The Association of Baseline Suicidality With Treatment Outcome in Psychotic Depression

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ABSTRACT

Objective: To examine the association between baseline suicidality and outcome of major depression in a randomized controlled trial of the pharmacotherapy of psychotic depression and to explore the interaction of suicidality, randomized treatment assignment, and depression outcome.

Methods: This study was a secondary analysis of data from 258 persons aged 18 years or older with *DSM-IV*–defined major depressive disorder with psychotic features who participated in a 12-week randomized controlled trial (RCT) comparing olanzapine plus sertraline with olanzapine plus placebo (the Study of the Pharmacotherapy of Psychotic Depression [STOP-PD], which ran from 2002 to 2007). The independent variable was baseline suicidality, defined by 4 groups (suicide attempt in the current episode, active suicidal ideation, passive suicidal ideation, and no suicidality). The outcome variables were change in 16-item Hamilton Depression Rating Scale ($HDRS_{16}$) total score (excluding the suicide item) over time and remission of psychotic depression over time.

Results: Suicidality groups did not significantly differ on baseline $HDRS_{16}$ total score. Baseline suicidality group was significantly associated with change in $HDRS_{16}$ score over time in the sample as a whole ($F_{3,1394}=8.17$; $P<.0001$), but was not significantly associated with probability of remission over time. Among participants assigned to olanzapine and placebo, persons with no suicidality had a significantly greater reduction in $HDRS_{16}$ total score compared to those with passive suicidal ideation (7.5-point difference in change scores between the 2 groups; 95% CI, 4.3–10.7 $t_{1394}=4.61$, $P<.0001$), active suicidal ideation (4.4 points; 95% CI, 1.4–7.4; $t_{1394}=2.85$, $P=.0176$), or suicide attempts (6.1 points; 95% CI, 2.8–9.4; $t_{1394}=3.66$, $P=.0015$). The 12-week change from baseline in $HDRS_{16}$ score for patients with no suicidality was not significantly different between the 2 treatment arms. However, the 12-week $HDRS_{16}$ improvement was significantly greater in the olanzapine plus sertraline arm, compared with the olanzapine plus placebo arm, for patients with suicide attempts (8.7-point difference in change scores between the 2 groups; 95% CI, 5.1–12.4; $t_{1394}=4.75$, $P<.0001$), active suicidal ideation (8.1 points; 95% CI, 4.5–11.7; $t_{1394}=4.38$, $P<.0001$), or passive suicidal ideation (5.7 points; 95% CI, 2.2–9.2; $t_{1394}=3.23$, $P=.0012$), respectively.

Conclusions: Baseline suicidality predicted worse acute treatment outcome of psychotic depression. However, participants with suicidality had a better outcome when treated with the combination of olanzapine and sertraline than when treated with olanzapine plus placebo.

Trial Registration: ClinicalTrials.gov identifier: NCT00056472

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Naturalistic studies suggest that baseline suicidality (characterized by suicidal ideation and/or suicide attempts) may be associated with worse short-term and long-term outcome of major depressive disorder.[1–3] However, few studies have specifically examined the effect of baseline suicidality on response to antidepressant treatment; in part, this is because many studies evaluating antidepressant pharmacotherapy specifically exclude patients with active suicidal ideation or recent suicide attempts. The results of open-label prospective studies that have examined this issue have been mixed, with some studies reporting that suicidality is associated with poorer response to antidepressant medication[4–8] and others finding no such association.[9,10] To our knowledge, only 1 randomized controlled trial (RCT)[11] has examined this issue: it found that baseline suicidality did not predict response to antidepressant pharmacotherapy overall or to specific antidepressants. The findings of this study are, however, limited by the fact that it was not a double-blind design and the predictor variable was limited to suicidal ideation in the 24-hour period prior to assessment.

The Study of the Pharmacotherapy of Psychotic Depression[12] (STOP-PD; ClinicalTrials.gov identifier: NCT00056472) provides a unique opportunity to further examine the relation between suicidality and treatment outcome of major depression. Unlike most RCTs of the pharmacologic treatment of major depression, STOP-PD allowed for the inclusion of persons with severe suicidal ideation and recent suicide attempts: 19% of participants had made 1 suicide attempt or more during the index episode of depression. Thus, participants in STOP-PD had a full range of suicidal intensity. Second, this RCT compared olanzapine and sertraline with olanzapine and placebo and therefore provides the opportunity to explore, under double-blind placebo-controlled conditions, whether those who have baseline suicidality have differential treatment response to combination treatment with olanzapine and sertraline compared with olanzapine and placebo.

