Personality Disorders Predict Relapse After Remission From an Episode of Major Depressive Disorder: A 6-Year Prospective Study

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Objective: To examine prospectively the course of major depressive disorder (MDD) and to test for the moderating effects of personality disorder (PD) comorbidity on relapse after remission from an episode of MDD.

Method: Participants were 303 patients (196 women and 107 men) with current *DSM-IV*–diagnosed MDD at baseline enrollment in the Collaborative Longitudinal Personality Disorders Study. Major depressive disorder and Axis I psychiatric disorders were assessed with the Structured Clinical Interview for *DSM-IV*, and Axis II PDs were assessed with the Diagnostic Interview for *DSM-IV* Personality Disorders. The course of MDD was assessed with the Longitudinal Interval Follow-up Evaluation at 6 and 12 months and then yearly through 6 years. Survival analyses were used to analyze time to remission and time to relapse. The study was conducted from July 1996 to June 2005.

Results: Of 303 patients, 260 (86%) remitted from MDD; life table survival analyses revealed that patients with MDD who had PDs at baseline had significantly longer time to remission from MDD than patients without PDs. Among the 260 patients whose MDD remitted, 183 (70%) relapsed. Patients with MDD with PDs—specifically those with borderline and obsessive-compulsive PDs—at baseline had significantly shorter time to relapse than patients with MDD without PDs. Cox proportional hazards regression analyses revealed that the presence of PDs at baseline (hazard ratio = 1.5) and recurrent-type MDD (hazard ratio = 2.2), but not sex (hazard ratio = 1.03) or dysthymic disorder (hazard ratio = 0.97), significantly predicted time to relapse.

Conclusions: Personality disorders at baseline were robust predictors prospectively of accelerated relapse after remission from an episode of MDD. Personality disorders at baseline significantly moderated eventual time to relapse in MDD among patients who remitted from an episode of MDD, even when controlling for other potential negative prognostic predictors.

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Major depressive disorder (MDD) is a serious, prevalent, and refractory public health problem.[1] Major depressive disorder is currently the leading cause of disability among 15–44 year olds in the United States[2] and is 1 of the 10 leading sources for worldwide disease burden.[3] Longitudinal prospective studies have characterized MDD as a chronic illness with complex patterns of remission and relapse.[4,5] Similarly, the treatment literature characterizes MDD as a refractory illness, and high relapse rates remain pressing concerns for clinicians and researchers.[6]

Finding reliable predictors for specific aspects of the course of MDD—in particular, remission and relapse—has been difficult.[4,5] Solomon and colleagues,[5] for example, noted that none of their "many sociodemographic and clinical factors" influenced time to recovery and speculated that the "course of illness may be autonomous."[5(p1006)] Recurrent MDD (ie, MDD with repeated episodes versus a single MDD episode or number of prior episodes of MDD) is associated with slowed remissions and strongly predicts accelerated relapses.[7–10] Patients with MDD with coexisting dysthymic disorder ("double depression") appear to have a more chronic course than patients without dysthymic disorder.[11,12]

Personality disorders (PDs) represent a potential negative prognostic factor for MDD course. Reviews have concluded that many studies, but not all, suggest that PDs negatively influence the course of psychiatric disorders such as depression.[13,14] Critical reviews and meta-analyses of the prognostic significance of PDs for MDD treatment outcomes are similarly mixed, perhaps due partly to methodological shortcomings that characterize much of the literature.[15–17]

Several small short-term studies that utilized diagnostic interviews have found that PDs predict MDD relapse. Alnaes and Torgersen[18] reported that PDs (but not comorbid Axis I psychiatric disorders) significantly predicted relapse in a group of 88 patients with MDD re-evaluated at a 6-year follow-up. Ilardi and colleagues,[19] in a follow-up study of 50 inpatients with depression followed 33 to 84 months (mean = 50 months) after discharge, reported that PD psychopathology predicted significantly shorter time to relapse. Hart and colleagues,[20] in an 18-month follow-up study of 65 adults with remitted MDD, found that PDs predicted shorter time to relapse, whereas Axis I psychiatric comorbidity and various depression-specific variables (MDD recurrence, suicidality, treatment) lacked predictive significance. Cyranowski and colleagues,[21] in a 2-year maintenance treatment study of 125 women with recurrent depression,

