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Overcoming functional impairment in postpartum depressed or anxious women: a pilot trial of desvenlafaxine with flexible dosing

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Abstract

Objectives: Antidepressants are the first line treatment for moderate to severe major depressive disorder (MDD) in perinatal and general populations. However, there appears to be paucity of evidence around antidepressant use in women with postpartum depression or anxiety. Selection of an appropriate antidepressant is crucial in promoting efficacy, optimizing tolerability, and managing comorbid anxiety or depression. Our aim was to investigate the treatment effect and tolerability profile of desvenlafaxine, and to examine the functionality of women with postpartum depression or anxiety after desvenlafaxine treatment.

Methods: Fifteen postpartum women with depression or anxiety completed this 12-week prospective pilot study with a flexible dose of desvenlafaxine (50–100 mg). Participants were recruited at a tertiary care level program. Measures of depression (Montgomery–Åsberg Depression Rating Scale, MADRS), anxiety (Hamilton Anxiety Rating Scale, HAM-A), worry (Penn State Worry Questionnaire, PSWQ) and functional impairment (Sheehan Disability Scale, SDS) were completed at baseline, 8 weeks, and 12 weeks.

Results: In the intention-to-treat analysis ($n = 17$), the majority of women responded to medication (88.2%, $n = 15$), and reached remission of depressive (82.4%, $n = 14$) and anxiety symptoms (82.4%, $n = 14$). Remission of depression was achieved in a mean of 6.9 weeks [standard deviation (SD) = 3.01] at a mean dose of 71 mg/day (SD = 25.7). Significant decreases were observed on PSWQ worry scores ($p < 0.0001$) and SDS scores for social ($p < 0.0001$) and family life impairment ($p < 0.0001$). The medication was generally well tolerated.

Conclusion: The results of our prospective pilot study suggest that treatment with desvenlafaxine of postpartum mothers with depression or anxiety can lead to symptom remission and restoration of functionality.

Keywords: antidepressants, anxiety, desvenlafaxine, functional restoration, mental health, postpartum depression

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Introduction

Postpartum depression (PPD) has a worldwide prevalence of 15% [Pearlstein *et al.* 2009]. Family physicians, midwives or obstetricians are generally the first point of healthcare contact for women after childbirth. In the early postpartum period, most clinicians spend time focusing on the mother and newborn's medical concerns. As a result, maternal mental health issues such as postpartum depression are often undetected. The impact of untreated maternal depression on functional impairment thus far has not been studied methodically. Even with conscientious screening, it is difficult for a clinician to measure the degree of maternal mental impairment in the absence of a specific validated tool. One study has measured quality of life in postpartum mothers after pharmacotherapy treatment with an antidepressant

[Misri *et al.* 2012]. However, functional impairment specifically has not yet been measured in this population.

Timely diagnosis and judicious treatment will diminish the harmful effects of a mentally ill mother on her growing infant, reduce negative neurodevelopmental impact on the baby, and prevent long-term detrimental outcomes in the child [Stein *et al.* 2014]. Offspring of women with untreated mental illness are more likely to have disturbed social interactions, exhibit greater internalizing behaviours as children, and have a higher chance of developing mental disorders as adolescents [Stein *et al.* 2014]. Therefore, the healthcare provider should aim for the appropriate type of treatment to restore maternal mental health and to prevent deleterious consequences on the baby.