The primary aim of this analysis is to examine whether baseline suicidality is associated with

Table 1. Questions 1–5 of the Scale for Suicide Ideation[a]

Based on the past week, including today:
1. Can you tell me about your desire to live, your wish to live *today*? Is it moderate to strong? Weak? Or none?
   0. Moderate to strong
   1. Weak
   2. None
2. Can you tell me about your wish to die? Is it moderate to strong? Weak? Or none?
   0. None
   1. Weak
   2. Moderate to strong
3. Would you say today that your reasons for living outweigh your reasons for dying?
   0. For living outweigh for dying
   1. About equal
   2. For dying outweigh for living
4. What is your current desire to make an active suicide attempt, to actively harm yourself, actively kill yourself? Is there no desire at all?
   0. None
   1. Weak
   2. Moderate to strong
5. Today do you have any passive suicidal feelings? For instance, would you, in fact, take precautions necessary to save your life? Would you take medicine to save your life? Would you drive safely to keep yourself alive?
   0. Would take precautions to save life
   1. Would leave life/death to chance (eg, carelessly crossing a busy street)
   2. Would avoid steps necessary to save or maintain life (eg, diabetic ceasing to take insulin)

[a]Reprinted with permission from Beck et al.[15]

treatment outcome of major depression with psychotic features. We hypothesized that suicidality at baseline would be associated with poorer depression treatment outcome. An exploratory aim was to investigate the interaction of baseline suicidality, randomized treatment assignment, and depression outcome.

METHODS

Sample and Study Design

This is a secondary analysis of STOP-PD data. The design, methods, and main findings have been reported elsewhere.[12] Briefly, STOP-PD was a 12-week 4-site RCT comparing olanzapine plus sertraline with olanzapine plus placebo in the treatment of non-bipolar major depressive disorder with psychotic features in persons aged 18 years or older (n = 117 aged 18–59 years and n = 142 aged 60 years or older) from 2002 to 2007. Initial target dosages of olanzapine plus sertraline/placebo were 15 mg/d and 150 mg/d, respectively, attained during the second week of treatment, as tolerated. If clinically indicated, olanzapine plus sertraline/placebo dosages could be increased to a maximum of 20 mg/d and 200 mg/d, respectively, beginning in week 3 of the trial. Among the exclusion criteria for the study were another Axis I mood disorder or psychotic disorder, *DSM-IV*–defined dementia preceding the index episode of depression, substance abuse or dependence within the preceding 3 months, neurologic disease that might affect neuromuscular function such as Parkinson's disease, and unstable physical illness, although many of the study participants had stable chronic physical problems. With use of procedures approved by local institutional review boards, written informed consent was obtained from all participants or their substitute decision-maker prior to the initiation of any research assessments or treatment.

Clinical Points

- Few studies have examined the association of baseline suicidality with response to antidepressant treatment in major depression; this issue has not previously been addressed in psychotic depression.
- In persons with psychotic depression treated with pharmacotherapy, baseline suicidality is associated with less improvement in depressive symptoms over time. Treatment with olanzapine plus sertraline, versus olanzapine plus placebo, attenuates this negative association.

The main outcome measures for these analyses are (1) the 17-item Hamilton Depression Rating Scale (HDRS)[13] total score modified to exclude the HDRS suicide item at each study visit (referred to as $HDRS_{16}$), and (2) remission of psychotic depression at each study visit. Remission was defined as a $HDRS_{17}$ total score of 10 or lower at 2 consecutive visits and the absence of delusions (a score of 1 on the Schedule for Affective Disorders and Schizophrenia [SADS][14]) at the second depression remission assessment. Study visits were conducted weekly for the first 6 weeks and every other week for the remainder of the trial.

