A Gender Analysis of the Study of Pharmacotherapy of Psychotic Depression (STOP-PD): Gender and Age as Predictors of Response and Treatment-Associated Changes in Body Mass Index and Metabolic Measures

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ABSTRACT

Background: Gender differences exist in psychiatric disorders; however, gender has not been well studied in psychotic depression. This analysis of the largest clinical trial in psychotic depression examined the effects of age and gender on clinical characteristics and predictors of treatment outcome and treatment-associated changes in body mass index (BMI) and metabolic measures.

Method: Secondary analyses were performed on data from 259 subjects with major depressive disorder with psychotic features (*DSM-IV-TR*) aged 18–93 years in the double-blind randomized controlled trial of olanzapine plus sertraline versus olanzapine plus placebo for psychotic depression (Study of Pharmacotherapy of Psychotic Depression). Sociodemographic factors, clinical characteristics, treatment outcome, and treatment-associated changes in BMI and metabolic measures were analyzed by gender and age. Subjects were enrolled from December 2002 to June 2007.

Results: Female gender was associated with divorced ($\chi^2_1 = 5.3$, $P = .03$) or widowed ($\chi^2_1 = 8.1$, $P \leq .01$) marital status. Comorbid anxiety disorders were more common in women than in men ($\chi^2_1 = 4.9$, $P = .03$). Hallucinations ($\chi^2_1 = 7.8$, $P = .005$) and delusions with disorganization ($t_{257} = -2.10$, $P = .04$) were significantly associated with female gender, as were higher cholesterol measures ($\chi^2_1 = 7.15$, $P = .008$). There were no significant interactions between treatment and gender in terms of change in BMI. Gender was not associated with treatment response.

Discussion: This study is the first analysis of gender and age as predictors of treatment outcome and treatment-associated changes in BMI and metabolic adverse effects in psychotic depression. Gender differences exist in patients with psychotic depression, most notably with regard to the presence of hallucinations. Female gender was associated with metabolic measures. Future studies with larger sample sizes may detect small gender differences in treatment outcome and treatment-associated changes in BMI and metabolic measures in psychotic depression.

Trial Registration: ClinicalTrials.gov identifier: NCT00056472

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Major depression with psychotic features, or "psychotic depression," is a serious illness characterized by the presence of delusions or hallucinations during a major depressive episode.[1] Compared to major depression without psychotic features, psychotic depression is associated with increased rates of relapses and recurrences,[2–4] mortality from medical causes,[5] suicide attempts, and completed suicide.[6–8] Effective treatments for psychotic depression are available,[9–15] but misdiagnosis is common[16] and many patients do not receive adequate pharmacotherapy.[17] Evidence supports that a combination of an antipsychotic and an antidepressant is the most effective pharmacotherapy for psychotic depression,[9,10,12–14] but not all patients respond and some experience adverse effects that can lead to early treatment discontinuation. Identification of predictors of response and treatment-associated adverse effects in this population would help clinicians detect likely treatment responders and may help identify patients at risk for adverse effects, especially metabolic effects associated with antipsychotic use. To date, predictors of response and adverse effects in this population are ill defined.

The effect of gender and age on clinical characteristics, treatment response, and treatment-associated adverse effects has been reported in several psychiatric illnesses. Gender differences in the clinical characteristics of major depression,[18,19] delusional disorder,[20] bipolar psychosis,[21,22] and schizophrenia[23–26] have been reported. A limited number of studies into gender differences in psychotic depression[27–30] suggest that females may experience more fatigue, psychomotor agitation, mood-incongruent delusions,[29] and somatic symptoms[28] but less suicidality[27] than males. Small gender differences exist in antidepressant and antipsychotic treatment response in psychiatric disorders, and they may be associated with age. Younger females generally respond to SSRIs,[31,32] including sertraline,[33,34] better than males. This gender effect is lost in older females, whose treatment response rates are similar to those of males. Furthermore, in schizophrenia, females respond better than males to olanzapine treatment, and younger females respond better than older females.[35] These gender effects may be due, in part, to the effects of estrogen on dopamine and serotonin neurotransmission.[36–38]