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found that comorbid PDs predicted higher relapse rates and shorter time to MDD relapse. The major longitudinal naturalistic study of MDD (ie, National Institute of Mental Health Collaborative Depression Study [NIMH-CDS][22]) did not assess PDs by standardized diagnostic interview and thus focused on depression-specific variables as predictors, such as number of prior depression episodes and the presence of dysthymia.[4,5,8,11]

The Collaborative Longitudinal Personality Disorders Study (CLPS) was designed to provide comprehensive data on the course and outcome of patients with PDs, many of whom had MDD, and a comparison group of patients with current MDD but no PD.[23,24] This design allows a clear test of whether PDs represent a negative prognostic factor for MDD course. In our initial report of the short-term (2-year) course of remission from MDD, PDs emerged as significant predictors of slowed remission from MDD even when controlling for other putative negative prognostic predictors (sex, ethnicity, Axis I psychiatric disorder comorbidity, dysthymic disorder, recurrent MDD, age at onset of MDD, treatment during follow-up), none of which had a statistically significant effect.[25] The present study examined prospectively the 6-year course of MDD as a function of PD. We built on our initial 2-year study of remission from MDD[25] by extending to 6 years of prospective yearly follow-ups to allow us to address the primary aim of testing specifically for the effects of PD comorbidity on relapse after remission from an MDD episode.

METHOD

Participants

Participants for this study, conducted from July 1996 to June 2005, were drawn from the CLPS—a multisite, prospective, naturalistic longitudinal study. Recruitment aimed to obtain a diverse, clinically representative sample from inpatient and outpatient clinical programs affiliated with 4 recruitment sites (Brown, Columbia, Harvard, and Yale). The CLPS enrolled 668 participants aged 18 to 45 years with at least 1 of 4 PDs or with current MDD without any PD. Exclusion criteria included conditions that precluded a valid interview (eg, active psychosis, acute substance intoxication or withdrawal) or a history of schizophrenia or schizoaffective disorder. The CLPS focused on recruiting 4 specific PD diagnoses (schizotypal [STPD], borderline [BPD], avoidant [AVPD], and obsessive-compulsive [OCPD]), selected because of their prevalence and research base in clinical samples and to span the 3 *DSM-IV* clusters.[23] The CLPS also focused on recruiting a comparison group of patients with current MDD without any PDs. This MDD group was recruited to reflect a "pure" MDD group with regard to PD psychopathology and required that participants have greater than or equal to 2 criteria below the threshold for any specific PD and less than or equal to 15 total criteria across all PDs. For the PD study group assignments, since PDs frequently co-occur,[26] if more than 1 study PD was present, a primary PD study group was assigned following an a priori algorithm making use of multiple sources of clinical data (diagnostic interview data including severity, self-report ratings, and independent clinician ratings).[23] Detailed descriptions of the CLPS methods and characteristics of the overall study group have been reported.[23,24,27]

Of the 668 participants in the CLPS, 573 met criteria for a PD study group and 95 for the MDD (without PD) group. Overall, the mean number of lifetime Axis I disorders for participants was 3.5 (SD = 1.7; range, 0–9). Among the PD participants, the mean number of PD diagnoses was 2.4 (SD = 1.6) out of the possible *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*) total of 12 (10 formal diagnoses and 2 research diagnoses). Thus, participants with a PD were assigned a mean of 1.4 additional PD diagnoses, with a median of 1 additional PD. Specific co-occurrence patterns among the Axis I psychiatric and Axis II PD diagnoses in this study, reported previously,[24] echo the co-occurrence patients observed in other clinical samples,[26] thus increasing confidence in their generalizability.

The current report includes all 303 participants who met criteria for current MDD at baseline, regardless of PD status, and for whom at least 12 months of follow-up data were available. Mean age was 33.3 (SD = 8.1) years. Of the participants, 196 (65%) were female, and 107 (35%) were male; 214 (71%) were white, and 89 (29%) were minorities (50 [17%] were African American, 32 [11%] were Hispanic American, and 7 [2%] were "other"). At baseline assessment, mean age at MDD onset was 19.3 (SD = 9.2) years, and 90% (n = 273) reported previous episodes of MDD. The MDD without PD and MDD with PD groups did not differ significantly in the number of previous MDD episodes (mean = 5.0 [SD = 6.4] versus mean = 5.7 [SD = 6.6], $t_1 = -0.67$, N = 303, $P = .50$).