Measurement of Suicidality

Suicidal ideation was assessed at baseline with the interviewer-administered Scale for Suicide Ideation (SSI),[15] a widely used, validated instrument assessing current intensity of suicidality with predictive validity for future completed suicide.[16,17] All participants completed the 5 screening questions of the SSI (Table 1), scored for the preceding week (including the day of assessment). Raters were trained to probe for details about any suicide item endorsed. Suicide attempts (defined as a self-injurious act with intent to die) during the current depressive episode were determined by the Structured Clinical Interview for *DSM-IV* (SCID).[18]

On the basis of the SSI and the SCID, participants were categorized into 1 of 4 mutually exclusive groups using the most severe category to which the subject belonged at baseline: suicide attempt during the current episode, active suicidal ideation, passive suicidal ideation (that included wishes of death), or no suicidal ideation. We chose to separate participants with active and passive suicidal ideation based on previous studies that identified qualitative differences between active and passive suicidal ideation.[19,20] The suicide attempt group consisted of participants who attempted suicide during the current depressive episode, as ascertained by the SCID. The active suicidal ideation group consisted of participants who scored 1 or 2 on question 4 of the SSI (Table 1). The passive suicidal ideation group consisted of participants who scored 1 or 2 on question 2 or 5 or scored 2 on question 1 or 3 of the SSI (Table 1). Finally, the nonsuicidal group included those participants who did not meet criteria for any of the other 3 suicidality groups.

Table 2. Comparison of Suicidality Groups on Selected Baseline Variables

Characteristic	Suicidality Group: Suicide Attempt (n = 48)	Active Suicidal Ideation (n = 44)	Passive Suicidal Ideation (n = 55)	No Suicidality (n = 111)	Test Statistic	*df*	*P*
Continuous, mean (SD)[a]							
Age, y	53.06 (18.90)	49.23 (16.16)	59.51 (16.98)	62.86 (16.52)	$F = 8.4$	3, 254	< .001
Duration of index episode, median (IQR), mo	4.5 (2.75–14.25)	5 (2–7)	6 (3–12)	5 (2–9)	$\chi^2 = 3.31$	3	.346
Age at onset of MDD, y	41.53 (22.10)	33.84 (17.82)	40.98 (23.12)	48.86 (19.78)	$F = 5.37$	3, 229	.001
No. of lifetime depressive episodes	2.06 (0.86)	2.05 (0.78)	2.22 (0.94)	2.07 (0.93)	$F = 0.44$	3, 254	.727
CIRS-G total score	4.83 (4.38)	3.26 (2.83)	4.78 (3.41)	5.82 (4.32)	$F = 4.51$	3, 252	.004
$HDRS_{16}$ total score	29.25 (4.81)	27.89 (4.54)	28.04 (5.74)	27.25 (4.41)	$F = 1.95$	3, 253	.123
MMSE total score	26.74 (2.68)	27.61 (2.81)	27.24 (3.27)	26.54 (3.16)	$F = 1.57$	3, 248	.197
Stroop color-word interference score[b]	26 (6.3)	30.14 (9.4)	25.22 (5.07)	26.49 (8.27)	$F = 3.65$	3, 229	.013
Categorical, n (%)							
Female	28 (58.3)	26 (59.1)	35 (63.6)	77 (69.4)	$\chi^2 = 2.52$	3	.472
Race					Fisher exact test	…	.526
White	38 (79.2)	37 (84.1)	49 (89.1)	93 (83.8)			
Black	7 (14.6)	3 (6.8)	5 (9.1)	14 (12.6)			
Asian	3 (6.2)	4 (9.1)	1 (1.8)	4 (3.6)			
Ethnicity					Fisher exact test	…	.013
Hispanic	11 (22.9)	7 (15.9)	2 (3.6)	10 (9.0)			
Non-Hispanic	37 (77.1)	37 (84.1)	53 (96.4)	101 (91.0)			
Treatment nonresponse during index episode[c]	20 (41.7)	13 (29.5)	24 (43.6)	46 (41.4)	$\chi^2 = 2.46$	3	.483
Inpatient	39 (81.2)	35 (79.5)	34 (61.8)	70 (63.1)	$\chi^2 = 8.81$	3	.032

[a]Unless otherwise indicated.
[b]Reported as T-scores.
[c]Defined using the Antidepressant Treatment History Form[28] (see Bingham et al[29]).
Abbreviations: CIRS-G = Cumulative Illness Rating Scale for Geriatrics, $HDRS_{16}$ = 16-item Hamilton Depression Rating Scale (ie, minus the suicide item), IQR = interquartile range, MMSE = Mini-Mental State Examination.
Symbol: … = not applicable.