For moderate to severe depression in the general population, research demonstrates that pharmacotherapy is the most studied and best evidenced treatment [Lam *et al.* 2009]. In contrast, however, there is a paucity of data around the efficacy and tolerability of antidepressants in postpartum depression. Published research reveals 11 studies in total, of which four are open-label studies and seven are randomized controlled trials (RCTs) [Kim *et al.* 2014; di Scalea and Wisner, 2009]. Of the four open-label studies, two involved selective serotonin reuptake inhibitors, that is, sertraline and escitalopram; one study utilized norepinephrine reuptake inhibitor, that is, bupropion slow release; and another study incorporated a selective serotonin norepinephrine reuptake inhibitor , that is, venlafaxine [Kim *et al.* 2014; di Scalea and Wisner, 2009]. Among the antidepressants investigated, all of them demonstrated an overall antidepressant efficacy [Cohen *et al.* 2001]. Venlafaxine, however, was the only antidepressant that demonstrated a specific anxiolytic effect in the postpartum depressed population [Cohen *et al.* 2001]. Since anxiety symptoms almost invariably accompany postpartum depression [Kornstein *et al.* 2014a; Tourian *et al.* 2010a], careful antidepressant selectivity is crucial in managing comorbid anxiety and depressive symptoms [Misri *et al.* 2015]. Desvenlafaxine, a metabolite of venlafaxine, appears to be an effective first-line antidepressant for the treatment of major depressive disorder (MDD) [Lam *et al.* 2009]. It has also been shown to have anxiolytic properties [Kornstein *et al.* 2014a; Tourian *et al.* 2010a] and an easy dosing profile with minimal to no titration [Kornstein *et al.* 2014b; Pfizer Canada Inc., 2014]. The tolerability profile of desvenlafaxine demonstrates that the adverse effects of weight gain and sexual dysfunction are minimal [Kornstein *et al.* 2014b; Clayton *et al.* 2013]. Since these specific side effects of weight gain and sexual dysfunction often lead to poor adherence in the postpartum population, desvenlafaxine could be considered as a suitable antidepressant treatment option for women transitioning into motherhood.

We designed this open-label, prospective pilot study administering a flexible dose of desvenlafaxine for treatment of MDD and anxiety symptoms in postpartum women. The primary objectives of this study were to estimate the proportion of women who respond to treatment with desvenlafaxine and achieve full functionality and remission; and the treatment effect and tolerability profile within these women. For depression, response represents at least a 50% reduction in baseline scores on the Montgomery–Åsberg Depression Rating Scale (MADRS); remission is defined as scores of less than 10 on MADRS [Montgomery and Åsberg, 1979]. For anxiety, response is at least a 50% reduction in baseline scores on the Hamilton Anxiety Rating Scale (HAM-A); remission is defined as scores of up to 7 on HAM-A [Hamilton, 1959]. Full functionality is defined as scores of less than 5 on the Sheehan Disability Scale (SDS) domains [Sheehan, 1983].

Materials and methods

Participants

Women were recruited up to 2 years postpartum through outpatient referrals to the British Columbia Reproductive Mental Health Program affiliated with the University of British Columbia. Inclusion criteria were age 19–45 years, onset of MDD within 1 year after childbirth, baseline MADRS score greater than 25, and fluency in English. Women were excluded if they were breastfeeding, suicidal, psychotic, or abusing substances. All participants provided informed consent. Ethics approval was granted by the Research Ethics Committee at University of British Columbia and BC Women's Hospital.

Study design

In this 12-week trial, women were assessed by the study psychiatrist as per the Diagnostic and Statistical Manual of Mental Disorders, 5th

Edition (DSM-5) structured clinical interview; diagnosis was confirmed by the Mini International Neuropsychiatric Interview [Sheehan *et al.* 1998]. Patients attended six follow-up visits, approximately 2 weeks apart. Each visit recorded weight, blood pressure, and side effects. MADRS, HAM-A, Penn State Worry Questionnaire (PSWQ) [Meyer *et al.* 1990], and SDS were completed at baseline, visits 4 (8 weeks) and 7 (12 weeks). MADRS and HAM-A are both validated, clinician-rated, diagnostic screening tools for depression and anxiety, respectively, used widely in clinical practice and research. PSWQ is a 16-item self-report measure designed to capture the intensity of worry associated with generalized anxiety disorder (GAD). PSWQ distinguishes between GAD and other anxiety disorders, as well as between patients with all, some, or none of the diagnostic features of GAD [Meyer *et al.* 1990]. The SDS is a three-item, patient-rated tool assessing functional impairment in domains of work/school, social life and family life/home responsibilities and is sensitive to change over treatment [Sheehan, 1983]. Patients rate the extent to which each domain impairs their symptoms on a 10-point visual analogue scale. Scores of at least 5 in a particular domain suggest functional impairment in that category. Because this study took place in Canada, where women are given maternity leave for up to a year, none of our participants were working outside of the home. The SDS work domain is specified as paid, unpaid volunteer work or training and therefore 'respondents have the option to skip this item if they have not worked/or studied at all in the last week for reasons unrelated to their disorder' [Sheehan and Sheehan, 2008]. As all of the women in our study were on maternity leave, the 'work/study' item, and two productivity items (days lost and days underproductive) were not applicable.