Although females may respond better to antipsychotics than males, clinically significant weight gain during

Clinical Points

- One of the main novel findings of this gender analysis was that hallucinations and delusions with disorganization were more common among women with psychotic depression than men and that this finding was not associated with age.
- Our analysis did not identify gender differences in treatment response in patients with psychotic depression, but it may have been limited by a small sample size.

antipsychotic treatment, including olanzapine, is associated with female gender and younger age.[13,35,39–41] Similarly, females with depression treated with a combination of an atypical antipsychotic and an antidepressant are at greater risk for weight gain than males.[42] Thus, younger females may respond better to antidepressant and antipsychotic treatment than older females or males, but they may experience greater treatment-associated increases in body mass index (BMI) or changes in metabolic measures, such as cholesterol and blood glucose. To our knowledge, no study has yet investigated the potential role of female gender and age on treatment-associated metabolic measures in psychotic depression.

Thus, gender differences in clinical characteristics and treatment outcomes are likely due to a complex interaction of psychosocial factors, neurochemical and anatomic factors, hormonal factors, and genetic factors. Across several psychiatric disorders, gender differences are striking and encompass a range of issues, from demography, premorbid functioning, onset, and clinical characteristics to long-term outcome. Understanding the differences is the first step to ultimately provide more personalized, gender-specific treatment.

The Study of Pharmacotherapy of Psychotic Depression (STOP-PD) reported higher remission rates after 12 weeks of treatment with olanzapine plus sertraline than with olanzapine plus placebo.[13] The aims of this analysis were to determine (1) whether gender differences existed in the sociodemographic and clinical characteristics of patients with psychotic depression, (2) whether gender and age were predictors of treatment response, and (3) whether gender and age were a predictor of treatment-associated changes in BMI and metabolic measures. On the basis of the above-cited literature in nonpsychotic depression and psychotic disorders, we hypothesized that (1) female gender would be associated with the presence of comorbid anxiety disorders, (2) younger females would have higher response and remission rates than older females, and (3) younger females would experience greater increases than older females in BMI, cholesterol, and blood glucose as metabolic adverse effects.

METHOD

Study Sample

Secondary analyses were performed on data from 259 subjects aged 18–93 years in the STOP-PD study, a double-blind, randomized controlled study of olanzapine plus sertraline versus olanzapine plus placebo for psychotic depression. The study was registered on ClinicalTrials.gov (identifier: NCT00056472). The CONSORT diagram for this analysis has been previously reported.[13] One hundred seventeen subjects 18–59 years old and 142 subjects 60–93 years old were enrolled from the inpatient and outpatient services of the 4 participating academic sites from December 2002 to June 2007. Investigators used the age range 18–59 years to characterize younger women and age ≥ 60 years to characterize older women, which resulted in 75 women being designated as younger and 91 women as older. The cutoff of age 60 was used to maintain consistency with other STOP-PD reports. Sixteen women received hormone replacement therapy, of whom 6 were ≤ 59 years old and 10 were ≥ 60 years old; they were all included in the main gender analyses. Diagnosis of psychotic depression, based on *DSM-IV-TR*[1] criteria, was assessed with the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders-Patient Edition.[43] Additionally, subjects with psychotic depression were required to have a delusional belief, a score of 2 or higher on 1 of the conviction items of the Delusional Assessment Scale (DAS),[44] and a score of 3 or higher on the Schedule of Affective Disorders and Schizophrenia (SADS)[45] delusion severity rating item. Subjects received a mean olanzapine dose of 14.3 mg/d (SD = 5.3) and a mean sertraline dose 168.9 mg/d (SD = 44.1)[13]; there were no statistically significant differences in dose of either sertraline or olanzapine based on gender (data not shown). The subjects underwent repeated assessments with the 17-item Hamilton Depression Rating Scale (HDRS-17),[46] DAS, SADS, Brief Psychiatric Rating Scale (BPRS),[47] Scale for the Assessment of Positive Symptoms (SAPS),[48] Clinical Global Impressions-Severity of Illness scale (CGI-S),[49] Mini-Mental State Examination (MMSE),[50] and other instruments as outlined elsewhere.[13] Study assessments were completed weekly for the first 6 weeks and then every other week until week 12 or termination. Analysis was completed on data collected at weeks 0, 4, 8, and 12, when metabolic measures were also collected. The local institutional review boards of the participating academic medical centers and a data safety monitoring board at the National Institute of Mental Health approved the study, and written informed consent was obtained from all subjects or their substitute decision makers.