Severity of suicidality was ranked in ordered categories, with the current suicide attempt group representing the highest intensity of suicidality, followed by the active suicidal ideation, passive suicidal ideation, and no suicidality groups.[21] This hierarchy was established based on a number of factors. First, there is evidence that history of suicide attempt(s) is a robust predictor of death by suicide.[17,22,23] Second, while there is a lack of consensus on precise terminology for suicidal thoughts and behavior, these 4 categories have been traditionally viewed in the literature as distinct but related stages of increasing suicidal intensity.[24] Finally, there is face validity in ranking severity of suicidality according to these 4 categories, as these descriptions are commonly used in clinical practice to determine the severity of suicidality and to formulate the management plan.[21]

Data Analysis

The outcome measurements were analyzed in a series of linear mixed-effects regression models for change in $HDRS_{16}$ scores and logistic mixed-effects regression models for remission, with suicidality categorical groups as the predictor variable. The mixed models had a patient-level random intercept and fixed effects for time, predictor, and treatment and for the following interactions: predictor × time, treatment × time, predictor × treatment, and predictor × treatment × time. In addition, each model included fixed effects for selected baseline variables that have been associated with depression treatment outcome in the literature, were measured in STOP-PD, and differed among the suicidality groups at $P < .1$ (see Table 2): the included covariates were age, ethnicity, inpatient status at study entry, age at depression onset, cumulative medical burden rated with the Cumulative Illness Rating Scale for Geriatrics,[25] and executive function measured with the color-word interference score from the Stroop task[26] converted to T-scores. The mixed-effects models were carried out using PRO MIXED and PROC GLIMMIX of SAS 9.3 (SAS Institute, Cary, North Carolina) and performed with 2-tailed α set at .05. Multiple comparisons to test suicidal group differences between treatment arms, 6 in total, were adjusted using the Holm stepdown procedure[27] to control the type I error rate.

RESULTS

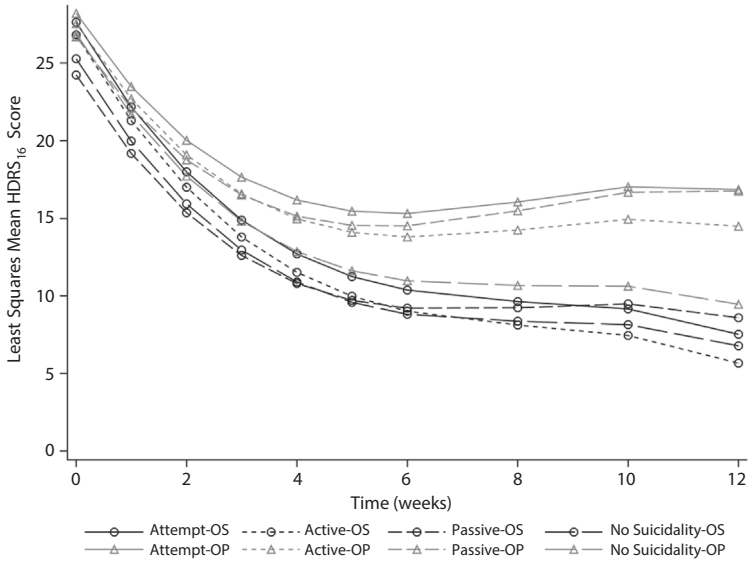
Suicidality Groups

Of the 259 participants enrolled in STOP-PD, 1 did not have complete baseline suicidality data. Therefore, analyses were based on 258 participants. Of these participants, 48 (18.6%) had 1 suicide attempt or more in the index episode, 44 (17.1%) had active suicidal ideation at baseline, 55 (21.3%) had passive suicidal ideation at baseline, and 111 (43.0%) had no suicidality. Of the participants who had a suicide attempt in the index episode, 77.1% had suicidal ideation at baseline assessment.