All participants were initiated on a 50 mg/day dose of desvenlafaxine following baseline assessment. The dose was increased to 100 mg/day from week 4 onwards by the study psychiatrist based on response and tolerability profile.

Statistical analysis

Outcome results are based on an intent-to-treat (ITT) population, with inclusion criteria based on complete baseline measures, at least one dose of desvenlafaxine taken, and minimum of one complete postmedication assessment. Last observation carried forward completed the remaining visits for those who withdrew but were included in ITT. Repeated measures analysis of variance (ANOVA) tested change from baseline for each outcome measure. Mean number of weeks to response (at least 50% reduction in baseline scores on MADRS and HAM-A), remission (total scores separately of less than 10 on MADRS, up to 7 on HAM-A), mean dosage at response and remission, and side effects are described. Change in weight from baseline to final visit was analysed by paired samples *t* test.

Results

Forty clinic referrals were screened, 25 women enrolled, and 15 completed all study visits. None of these women were on antidepressant medications within the past month prior to enrolment, with the exception of one participant who was tapered off from escitalopram over 2 weeks. Reasons for dropout included: allergic reaction (1), accidental conception (1), lost to follow up (1), changed mind about pharmacotherapy (4), tolerability (2), and lack of partner support (1). Of these, eight did not continue after baseline, one completed two follow-up visits while another completed one follow-up visit; therefore analyses are based on an ITT sample of 17. Mean age of ITT women was 33.2 years [standard deviation (SD) = 1.05]; among those who withdrew, the mean age was 36.8 (SD = 2.00). Of the ITT participants, the mean number of children was 1.76 (SD = 0.94). All were married and represented a variety of ethnicities such as white (9), Chinese (2), Fijian (1), Iranian (1), Polish (1), Slovakian (1), and South Asian (2).

In addition to PPD, the majority of ITT (70.6%) had comorbid GAD. Other comorbidities in the sample included dysthymia (23.5%), panic disorder (17.6%), agoraphobia (5.9%), social phobia (5.9%), and obsessive compulsive disorder (17.6%). Comorbidities were similar in the withdrawals: GAD (75%), dysthymia (37.5%), panic disorder (50%), and social phobia (12.5%).

Of the ITT population, one woman increased the dose at week 4, another two at week 6, another four at week 8, three at week 10, and one at week 12. In total, the doses of 11 women were increased to 100 mg/day desvenlafaxine by the conclusion of the trial.

Depression and anxiety symptoms

Table 1 shows initial and final visit mean scores for all outcomes. Repeated measures ANOVAs

Table 1. Initial and final scores for study measures with change from baseline.

Measure	Mean initial score (SD)	Mean final score (SD)	Mean change (SD)	Weeks to remit (SD)	% Remitted	ANOVA *p*
MADRS	30.6 (6.55)	6.2 (8.00)	−24.4 (9.20)	6.9 (3.01)	82.4%	<0.0001
HAM-A	23.5 (8.13)	5.5 (6.05)	−18.0 (8.42)	6.9 (3.57)	82.4%	<0.0001
PSWQ	60.3 (10.69)	44.1 (11.68)	−16.2 (12.78)			<0.0001
SDS						
Social life	6.5 (2.41)	3.1 (2.41)	−3.4 (2.42)			<0.0001
Family life	7.4 (2.06)	3.5 (2.55)	−3.9 (3.00)			<0.0001

ANOVA, analysis of variance; HAM-A, Hamilton Anxiety Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale; PSWQ, Penn State Worry Questionnaire; SD, standard deviation; SDS, Sheehan Disability Scale.