Statistical Analyses

Subjects' baseline sociodemographic and clinical characteristics were compared according to gender, age, and treatment using χ^2 tests for categorical variables and *t* tests for continuous variables (with Satterthwaite adjustment for unequal variances, as appropriate). Because of the potential for small cell sizes with categorical variables, we report the *P* value for the likelihood ratio χ^2 test statistic throughout this article. For cross-sectional data, we used a *t* test for comparison of mean values and a χ^2 test for comparison of proportions. We analyzed the longitudinal BMI, HDRS-17, and metabolic measures using generalized estimating equation methods. This approach allowed us to analyze all available data across

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Women (n = 166)	Men (n = 93)	*P* Value	*df*	Statistic
Age, mean (SD), y	57.69 (17.62)	58.40 (17.99)	.7594	257	$t = 0.31$
HDRS-17 score, mean (SD)	29.69 (5.23)	29.89 (5.29)	.7624	257	$t = 0.30$
Enrollment setting status, %					
Inpatient	68.07	70.97			
Outpatient	30.12	27.96			
Nursing home	0.60	0.00	}.7852[a,b]	3	$\chi^2 = 1.1$
Partial hospitalization	1.20	1.08			
Randomization to olanzapine plus sertraline, %	50.00	49.46	.9338[a]	1	$\chi^2 = 0.01$
Race, %					
White	80.72	90.32			
Black or African American	14.46	5.38	}.0604[a,b]	2	$\chi^2 = 5.6$
Other	4.82	4.30			
Marital status, %					
Never married	23.49	30.11			
Married	37.35	47.31			
Separated	3.01	8.60	}**.0014**[a,b]	4	$\chi^2 = 17.7$
Widowed	18.67	6.45			
Divorced	17.47	7.53			
Marital status (combined), %					
Single/married/separated	63.86	86.02			
Divorced/widowed	36.14	13.98	}**<.0001**[a,b]	1	$\chi^2 = 15.6$
Employment status, %					
Currently employed	16.56	15.22	.7778[a]	1	$\chi^2 = 0.1$
Education, %					
Less than high school graduate	31.10	29.35			
High school graduate	29.27	25.00			
Some college	18.90	21.74	}.7063[a,b]	4	$\chi^2 = 2.2$
College graduate	11.59	9.78			
Graduate/professional school	9.15	14.13			

[a]Likelihood ratio test.
[b]Bracket denotes the *P* value for the entire category (eg, enrollment setting status, race, education, etc).
Abbreviation: HDRS-17 = 17-item Hamilton Depression Rating Scale.

the study for each patient while controlling for the inherent correlation among the data collected at weeks 0, 4, 8, and 12. Both main and interaction effects (ie, age group × gender, age group × visit, gender × visit, gender × treatment group, age group × treatment group in relation to BMI and HDRS-17, gender × age group in relation to metabolic measures, time × treatment group in relation to BMI) were investigated. *P* values are reported for tests in which a single regression coefficient was equal to 0 or, for an overall test, a type 3 test of any difference among the levels of a factor (such as weeks), with adjustment for the other factors in the model. Because of the sample size, the study had limited power to detect significant interactions. To determine whether data missing at later visits were random and not related to gender or treatment, we conducted a sensitivity analysis on all subjects for BMI, each metabolic measure, and HDRS-17. We used SAS Version 9.2 (SAS Institute, Inc, Cary, North Carolina) for all data analyses.