Association of Baseline Suicidality With $HDRS_{16}$ Outcome

Suicidality groups did not significantly differ on $HDRS_{16}$ total score at baseline (Table 2). Baseline suicidality group was significantly associated with change over time in $HDRS_{16}$ scores in the sample as a whole ($F_{3,\ 1,394} = 8.17$, $P < .0001$); suicidality was associated with worse outcome.

Figure 1. Change in Least Squares Mean $HDRS_{16}$ Scores in STOP-PD Participants According to Baseline Suicidality and Randomized Treatment Assignment



Abbreviations: Active = baseline active suicidal ideation, Attempt = suicide attempt in index episode, $HDRS_{16}$ = 16-item Hamilton Depression Rating Scale, No Suicidality = no index episode suicide attempt or baseline suicidal ideation, OP = treatment with olanzapine and placebo, OS = treatment with olanzapine and sertraline, Passive = baseline passive suicidal ideation, STOP-PD = Study of the Pharmacotherapy of Psychotic Depression.

There was a significant interaction between suicidality, randomized treatment assignment, and change in $HDRS_{16}$ scores over time ($F_{3,1394} = 5.83$, $P = .0006$). Specifically, among participants assigned to olanzapine plus placebo, persons with no suicidality had a significantly greater reduction in $HDRS_{16}$ scores than those in each of the 3 suicidality groups (Figure 1). In the olanzapine plus placebo arm, there were statistically significant differences in change in $HDRS_{16}$ scores over 12 weeks (ie, between baseline and termination visits) between (*a*) the no suicidality and passive suicidal ideation groups (7.5-point difference in change scores between the 2 groups; 95% CI, 4.3–10.7; $t_{1394} = 4.61$; $P < .0001$); (*b*) the no suicidality and active suicidal ideation groups (4.4 points; 95% CI, 1.4–7.4; $t_{1394} = 2.85$; $P = .0176$); and (*c*) the no suicidality and suicide attempt groups (6.1 points; 95% CI, 2.8–9.4; $t_{1394} = 3.66$; $P = .0015$). However, among participants assigned to olanzapine plus sertraline, persons with no suicidality did not significantly differ from persons with passive suicidal ideation, active suicidal ideation, or suicide attempts.

The 12-week change from baseline in $HDRS_{16}$ score for patients with no suicidality was not significantly different between the 2 treatment arms. However, the 12-week $HDRS_{16}$ improvement was significantly greater in the olanzapine plus sertraline arm, compared with the olanzapine plus placebo arm, for patients with suicide attempts (8.7-point difference in change scores between the 2 groups; 95% CI, 5.1–12.4; $t_{1394} = 4.75$; $P < .0001$), active suicidal ideation (8.1 points; 95% CI, 4.5–11.7; $t_{1394} = 4.38$; $P < .0001$), and passive suicidal ideation (5.7 points; 95% CI, 2.2–9.2; $t_{1394} = 3.23$; $P = .0012$). In other words, compared with olanzapine plus placebo, the combination of olanzapine plus sertraline was associated with significantly greater improvement in $HDRS_{16}$ scores in each of the 3 suicidality groups, but not in the group of patients with no suicidality (Figure 1).

Association of Baseline Suicidality With Remission

Baseline suicidality was not significantly associated with probability of remission over time ($F_{3,1384} = 2.52$; $P = .06$). There was no significant interaction between suicidality, treatment assignment, and probability of remission ($F_{3,1384} = 1.43$; $P = .23$) (Figure 2).