Table 2. TEAE reported by participants at postmedication assessments.

Study visit	Total number reporting TEAE	TEAE details (number reported)
2 weeks	14	Sweating (6), heartburn (2), dry mouth (2), nausea (6), decreased appetite at night (2), hot flushes (2), irritability (2), light headedness (2), headache (3), drowsiness and diarrhoea for 3 days , insomnia for 4 days
4 weeks	12	Sweating (5), headache (3), nausea (2), dry mouth (2), muscle tension, hot flushes when not taken with food, light headedness, drowsiness/tiredness at night after meds, nausea for 1 day
6 weeks	6	Sweating (3), headache (4), dry mouth (2), tiredness, hot flushes, low appetite in pm
8 weeks	6	Nausea as a result of increased exercise, dry mouth (3), sweating (4), headache (3)
10 weeks	6	Mild sweating, headache (2), dry mouth (2), nausea for few hours after meds, night sweating since increase to 100 mg
12 weeks	8	Sweating (3), headaches occasional, hot flushes, nausea after meds

TEAE, treatment-emergent adverse effect.

showed significant improvement across the trial for both MADRS [$F(6, 96) = 39.18$, $p < 0.0001$] and HAM-A [with Greenhouse–Geisser correction, $F(3.2, 51.2) = 29.59$, $p < 0.0001$]. By the final visit, 88.2% ($n = 14$) responded, with a mean 4.9 weeks (SD = 2.25) to response on MADRS and 5.3 weeks (SD = 2.23) on HAM-A. The mean dose at response was 66 mg (SD = 24.4) for MADRS and 63 mg (SD = 22.9) for HAM-A. The majority of women reached remission by the final visit (82.4% on each measure); among them, remission was achieved with a mean dose of 71 mg (SD = 25.7). Overall, PSWQ worry scores decreased significantly from baseline to final visit [$F(2, 32) = 17.68$, $p < 0.0001$].

Functional improvement

Table 1 shows functional outcomes on the SDS. Significant decreases were observed on both social [$F(2, 32) = 13.24$, $p < 0.0001$] and family life impairment [$F(2, 32) = 18.94$, $p < 0.0001$].

Treatment-emergent adverse effects

Details of reported treatment-emergent adverse effects (TEAEs) are presented in Table 2. Mean weight showed no significant change from baseline (172 lb, SD = 69.2) to final visit (171 lb, SD = 68.7), $t(16) = 0.64$, $p = 0.54$.

Overall, the reported side effects appeared to be mild, transient, and manageable. However, two women opted to discontinue the study despite reassurance.

Decrease in libido and difficulty reaching climax was reported by one participant at the 2-week visit after switching from escitalopram; this resolved by the week 4 visit.

Discussion

This pilot study is the first to estimate the treatment effect of desvenlafaxine in postpartum depression or anxiety. A significant proportion of our participants returned to full functionality after completion of treatment. Other than one study [Misri *et al.* 2012], there are no published data measuring quality of life in postpartum mothers with depression treated with pharmacotherapy. Routine functional assessment of postpartum women is not generally undertaken due to lack of validated measures that can assist the healthcare provider. Underreporting of the degree of maternal dysfunction due to fear and stigma is an additional barrier.

We demonstrated significant improvements in social and family life domains of the SDS with a flexible dose regimen of desvenlafaxine, with mean change similar to a general population of employed adults with MDD on 50 mg/day of desvenlafaxine [Dunlop *et al.* 2011]. Since the majority of our participants were on maternity leave, the work/productivity domains were not applicable.