We chose not to adjust the critical significance level (ie, $P = .05$) for multiple comparisons because (1) the adjustment would be extreme, eliminating any indication of results that might be of interest for further study, and (2) the presentation of the results using the conventional critical value allows readers to make their own decision on the significance (and plausible causality) of the results. In fact, the literature is undecided, ranging from Rothman,[51] who advocates never adjusting for multiple comparisons, to Cook and Farewell,[52] who advocate a strong adjustment. The balance between the approaches lies between a substantial adjustment, which, while potentially controlling (in some sense) the experiment-wise type I error rate at .05, also substantially increases the type II error rate, and a position of not making any adjustment, which will control the type II error rate but increases the type I error rate. In a clinical trial in which lives are at risk, controlling the type I error is certainly a priority. In this study, the answer is not so clear, and, thus, we have left the decision to the reader.

RESULTS

Baseline Sociodemographic and Clinical Variables

Women comprised 64.1% of the study sample. Female gender was associated with divorced ($\chi^2_1 = 5.3$, $P = .03$) or widowed marital status ($\chi^2_1 = 8.1$, $P \leq .01$), but there were no gender differences in race or achieved education level (Table 1). Female gender was associated with anxiety disorder in the lifetime and in the past month ($\chi^2_1 = 5.5$, $P = .019$, and $\chi^2_1 = 4.9$, $P = .027$, respectively), lifetime panic disorder ($\chi^2_2 = 7.2$, $P = .03$), and specific phobia in the past month ($\chi^2_1 = 4.7$, $P = .027$) (Table 2). Gender effects on baseline clinical characteristics as measured by the SADS, SAPS, BPRS, and DAS were examined. Female gender was associated with

Table 2. Baseline Comorbid Psychiatric Diagnoses by Gender

SCID-I/P Diagnosis	Women (n = 166), n (%)	Men (n = 93), n (%)	χ^{2a}	*P* Value[b]	*df*
Anxiety disorder, lifetime	24 (14.5)	5 (5.4)	5.5	**.019***	1
Anxiety disorder, past month	23 (13.9)	5 (5.4)	4.9	**.027***	1
PTSD, lifetime	25 (15.2)	6 (6.5)	4.8	.09	2
Panic disorder, lifetime	23 (13.9)	7 (7.5)	7.2	**.027***	2
Panic disorder, past month	21 (12.7)	5 (5.4)	3.8	.05	1
Specific phobia, lifetime	17 (10.2)	3 (3.2)	4.7	.10	2
Specific phobia, past month	17 (10.2)	3 (3.2)	4.7	**.031***	1

[a]Between-gender χ^2 tests of difference.
[b]Likelihood ratio χ^2 test.
*$P \leq .05$.
Abbreviations: PTSD = posttraumatic stress disorder, SCID-I/P = Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders-Patient Edition.

Table 3. End of Study Metabolic Measures Adjusted for Age, Gender, and Appropriate Interactions

	Gender			Age Group			Gender × Age Group[a]			Age Group × Treatment Group[b]		
Measure	*P* Value[c]	χ^2	*df*	*P* Value[c]	χ^2	*df*	*P* Value[c]	χ^2	*df*	*P* Value[c]	χ^2	*df*
BMI	.69	0.2	1	**<.0001**	18.9	1	…	…	…	.10	2.7	1
Glucose	.17	1.9	1	**.021**	5.3	1	.18	1.8	1	…	…	…
Total cholesterol	**.008**	**7.2**	1	.15	2.1	1	**.004**	8.4	1	…	…	…
HDL	**<.0001**	23.6	1	.07	3.3	1	.32	1.0	1	…	…	…
LDL	**.01**	6.5	1	.14	2.2	1	.14	2.2	1	…	…	…
Triglycerides	.34	0.9	1	.34	0.9	1	.94	0.1	1	…	…	…