Procedures

All participants provided written informed consent following a full description of study procedures. The study protocol, including consent procedures, was approved by each collaborating site's institutional review board. Experienced research clinicians with master's or doctoral degrees in mental health disciplines interviewed participants. Interviewers underwent extensive standardized training to achieve reliability in the administration of the diagnostic measures. Interviewers were monitored and received ongoing supervision by the investigators at each site, as well as supervision across sites to maintain reliability and prevent temporal drift.

Assessment Protocol

At baseline, interviewers administered the Structured Clinical Interview for *DSM-IV* Axis I Disorders–Patient Version (SCID-I/P)[28] to assess Axis I psychiatric disorders and the Diagnostic Interview for *DSM-IV* Personality Disorders (DIPD-IV[29]) to assess all PDs (despite the primary focus on 4 PD diagnoses). Participants were reinterviewed at 6 and 12 months and then yearly thereafter for 6 years following baseline assessment. The course of MDD was assessed using the Longitudinal Interval Follow-up Evaluation (LIFE).[30] In order to maximize the reliability of the course of MDD, these follow-up interviews were not blind and were conducted by

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the same interviewer from the previous interval whenever possible.

Measures

Structured Clinical Interview for DSM-IV Axis I Disorders–Patient Version. The SCID-I/P,[28] a diagnostic interview to assess current and lifetime psychiatric disorders, was administered at baseline. κ coefficients for interrater reliability for psychiatric diagnoses ranged from 0.57 to 1.0; κ was 0.80 for MDD and 0.76 for dysthymic disorder.[31]

Diagnostic Interview for DSM-IV Personality Disorders. The DIPD-IV,[29] a semistructured diagnostic interview to assess *DSM-IV* Axis II PDs, was given at baseline. Each of the PD criteria is assessed with 1 or more questions rated on a 3-point scale (0 = not present; 1 = present but of uncertain clinical significance; 2 = present and clinically significant). The DIPD-IV requires that criteria be pervasive for at least 2 years and that they be characteristic of the person for most of his or her adult life in order to count toward a diagnosis. Interrater reliability (based on 84 pairs of raters independently rating 27 videotaped assessments) κ coefficients for PD diagnoses ranged from 0.58 to 1.0.[31] Test-retest reliability κ coefficients (based on 2 direct interviews of 52 participants performed 7 to 10 days apart with the second interview blind to the first interview) ranged from 0.69 (BPD) to 0.74 (OCPD).

Longitudinal Interval Follow-up Evaluation. The LIFE[30] is a semistructured interview rating system for assessing the longitudinal course of mental disorders. The LIFE has served as the primary measure for major longitudinal studies of depression[4] and has good-to-excellent reliability.[32] Interviewers were trained and certified by the LIFE developers and official training staff at the Brown site. The LIFE training staff provided ongoing training and consultation regarding the interview and ratings. These methods have maintained long-term reliability and prevented drift over time.[32]

As in the NIMH-CDS,[4,5,8,11] the LIFE was administered to measure the presence and severity of psychopathology on a weekly basis. The severity of psychopathology is quantified on weekly Psychiatric Status Ratings (PSRs) for each Axis I disorder present. For MDD, PSRs use the following 6-point scale: PSR = 1 signifies no symptoms; PSR = 2 corresponds to 1–2 symptoms of mild degree with no impairment in functioning; PSR = 3 indicates moderate symptoms but considerably less than full diagnostic criteria, with up to moderate functional impairment; PSR = 4 corresponds to marked symptoms but not meeting full diagnostic criteria, with major functional impairment; PSR = 5 corresponds to symptoms meeting full criteria for disorder; PSR = 6 corresponds to full criteria for disorder plus psychosis or extreme functional impairment.