We included women with comorbid anxiety disorders, a majority of whom suffer from GAD; this high level of GAD comorbidity in PPD has been reported by Grigoriadis and colleagues [Grigoriadis *et al.* 2011]. Research on desvenlafaxine efficacy in MDD with concomitant GAD is sparse, as comorbid conditions have been an exclusion criteria in most published clinical trials. Efficacy of desvenlafaxine in 'anxious depressed' patients was previously reported in two papers [Kornstein *et al.* 2014a; Tourian *et al.* 2010a], where clinically relevant anxiety was identified by the anxiety–somatization subscale of the Hamilton Rating Scale for Depression 17 (HAM-D-17) [Hamilton, 1960]. Ours is the first study of desvenlafaxine which included comorbid anxiety disorders and used a validated anxiety scale, HAM-A, and a worry questionnaire, PSWQ. Using the ITT population, we found an anxiety remission rate of 82.4% on HAM-A. PSWQ scores reduced significantly, from an excessive anxiety score of 60 to the normal range of 44. Additionally, our depression remission rate of 82.4% on MADRS was higher than that reported in a 100 mg/day, placebo-controlled trial in a general population of adults with MDD [Thase *et al.* 2009]. This discrepancy might be reflecting the longer trial time of 12 weeks rather than 8 weeks. Other aspects of the current study design that may account for better remission rates than those observed in the controlled studies include its open-label design, small sample size, and a highly-specialized clinic for this very special population.

Generally, anxious depressed patients have more severe depressive symptoms, poorer response to antidepressant treatment, and lower chance of reaching remission [Fava *et al.* 2008]. In clinical practice, these patients often necessitate higher dosing. Most women in our sample responded to 50 mg/day; among those with remitting disease, almost half required 100 mg/day by the final visit. This can be explained, at least in part, by greater levels of anxiety in our population. Without remission of anxiety, complete functional restoration was not observed. Despite greater difficulty in treating patients with anxiety symptoms [Emmanuel *et al.* 1998], the majority of the patients, including those with anxiety symptoms, reached remission and full functionality with flexible dosing of 50–100 mg. Therefore, healthcare providers should target optimal medication dosing for maternal functional recovery.

Reported side effects appeared to be mild and tolerable; most were transient. Three participants dropped out of the study as a result of TEAEs, including one due to an allergic reaction. It is important to note that there was no significant change in weight from baseline to completion; earlier general population research with desvenlafaxine has been consistent with our finding [McIntyre *et al.* 2015; Tourian *et al.* 2010b]. In clinical practice, weight gain and sexual dysfunction are often reported as reasons for discontinuation of antidepressant treatment [Ginsberg, 2009]. Overall sexual functioning appears to be unaffected in patients treated with desvenlafaxine in the general population [Kornstein *et al.* 2014b; Clayton *et al.* 2013]. In our study, when specifically questioned by the study psychiatrist, only one patient reported lack of sexual desire with 2 weeks of treatment; this resolved by the week 4 visit. There was no spontaneous reporting of sexual dysfunction, an important consideration when treating postpartum women with antidepressants. This finding is consistent with recent research using an objective measure of sexual functioning at 50 and 100 mg/day of desvenlafaxine [Clayton *et al.* 2013].

Estimates of change on study measures (MADRS and SDS), remission rates, and dose at response for the current study were compared with data