[a]Final metabolic models include visit, treatment group, age group, gender, gender × age group.
[b]Final BMI model includes visit, treatment group, gender, treatment group × gender, age group, treatment group × age group.
[c]Generalized estimating equation analysis.
Abbreviations: BMI = body mass index, HDL = high-density lipoprotein, LDL = low-density lipoprotein.
Symbol: … = Data not shown.

probable or definite presence of hallucinations on the SADS ($\chi^2_1 = 7.8$, $P = .005$), as well as auditory ($\chi^2_1 = 4.8$, $P = .028$), somatic or tactile ($\chi^2_1 = 6.7$, $P < .01$), and olfactory ($\chi^2_1 = 11.9$, $P < .001$) hallucinations as measured by the SAPS.

Hallucinations were also associated with female gender on the BPRS ($t_{257} = -2.54$, $P = .012$). In all cases, the significant effect noted on the Breslow-Day test was caused by the low levels of hallucinations reported by men aged 60 or older. The presence of a fixed delusion with conviction was an inclusion requirement of the study. Delusion characteristics including disorganization was associated with female gender ($t_{257} = -2.10$, $P = .037$), while temporal pressure was associated with male gender ($t_{257} = 1.94$, $P = .053$) on the DAS.

There were no gender differences in baseline HDRS-17, HDRS psychotic or somatic anxiety subscale, CGI-S, or MMSE total scores, and both genders were equally randomized to either olanzapine plus sertraline or olanzapine plus placebo. There was no gender difference in the number of antidepressant trials, antipsychotic trials, combination of antidepressant and antipsychotic trials, or use of electroconvulsive therapy prior to entering the study.

Treatment Response

There was no difference in change in HDRS-17 scores by gender with regard to overall (overall type 3 $\chi^2_1 = 0.1$, $P = .73$) or visit by gender (overall type 3 $\chi^2_3 = 5.3$, $P = .15$) assessments. There was no difference in change in HDRS-17 scores in women by age group with regard to overall (overall type 3 $\chi^2_1 = 0.01$, $P = .93$) or by visit (overall type 3 $\chi^2_3 = 1.5$, $P = .70$) assessments. Using age groupings based on published gender analyses,[31,33,34,53] which differed from that used in STOP-PD, did not change the results (data not shown). Similarly, there were no significant interactions between treatment and age (overall type 3 $\chi^2_1 = 1.5$, $P = .22$) or gender (overall type 3 $\chi^2_1 = 1.0$, $P = .31$), indicating that the treatment effect on HDRS-17 was consistent across age groups and for both genders.

Treatment-Associated Change in BMI and Metabolic Measures

Compared to their assessments at baseline, subjects experienced a significant overall mean increase in BMI (kg/m^2) across all study visits ($\chi^2_3 = 96.1$, $P < .0001$). Compared to subjects aged 60 or older, subjects aged 59 or younger had a BMI 3.6 (0.8) units greater, with significant increase in BMI across visits ($\chi^2_1 = 18.9$, $P \leq .0001$). There was no gender difference in BMI overall or across visits or between treatment groups, and there was no gender-by-treatment interaction or time-by-treatment interaction with BMI. On average, across visits, younger subjects had significantly lower glucose than older subjects (mean = −7.3 mg/dL, SE = 3.3, $\chi^2_1 = 5.3$, $P = .021$); however, there were no significant differences in glucose as a function of an age by gender interaction ($P = .18$). There were significant gender differences in total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Overall, men had lower total cholesterol than women

(mean = −16.4 mg/dL, SE = 6.0, $\chi^2_1 = 7.2$, $P = .008$), with men in the younger age group having higher cholesterol (mean = 35.2 mg/dL, SE = 11.7, $\chi^2_1 = 8.4$, $P = .004$) than the other subjects: there was no difference in total cholesterol as a function of age group. There was a significant difference in total cholesterol ($P < .0001$), LDL ($P < .0001$), and triglycerides ($P = .01$) across visits, but it was not consistent, with increases at weeks 4 and 8, but a decrease at week 12. Male subjects had mean HDL and LDL levels that were −10.4 mg/dL (SE = 2.1, $\chi^2_1 = 23.6$, $P < .0001$) and −13.3 mg/dL (SE = 5.2, $\chi^2_1 = 6.5$, $P = .01$) lower than female subjects, respectively (Table 3). For glucose, total cholesterol, triglycerides, HDL cholesterol, and LDL cholesterol, there were no significant differences by treatment (data not shown). Results of the sensitivity analysis showed no relationship between missing data and treatment or gender, implying that any missing data were missing at random.