Remission from MDD was defined as 8 consecutive weeks with PSR ratings no higher than 2 (reflecting minimal or no symptoms). Relapse was defined as 2 consecutive weeks with PSR ratings of 5 or greater. These definitions follow those used in the NIMH-CDS[8,11] and other major longitudinal studies of MDD[9] and parallel those used in longitudinal studies of other psychiatric disorders,[33,34] although alternative definitions have been proposed.[35]

Data Analyses

Life table survival methods[36] were used to analyze time to remission from MDD and time to relapse following the remission from an MDD episode. The Kaplan-Meier[37] method was used to estimate cumulative remission and relapse rates. Participants with MDD were divided into 2 groups, those with and without PDs at baseline, and this categorization was used to predict time to MDD remission and to relapse following remission from an episode of MDD. Analyses considered only 1 (ie, the first) relapse in instances with multiple relapses. Sex was included as a covariate in analyses but did not prove to have a significant effect. For the omnibus predictor analysis of time to relapse, we used Cox[38] proportional hazards regression tests for significance. Two-tailed tests with α of .05 were considered statistically significant.

RESULTS

MDD Remission by PD Comorbidity

Overall, 260 (86%) of the 303 participants had a remission from MDD during this 6-year study. The remission rate for the MDD group without PD comorbidity was 91%; MDD remission rates by PD comorbidity were as follows: 76% (for the STPD-MDD group), 81% (for the BPD-MDD group), 77% (for the AVPD-BPD group), and 90% (for the OCPD-MDD group). The "degree" of remission, as reflected by PSR scores during the first 8 weeks of remission, did not differ significantly between the MDD group (mean = 1.4, SD = 0.5) and the MDD-PD groups as follows: mean = 1.4 (SD = 0.5) for STPD-MDD, mean = 1.4 (SD = 0.5) for BPD-MDD, mean = 1.5 (SD = 0.5) for AVPD-MDD, and mean = 1.5 (SD = 0.5) for OCPD-MDD ($F_4 = 1.0$, $P = .41$).

Figure 1 shows the survival curves for time to remission for MDD as a function of PD comorbidity. The median time to remission for the MDD group without PD comorbidity was 18.7 weeks; median times to MDD remission across the PD comorbidity groups were as follows: 64.0 weeks (for STPD-MDD), 55.1 weeks (for BPD-MDD), 39.3 weeks (for AVPD-BPD), and 26.3 weeks (for OCPD-MDD). Participants with MDD who had coexisting PDs had a significantly longer time to remission from MDD than did patients with MDD without any PD ($\chi^2_1 = 14.946$, N = 303, $P < .0001$). Specific post hoc contrasts revealed that MDD participants assigned to primary PD study groups with STPD and with BPD, but not AVPD or OCPD, had significantly longer time to remission than MDD participants without any PD. The STPD-MDD study group had significantly longer time to remission than the MDD without PD group (Wilcoxon $\chi^2_1 = 17.45$, n = 125, $P < .0001$) as did the BPD-MDD study group (Wilcoxon $\chi^2_1 = 12.59$, n = 160, $P = .0004$).

MDD Relapse by PD Comorbidity

Among the 260 patients whose MDD remitted, 183 (70%) relapsed during this 6-year study. The relapse rate for the MDD group without PD comorbidity was 63%; MDD relapse rates by PD comorbidity were as follows: 72% (for the