from four previously published general population RCTs (see Table A1, Appendix). The four studies used for comparison were placebo controlled trials with adult outpatient populations [Clayton *et al.* 2013; Dunlop *et al.* 2011; Liebowitz *et al.* 2013; Thase *et al.* 2009]. Our study had the highest percentage of patients achieving remission at 82.4% compared with the 17–45% remission rates on the other studies [Clayton *et al.* 2013; Dunlop *et al.* 2011; Liebowitz *et al.* 2013; Thase *et al.* 2009]. Our study also showed the largest mean change in both MADRS scores (–24.4 ± 2.23) and SDS domains (social: –3.4 ± 0.59 and family: 3.9 ± 0.72). Another notable comparison is that other studies used a fixed dosing of desvenlafaxine, either 50 or 100 mg [Clayton *et al.* 2013; Dunlop *et al.* 2011; Liebowitz *et al.* 2013; Thase *et al.* 2009], whereas the present study is the first to use flexible dosing of desvenlafaxine between 50 and 100 mg. Overall, our study showed comparable changes on SDS domains, including higher remission rates and larger changes on MADRS scores than these studies.

Due to a lack of robust data on suitable antidepressants in the postpartum population, there is a real need to examine the utility of different antidepressants for postpartum women. The limitation of a small sample size and open-label design seen in our pilot study is a common concern for research in the perinatal population [di Scalea and Wisner, 2009]; encouraging results from our study, nonetheless, warrant a larger clinical trial with controls. Our study provides clinically relevant information on an otherwise difficult to research area. Comparisons with previously published desvenlafaxine data in the general population help to validate the effects observed in our sample. Previous antidepressant studies in this population show attrition rates of 19–56% [Stowe *et al.* 1995; Appleby *et al.* 1997; Cohen *et al.* 2001; Nonacs *et al.* 2005; Yonkers *et al.* 2008]. High attrition rates in postpartum women are due to increased role responsibility, breastfeeding issues, fear of pharmacotherapy, medication adverse effects, and the continued stigma of mental illness [Warden *et al.* 2009]. We did not include women with a sole primary depression diagnosis; our sample reflects the clinical reality of comorbidity in postpartum women seeking psychiatric treatment.

Conclusion

Transitioning to motherhood is filled with uncertainties and challenges even for women without psychiatric diagnoses. Onset of clinically relevant depression and anxiety further complicates this picture, both for the patient and healthcare provider alike. This is because the severity of functional impairment is correlated to the psychiatric comorbidities in the postpartum population. Many new mothers are embarrassed or ashamed to accept a diagnosis of mental illness, let alone consider pharmacological intervention. In this context, instituting timely and appropriate antidepressant treatment has to be carefully considered. Functional impairment of postpartum psychiatric illness should be assessed by an appropriate instrument, which measures the impact of depression on a postpartum mother who must return to work shortly after giving birth. We found desvenlafaxine to be efficacious with a good tolerability profile leading to symptom remission and a positive impact on functionality. Healthcare providers are advised to aim for restoring maternal quality of life by offering comprehensive management of postpartum depression and anxiety.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

References

Appleby, L., Warner, R., Whitton, A. and Faragher, B. (1997) A controlled study of fluoxetine and cognitive-behavioural counselling in the treatment of postnatal depression. *BMJ* 314: 932–936.

Clayton, A., Kornstein, S., Dunlop, B., Focht, K., Musqnung, J., Ramey, T. *et al.* (2013) Efficacy and safety of desvenlafaxine 50 mg/d in a randomized, placebo-controlled study of perimenopausal and

postmenopausal women with major depressive disorder. *J Clin Psychiatry* 74: 1010–1017.

Cohen, L., Viguera, A., Bouffard, S., Nonacs, R., Morabito, C., Collins, M. *et al.* (2001) Venlafaxine in the treatment of postpartum depression. *J Clin Psychiatry* 62: 592–596.

Di Scalea, T. and Wisner, K. (2009) Pharmacotherapy of postpartum depression. *Expert Opin Pharmacother* 10: 2593–2607.

Dunlop, B., Reddy, S., Yang, L., Lubaczewski, S., Focht, K. and Guico-Pabia, C. (2011) Symptomatic and functional improvement in employed depressed patients: a double-blind clinical trial of desvenlafaxine versus placebo. *J Clin Psychopharmacol* 31: 569–576.