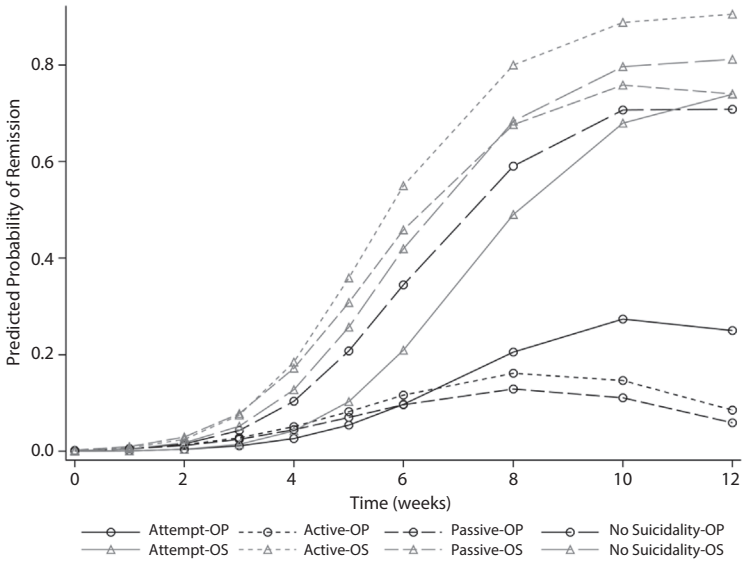
DISCUSSION

After covariates were controlled for, baseline suicidality was associated with less improvement in $HDRS_{16}$ scores over 12 weeks of pharmacologic treatment in persons with major depression with psychotic features. This finding is not explained by baseline depression severity. Furthermore, participants with suicidality, regardless of its severity, had greater improvement in $HDRS_{16}$ scores with the combination of sertraline and olanzapine compared with combined olanzapine and placebo. In contrast, the rate of improvement in $HDRS_{16}$ scores in participants with no suicidality did not significantly differ between the 2 treatment arms.

Our finding that suicidality predicts poorer response of major depression to antidepressant pharmacotherapy is in keeping with several,[4–8] but not all,[9–11] studies that investigated suicidality as a predictor of depression treatment outcome. However, it is difficult to compare the findings of these studies, given significant differences in methodologies and treatments. Of specific note, there has been little consistency between studies in the definition of suicidality as a predictor variable, with some studies focusing on suicide attempts or "suicidal behavior" over the lifetime,[7,8,10] others focusing on both suicide attempts and ideation in the index depressive episode,[4,5] and yet others examining suicidal ideation only.[9,11] Furthermore, with the exception of our study and 1 prior study,[11] all studies have based their findings on open-label treatment.

We did not find a direct correspondence between severity of suicidality and the magnitude of decline in $HDRS_{16}$ scores. For example, in the olanzapine-placebo group, the decline in $HDRS_{16}$ scores was similar across the suicide attempt and ideator groups. The most important distinction in predicting outcome was no suicidality versus any type of suicidality. Thus, even though a history of suicide attempt is a strong predictor of future attempts and completed suicide,[17,22,23,30] we did not find that suicide attempts and suicidal ideation predicted depression treatment outcome differentially. A

Figure 2. Predicted Probability of Remission in STOP-PD Participants According to Baseline Suicidality and Randomized Treatment Assignment



Abbreviations: Active = baseline active suicidal ideation, Attempt = suicide attempt in index episode, No Suicidality = no index episode suicide attempt or baseline suicidal ideation, OP = treatment with olanzapine and placebo, OS = treatment with olanzapine and sertraline, Passive = baseline passive suicidal ideation, STOP-PD = Study of the Pharmacotherapy of Psychotic Depression.

caveat to this finding, however, is that a suicide attempt could occur at any time during the index episode, whereas suicidal ideation had to occur within the week before starting the study: of the persons with a suicide attempt, 23% did not have suicidal ideation at baseline assessment. Thus, one may speculate that the temporal dissociation between suicide attempt and the baseline assessment "diluted" the impact of suicide attempt on treatment outcome.

An intriguing finding of this study is that the combination of olanzapine and sertraline was associated with significantly greater decrease in $HDRS_{16}$ scores in each of the 3 suicidality groups compared with olanzapine and placebo. In contrast, the decrease in $HDRS_{16}$ score for participants with no suicidality did not differ significantly between the 2 treatment arms. This study is the first to examine the effect of suicidality on depression outcome in persons treated with an antidepressant versus placebo. However, the concurrent administration of olanzapine potentially confounds interpretation of this finding. Several lines of evidence implicate abnormalities of the serotonergic system in the pathophysiology of suicidality.[31] For reasons that are currently unknown, it is possible that a serotonergic antidepressant such as sertraline moderates neurobiological abnormalities that may contribute to the association between suicidality and depression outcome. It's also possible that a third factor that we did not measure, such as anxiety[32] or personality traits like affective lability,[33] contributed to the association between suicidality and depression outcome and that sertraline led to improvement in that variable.