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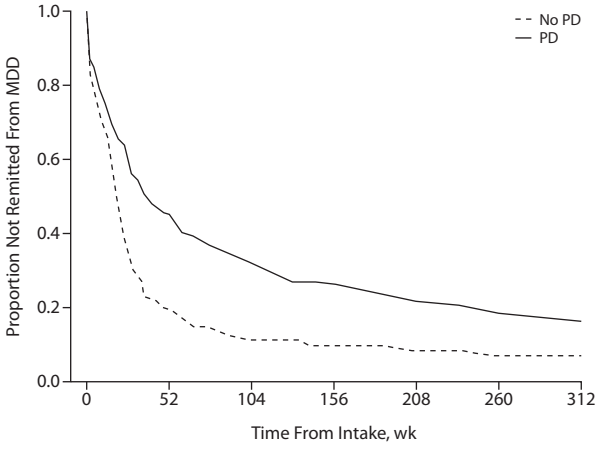
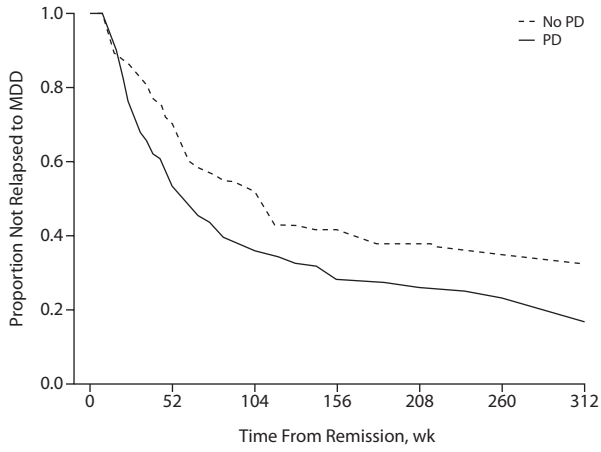
Figure 1. Time to Remission for MDD as a Function of PD Comorbidity (N = 303)[a]



[a]$\chi^2_1 = 14.946$, $P < .0001$.
Abbreviations: MDD = major depressive disorder, PD = personality disorder.

Figure 2. Time to MDD Relapse as a Function of PD Comorbidity Among Patients Who Had MDD Remission (n = 260)[a]



[a]$\chi^2_1 = 5.310$, $P = .0212$.
Abbreviations: MDD = major depressive disorder, PD = personality disorder.

STPD-MDD group), 72% (for the BPD-MDD group), 76% (for the AVPD-MDD group), and 77% (for the OCPD-MDD group).

Figure 2 shows the survival curves for time to relapse to MDD as a function of PD comorbidity for the 260 participants who remitted from an MDD episode. The median time to MDD relapse for the MDD group without PD comorbidity was 106.8 weeks; median times to MDD relapse across the PD comorbidity groups were as follows: 58.7 weeks (for STPD-MDD), 48.0 weeks (for BPD-MDD), 71.1 weeks (for AVPD-BPD), and 58.1 weeks (for OCPD-MDD). Participants with coexisting PDs at baseline had a significantly shorter time to MDD relapse than did participants without any PD ($\chi^2_1 = 5.310$, n = 260, $P = .02$). Specific post hoc contrasts revealed that MDD participants assigned to primary PD study groups with BPD and with OCPD, but not STPD or AVPD, had significantly shorter time to MDD relapse than MDD participants without any PD. The BPD-MDD study group had significantly shorter time to MDD relapse than the MDD without PD group (Wilcoxon $\chi^2_1 = 3.84$, n = 142, $P < .05$) as did the OCPD-MDD study group (Wilcoxon $\chi^2_1 = 4.54$, n = 127, $P < .05$).

Multivariate Prediction of Time to MDD Relapse

We performed an overall multivariate analysis (Cox proportion hazards regression) to predict time to MDD relapse after remission from an episode of MDD (n = 260). In this analysis, we considered the following variables: sex, presence or absence of PDs, presence or absence of dysthymic disorder, and whether the MDD was first episode ("single") or recurrent. Examination of the correlation matrix for the predictor variables revealed no correlations among predictor variables that exceeded 0.22, and colinearity diagnostics indicated no problems. The overall model was significant (likelihood ratio $\chi^2_4 = 19.18$ [N = 260], $P < .0007$). The presence of PDs ($\chi^2_1 = 6.13$, $P = .013$) and recurrent MDD ($\chi^2_1 = 7.55$, $P = .006$) each had statistically significant effects on time to MDD relapse; in contrast, sex ($\chi^2_1 = 0.03$, $P = .87$) and the presence of dysthymic disorder ($\chi^2_1 = 0.03$, $P = .87$) did not make significant contributions. In Cox survival regression analyses, hazard ratios are a standard measure of effect size. The following hazard ratios were observed: 1.5 for PDs, 2.2 for recurrent MDD, 0.97 for dysthymic disorder, and 1.03 for sex. Thus, for example, with all factors in the multivariate model being equal, patients with MDD with coexisting PDs relapsed 1.5 times more than patients with MDD without PDs (ie, they had a 50% greater chance of relapsing).