Emmanuel, J., Simmonds, S. and Tyrer, P. (1998) Systematic review of the outcome of anxiety and depressive disorders. *Br J Psychiatry Suppl* 34: 35–41.

Fava, M., Rush, A., Alpert, J., Balasubramani, G., Wisniewski, S., Carmin, C. *et al.* (2008) Difference in treatment outcome in outpatients with anxious versus nonanxious depression: a STAR* D report. *Am J Psychiatry* 3: 342–351.

Ginsberg, L. (2009) Impact of drug tolerability on the selection of antidepressant treatment in patients with major depressive disorder. *CNS Spectr* 14: 8–14.

Grigoriadis, S., de Camps Meschino, D., Barrons, E., Bradley, L., Eady, A., Fishell, A. *et al.* (2011) Mood and anxiety disorders in a sample of Canadian perinatal women referred for psychiatric care. *Arch Womens Ment Health* 14: 325–333.

Hamilton, M. (1959) The assessment of anxiety states by rating. *Br J Med Psychol* 32: 50–55.

Hamilton, M. (1960) A rating scale for depression. *J Neurol Neurosurg Psychiatry* 23: 56.

Kim, D., Epperson, C., Weiss, A. and Wisner, K. (2014) Pharmacotherapy of postpartum depression: an update. *Expert Opin Pharmacother* 15: 1223–1234.

Kornstein, S., Guico-Pabia, C. and Fayyad, R. (2014a) The effect of desvenlafaxine 50 mg/day on a subpopulation of anxious/depressed patients: a pooled analysis of seven randomized, placebo-controlled studies. *Hum Psychopharmacol* 29: 492–501.

Kornstein, S., McIntyre, R., Thase, M. and Boucher, M. (2014b) Desvenlafaxine for the treatment of major depressive disorder. *Expert Opin Pharmacother* 15: 1449–1463.

Lam, R., Kennedy, S., Grigoriadis, S., McIntyre, R., Miley, R., Ramasubbu, R. *et al.* (2009) Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults: III. Pharmacotherapy. *J Affect Disord* 117: S26-S43.

Liebowitz, M., Tourian, K., Hwang, E. and Mele, L. (2013) A double-blind, randomized, placebo-controlled study assessing the efficacy and tolerability of desvenlafaxine 10 and 50 mg/day in adult outpatients with major depressive disorder. *BMC Psychiatry* 13: 94.

McIntyre, R., Fayyad, R., Guico-Pabia, C. and Boucher, M. (2015) A post hoc analysis of the effect of weight on efficacy in depressed patients treated with desvenlafaxine 50 mg/d and 100 mg/d. *Prim Care Companion CNS Disord* 17.

Meyer, T., Miller, M., Metzger, R. and Borkovec, T. (1990) Development and validation of the Penn State Worry Questionnaire. *Behav Res Ther* 28: 487–495.

Misri, S., Abizadeh, J., Albert, G., Carter, D. and Ryan, D. (2012) Restoration of functionality in postpartum depressed mothers: an open-label study with escitalopram. *J Clin Psychopharmacol* 32: 729–732.

Misri, S., Abizadeh, J., Sanders, S. and Swift, E. (2015) Perinatal generalized anxiety disorder: assessment and treatment. *J Womens Health* 24: 762–770.

Montgomery, S. and Åsberg, M. (1979) A new depression scale designed to be sensitive to change. *Br J Psychiatry* 134: 382–389.

Nonacs, R., Soares, C., Viguera, A., Pearson, K., Poitras, J. and Cohen, L. (2005) Bupropion SR for the treatment of postpartum depression: a pilot study. *Int J Neuropsychopharmcol* 8: 445–449.

Pearlstein, T., Howard, M., Salisbury, A. and Zlotnick, C. (2009) Postpartum depression. *Am J Obstet Gynecol* 200: 357–364.