Hormone Replacement Therapy

Of 159 women with baseline data on hormone replacement therapy use, 16 (10.1%) received hormone replacement therapy. Because of the small number of women on hormone replacement therapy, there was not enough statistical power to analyze potential interactions between hormone replacement therapy status and BMI, change in HDRS-17 score, or other outcome measures.

DISCUSSION

To our knowledge, this analysis of the STOP-PD data is the largest study of gender differences in subjects with psychotic depression. The female gender prevalence (64.1%) found in the STOP-PD study is strikingly similar to that reported in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study (63.8%)[18] and other depression studies.[19] Women and men had a similar severity of illness entering the study as measured by the HDRS-17. Although men and women were of a similar age, women were more often divorced or widowed, but equally likely to have achieved the same level of education and to be currently employed, as men. This finding is similar to that reported in a study[19] of chronic major or double depression without psychotic features, even though the average age of females in that study was approximately 15 years younger than that in the STOP-PD. Our finding is in contrast to the mixed reports of gender differences in bipolar disorder studies in which females were equally[54] or more likely[55] to be married and had attained a similar[54] or lower education level than males,[55] but males were more often employed.[54,55] In comparison, females with schizophrenia are more likely to be married than males,[56,57] have either a higher[58] or a similar level of education,[56] and have a better work history than males.[56,57] In STOP-PD, there were no gender differences in enrollment setting status or race.

Epidemiologic studies have shown that females have a higher prevalence than males of comorbid depression and anxiety disorders.[59–64] Congruent with these findings and our hypothesis, in this study, women with psychotic depression were more likely than men to have comorbid anxiety disorders, including panic disorder and specific phobia. As previously reported from the STOP-PD study, women ≥ 60 years of age had fewer anxiety disorder diagnoses than women ≤ 59 years of age.[65] Some previous studies have reported female gender to be associated with a diagnosis of posttraumatic stress disorder,[66,67] while others have not.[64] In our sample, this association did not reach significance, most likely because of a smaller sample size than those in larger pooled or epidemiologic studies. Subjects with substance abuse/dependence were excluded from entry; thus, gender analyses were not available for comorbid substance use disorders, where gender differences have been previously reported in psychotic depression.[29]

One of the main novel findings of this analysis was that hallucinations were more common among women with psychotic depression than men and that this finding was not associated with age. Auditory hallucinations were most common, followed by visual, somatic or tactile, and olfactory hallucinations. Each of these types of hallucinations was more common in women than in men, except for visual hallucinations. To our knowledge, this is the first report of an association between female gender and hallucinations in unipolar psychotic depression. This finding is congruent with results from a study[22] in patients with bipolar disorder: in 155 subjects with psychotic mania, hallucinations were more common in females than in males. In that study, females with psychotic bipolar disorder more often had a lifetime history of depression than males, but gender differences in psychotic symptoms in the depressed phase have not yet been reported in the literature. Participants were excluded from the STOP-PD study if they had any other Axis I psychotic or mood disorder, obsessive-compulsive disorder, cognitive disorder, or substance abuse during the preceding 3 months. However, it is possible that hallucinations as part of comorbid personality disorders that were not evaluated in the STOP-PD study contributed to the gender effect, and this is a limitation of the study.

