fluvoxamine OR levomilnacipran OR milnacipran OR mirtazapine OR nefazodone OR paroxetine OR reboxetine OR sertraline OR trazodone OR venlafaxine OR vilazodone OR vortioxetine))) AND (tw:(random*)) AND (instance:"regional") AND (db:"LILACS")

H. **Clinicaltrials.gov**

Major Depressive Disorder | Agomelatine
Major Depressive Disorder | amitriptyline
Major Depressive Disorder | bupropion
Major Depressive Disorder | citalopram
Major Depressive Disorder | clomipramine
Major Depressive Disorder | desvenlafaxine
Major Depressive Disorder | duloxetine
Major Depressive Disorder | escitalopram
Major Depressive Disorder | fluoxetine
Major Depressive Disorder | fluvoxamine
Major Depressive Disorder | levomilnacipran
Major Depressive Disorder | milnacipran
Major Depressive Disorder | mirtazapine
Major Depressive Disorder | nefazodone
Major Depressive Disorder | paroxetine
Major Depressive Disorder | reboxetine
Major Depressive Disorder | sertraline
Major Depressive Disorder | trazodone
Major Depressive Disorder | venlafaxine
Major Depressive Disorder | vilazodone
Major Depressive Disorder | vortioxetine

I. **WHO International Clinical Trials Registry Platform**

Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: agomelatine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: bupropion
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: citalopram
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: clomipramine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: desvenlafaxine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: duloxetine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: escitalopram
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: fluoxetine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: fluvoxamine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: levomilnacipran
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: milnacipran
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: mirtazapine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: nefazodone
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: paroxetine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: reboxetine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: sertraline
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: trazodone
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: venlafaxine
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: vilazodone
Recruitment status ALL | Condition: Major Depressive Disorder | Intervention: vortioxetine

J. EUDRACT, Australian Clinical Trials Registry, ISRCTN, and UK National Research Register

Major Depressive Disorder and Agomelatine
Major Depressive Disorder and amitriptyline
Major Depressive Disorder and bupropion
Major Depressive Disorder and citalopram
Major Depressive Disorder and clomipramine
Major Depressive Disorder and desvenlafaxine
Major Depressive Disorder and duloxetine
Major Depressive Disorder and escitalopram
Major Depressive Disorder and fluoxetine
Major Depressive Disorder and fluvoxamine
Major Depressive Disorder and levomilnacipran
Major Depressive Disorder and milnacipran
Major Depressive Disorder and mirtazapine
Major Depressive Disorder and nefazodone
Major Depressive Disorder and paroxetine
Major Depressive Disorder and reboxetine
Major Depressive Disorder and sertraline
Major Depressive Disorder and trazodone
Major Depressive Disorder and venlafaxine
Major Depressive Disorder and vilazodone
Major Depressive Disorder and vortioxetine

K. JMACCT

Major Depressive Disorder

L. UMIN-CTR

Condition: Major Depressive Disorder | Free keyword: Agomelatine
Condition: Major Depressive Disorder | Free keyword: amitriptyline
Condition: Major Depressive Disorder | Free keyword: bupropion
Condition: Major Depressive Disorder | Free keyword: citalopram
Condition: Major Depressive Disorder | Free keyword: clomipramine
Condition: Major Depressive Disorder | Free keyword: desvenlafaxine
Condition: Major Depressive Disorder | Free keyword: duloxetine
Condition: Major Depressive Disorder | Free keyword: escitalopram
Condition: Major Depressive Disorder | Free keyword: fluoxetine
Condition: Major Depressive Disorder | Free keyword: fluvoxamine
Condition: Major Depressive Disorder | Free keyword: levomilnacipran
Condition: Major Depressive Disorder | Free keyword: milnacipran
Condition: Major Depressive Disorder | Free keyword: mirtazapine
Condition: Major Depressive Disorder | Free keyword: nefazodone
Condition: Major Depressive Disorder | Free keyword: paroxetine
Condition: Major Depressive Disorder | Free keyword: reboxetine
Condition: Major Depressive Disorder | Free keyword: sertraline
Condition: Major Depressive Disorder | Free keyword: trazodone
Condition: Major Depressive Disorder | Free keyword: venlafaxine
Condition: Major Depressive Disorder | Free keyword: vilazodone
Condition: Major Depressive Disorder | Free keyword: vortioxetine