Our results show that the no suicidality group was more likely to include participants who were older or non-Hispanic and had a higher medical comorbidity burden, a later age at of onset of major depressive disorder, and a lower score on the Stroop task. These results are in keeping with a previously published analysis[21] of baseline correlates of suicidality in a subsample of STOP-PD participants. In that analysis, Schaffer et al[21] found that participants with no suicidality were more likely to be 60 years or older and less likely to be Hispanic compared with participants with suicidality. Our current results, based on the entire STOP-PD sample, are consistent with those findings, reflecting the association of older age and its correlates (medical burden, poorer executive function, and later age at major depressive disorder onset) with suicidality in our patient sample. In addition, older age was associated with a lower frequency of Hispanic participants in STOP-PD.

The main limitation of this study is that it is based on a secondary analysis of data. The study was not specifically designed to test aims and hypotheses pertaining to suicidality as a predictor of treatment outcome. In particular, the study may have had insufficient statistical power to adequately examine the association between suicidality and remission: there was a trend toward an association between these variables, but the relationship did not reach statistical significance ($F_{3,1384} = 2.52$; $P = .06$). In our analyses, we controlled for variables that were measured as part of STOP-PD that are relevant to treatment outcome of depression, but there are other pertinent variables (for example, personality traits) that were not measured and therefore were not considered in our analyses. In addition, we did not have data on lifetime suicide attempts independent of suicide attempts in the index episode. Therefore, our analyses are limited to suicidality associated with the index depressive episode. On the other hand, the goal and design of the parent study contributed to strengths compared with other studies that have examined suicidality as a predictor of outcome. In particular, by virtue of focusing on psychotic depression we were able to study a group of participants with a high frequency of suicide attempts or active suicidal ideation. Almost all industry-sponsored studies that compare an antidepressant with placebo in the treatment of depression exclude persons with active suicidal ideation or a recent suicide attempt. STOP-PD therefore provides a rare opportunity to explore the interaction of suicidality with antidepressant versus placebo in depression outcome.

In conclusion, we found that baseline suicidality predicts poorer response to treatment in adults with psychotic depression. Our finding pertaining to the interaction of suicidality with a serotonergic antidepressant medication and depression outcome raises questions for future research concerning the mechanism underlying suicidality and treatment outcome.

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Potential conflicts of interest: **Dr Flint** currently receives grant support from the US National Institutes of Health (NIH), the Canadian Institutes of Health Research, Brain Canada, the Ontario Brain Institute, and Lundbeck and within the past three years has received honoraria from Pfizer Canada. **Dr Meyers** receives research support from the National Institute of Mental Health (NIMH). **Dr Mulsant** currently receives research funding from Brain Canada, the CAMH Foundation, the Canadian Institutes of Health Research, and the US NIH; during the last 5 years, has also received research support from Bristol-Myers Squibb (medications for an NIH-funded clinical trial), Eli Lilly (medications for an NIH-funded clinical trial), and Pfizer (medications for an NIH-funded clinical trial); and directly owns stocks in General Electric (less than $5,000). **Dr Rothschild** receives grant or research support from Alkermes, AssureRx, Cyberonics, Janssen, NIMH, St Jude Medical, and Takeda; is a consultant to Eli Lilly, GlaxoSmithKline, Omnicare, Pfizer, and Sunovion; 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; *The Evidence-Based Guide to Antipsychotic Medications*, American Psychiatric Press, 2010; and *The Evidence-Based Guide to Antidepressant Medications*, American Psychiatric Press, 2012; and from Up-to-Date. **Dr Whyte** has received research support from NIMH, the National Institute of Child Health and Human Development (NICHD), and the Department of Defense (DOD) and through a Small Business Innovation Research (SBIR) grant from Fox Learning Systems/National Institute of Neurological Disorders and Stroke (NINDS). **Dr Szanto** has received research support from NIMH and the American Foundation of Suicide. **Drs Bingham** and **Banerjee** have no disclosures.

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Acknowledgment: The members of the STOP-PD Study Group are listed in the original publication of the study.[12]

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