On the basis of the literature in nonpsychotic depression and psychotic disorders, we hypothesized that women ≤ 59 years of age with psychotic depression would have higher response and remission rates with olanzapine plus placebo or olanzapine plus sertraline than women ≥ 60 years of age but that younger women would experience more treatment-associated changes in BMI and metabolic side effects, such as elevated cholesterol and blood glucose. Contrary to our hypotheses, we were not able to demonstrate an effect of gender or age on treatment outcome, on treatment-associated changes in BMI, or on treatment-associated metabolic measures. However, these secondary analyses were not adequately powered to detect a small to moderate effect size. Additionally, weight prior to the baseline visit was not recorded; thus, it is possible that men or women lost weight prior to treatment, and weight gain, as measured in the study, may have represented restoration of premorbid weight. Similarly, because of the small number of women taking hormone replacement therapy (n = 16), there was

not enough power to analyze potential interactions between hormone replacement therapy status and BMI change or other outcome measures. We did not collect estrogen, follicle stimulating hormone, or luteinizing hormone data on study women, so we could not examine the potential effects of reproductive status on outcome measures. Another important limitation to the analysis is that only hormone replacement therapy status and not reproductive status or other factors that affect the measurement of serum lipids (eg, diet, smoking, physical activity, age, menopausal status,[68,69] and medication[70,71]) was recorded in this study.

This study in psychotic depression is the largest to investigate the impact of gender on sociodemographic and clinical characteristics and the first to investigate the impact of gender and age on treatment response and treatment-associated change in BMI. This analysis gives evidence of gender differences and similarities in sociodemographic and clinical characteristics in psychotic depression and compares them to those found in other affective and psychotic illnesses. Our findings that a greater percentage of women than men with psychotic depression have all types of hallucinations and delusions with disorganization suggest that women experience the disorder differently than men through varied symptomatology across the age spectrum. Our finding that women have higher cholesterol measures should be taken into consideration when monitoring for metabolic adverse effects of psychotropic medications. Larger studies are needed to confirm and extend the present analysis of gender differences in psychotic depression, with a focus on hypothesized differences in treatment outcomes and side effect burden among men and premenopausal, perimenopausal, and postmenopausal women.

Drug names: olanzapine (Zyprexa and others), sertraline (Zoloft and others).
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Potential conflicts of interest: **Dr Deligiannidis** has received grant/research support from National Institute of Mental Health (NIMH), Forest Research Institute, and University of Massachusetts Medical School. **Dr Rothschild** has consulted for Allergan, GlaxoSmithKline, Eli Lilly, Noven, Pfizer, Shire, and Sunovion; has received grant/research support from NIMH, Cyberonics, Takeda, and St Jude Medical; and has received royalties for the Rothschild Scale for Antidepressant Tachyphylaxis (RSAT); *Clinical Manual for the Diagnosis and Treatment of Psychotic Depression*, American Psychiatric Press, 2009; *Evidence-Based Guide to Antipsychotic Medications*, American Psychiatric Press, 2010; and *Evidence-Based Guide to Antidepressant Medications*, American Psychiatric Press, 2012. **Dr Flint** has received grant/research support from Lundbeck, Servier Canada, NIMH, and Canadian Institutes of Health Research (CIHR); and has received honoraria from Pfizer Canada. **Dr Whyte** has received grant/research support from NIMH, Lilly, Pfizer, and National Institute of Child Health and Human Development/National Center for Medical Rehabilitation Research. **Dr Mulsant** is an employee of Centre for Addiction and Mental Health, University of Toronto; has received grant/research support from NIMH, CIHR, Pfizer, and Bristol-Myers Squibb; and is a shareholder in General Electric. **Drs Barton** and **Meyers** and **Ms Kroll-Desrosiers** have no conflicts of interest to report.
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Additional information: The STOP-PD is located on a computer server at Weill Cornell Medical Center. As the STOP-PD study was funded by the NIMH, the database is accessible to the public. Once the STOP-PD limited access datasets are processed at NIMH, they will be posted on the following Web site: http://www.nimh.nih.gov/health/trials/datasets/nimh-procedures-for-requesting-data-sets.shtml.

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