Pfizer Canada Inc. (2014) *PRISTIQ® Desvenlafaxine Extended-Release Tablets (50 and 100 mg Desvenlafaxine as Desvenlafaxine Succinate)*. Report of Product Monograph. Available at: http://www.pfizer.ca/sites/g/files/g10017036/f/201505/Pristiq_DC_PM_E_170902_3Dec2014.pdf. (accessed 10 June 2015).

Sheehan, D.V. (1983) *The Anxiety Disease*. New York: Scribner.

Sheehan, D., Lecrubier, Y., Sheehan, K., Amorim, P., Janavs, J., Weiller, E. *et al.* (1998) The Mini-International Neuropsychiatric Interview (M.I.N.I): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 59: 22–33.

Sheehan, K. and Sheehan, D. (2008) Assessing treatment effects in clinical trials with the discan metric of the Sheehan Disability Scale. *Int Clin Psychopharmacol* 23: 70–83.

Stein, A., Pearson, R., Goodman, S., Rapa, E., Rahman, A., McCallum, M. *et al.* (2014) Effects of perinatal mental disorders on the fetus and child. *Lancet* 384: 1800–1819.

Stowe, Z., Casarella, J., Landry, J. and Nemeroff, C. (1995) Sertraline in the treatment of women with postpartum major depression. *Depression* 3: 49–55.

Thase, M., Kornstein, S., Germain, J., Jiang, Q., Guico-Pabia, C. and Ninan, P. (2009) An integrated analysis of the efficacy of desvenlafaxine compared with placebo in patients with major depressive disorder. *CNS Spectr* 14: 144–154.

Tourian, K., Jiang, Q. and Ninan, P. (2010a) Analysis of the effect of desvenlafaxine on anxiety symptoms associated with major depressive disorder: pooled data from 9 short-term, double-blind, placebo-controlled trials. *CNS Spectr* 15: 187–193.

Tourian, K.A., Leurent, C., Graepel, J. and Ninan, P.T. (2010b) Desvenlafaxine and weight change in major depressive disorder. *Prim Care Companion J Clin Psychiatry* 12.

Warden, D., Trivedi, M., Wisniewski, S., Lesser, I., Mitchell, J., Balasubramani, G. *et al.* (2009) Identifying risk for attrition during treatment for depression. *Psychother Psychosom* 78: 372–379.

Yonkers, K., Lin, H., Howell, H., Heath, A. and Cohen, L. (2008) Pharmacologic treatment of postpartum women with new-onset major depressive disorder: a randomized controlled trial with paroxetine. *J Clin Psychiatry* 69: 659–665.

Appendix

Table A1. ITT outcomes comparison with published data (ITT).

Study	Population	Sample size*	Length of trial	Dosage	% Remission	Mean (SE) change in MADRS	Mean (SE) change in SDS domains
Present study	Postpartum women	17	12 weeks	50–100 mg/day, flexible	82.4%	–24.4 (2.23)	Social: –3.4 (0.59) Family: –3.9 (0.72)
Clayton *et al.* [2013]	Women 40–70 years	216	8 weeks	50 mg/day	23.6%	–15.1 (0.67)	Total only reported
Dunlop *et al.* [2011]	Employed adults	285	12 weeks	50 mg/day	40%	Sig. diff from placebo, values not reported	Social: –3.3 (0.2) Family: –3.2 (0.2)
Liebowitz *et al.* [2013]	Adult outpatients	224	8 weeks	50 mg/day	17%	–10.8 (0.63)	Social: –1.4 (0.18) Family: –1.2 (0.17)
Thase *et al.* [2009]	Pooled data of 9 RCTs on adult outpatients	312	8 weeks	50 mg/day	45%	–15.8 (0.57)	Not measured
		411	8 weeks	100 mg/day	42%	–15.2 (0.49)	

*Sample size is limited to ITT patients who received desvenlafaxine.
ITT, intent to treat; MADRS, Montgomery–Åsberg Depression Rating Scale; RCT, randomized controlled trial; SDS, Sheehan Disability Scale; SE, standard error.