DISCUSSION

In this 6-year prospective study of the course of 303 participants with current MDD, we found that[1] coexistence of PDs predicted a significantly longer time to remission from MDD and,[2] among participants who achieved remission from an episode of MDD, those with coexisting PDs had a significantly shorter time to relapse than those without any PDs. Personality disorders emerged as robust predictors of accelerated relapse even when controlling for other potential negative prognostic predictors derived from the depression literature. Specifically, PDs significantly predicted relapse when considered jointly with whether the MDD was recurrent (also a significant predictor), whether there was coexisting dysthymic disorder, and sex (not significant predictors). These findings suggest that PDs might compromise naturalistically delivered treatments and undermine the stability of MDD remission.

Overall, the 6-year course of MDD in our study group is comparable to the 5-year course reported by the NIMH-CDS[39] on the basis of the same assessment methodology

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and analytic procedures, although our findings relied on the more recent *DSM-IV*. The NIMH-CDS did not include standardized diagnostic interview assessments for PDs, focusing instead on Axis I disorders. Our primary focus on the prediction of relapse following MDD remission considered 2 specific depression-illness variables (MDD recurrence and comorbid dysthymic disorder) found to predict chronic course of MDD in the NIMH-CDS.[11,39] A previous shorter-term follow-up study of 65 adults with remitted MDD also found that PDs predicted shorter time to relapse,[20] although various depression-specific variables such as MDD recurrence lacked predictive significance, perhaps because of the limited statistical power due to the small sample size.

Our study contributes to the growing empirical literature suggesting the negative prognostic significance of PDs on the course of psychiatric disorders. The study design, incorporating a relatively large sample size, followed prospectively for 6 years, with repeated assessments using standardized measures administered by certified and monitored research-clinicians, corrects many of the methodological limitations of earlier studies.[13] It appears that PDs have important effects on outcomes of some, but not other, psychiatric disorders.[40] Studies have reported mixed findings for PDs predicting remission from panic disorder,[34,41] not only that PDs have negative effects on remission from generalized anxiety and social phobia[34] but also that PDs are unrelated to both remission and relapse in eating disorders.[33] Our findings here suggest that PDs are robust moderators of accelerated relapse in MDD.

We investigated MDD relapse following "remission" from MDD, which we defined as 8 consecutive weeks with PSR ratings no higher than 2 (reflecting minimal or no symptoms). This definition follows the NIMH-CDS[5] and therefore allows direct comparison to that prospective longitudinal study. This definition, questioned by some researchers[35] but used by other research groups,[9] has some merits. Whereas the duration criterion (8 consecutive weeks) might seem brief, the requirement of 2 or fewer PSRs is strict. Supporting this view, we note that impressive analyses using the NIMH-CDS longitudinal data revealed that even "subthreshold" depression (ie, below threshold for MDD but failing "remission criteria") has a chronic course with high levels of impairment.[42,43]

We briefly note methodological limitations. The LIFE interviews conducted during this study were not blind to baseline status. Although some might suggest that this method holds the potential to introduce bias, the use of the same unblinded interviewer provides the advantage of repeated contacts with the subject, which may allow the interviewer to better gauge the symptom reports. This may increase the validity of the MDD ratings on the LIFE and diminish the error due to rater variance. A second limitation of naturalistic longitudinal studies of treatment-seeking or clinically ascertained subjects is the potential for treatment confounds. During the course of this study, the vast majority of participants received a variety of treatments, but these were neither prescribed nor provided as part of this study. We have described the treatment utilization patterns for these participants elsewhere and highlight here that we have reported prospective findings that patients with MDD without PDs utilize less treatment than patients with PDs.[44] Such findings suggest that naturalistic treatment use is driven by overall symptom severity, a typical finding in naturalistic studies.[45] We previously reported[25] that a treatment intensity composite variable entered into omnibus multiple regression analysis had no statistically significant effect on the course of MDD. We emphasize that this study was designed to examine the course of MDD in patients in real-world clinical settings. However, our study was not designed to address the important, but distinct, questions of the course of untreated MDD[46] or of experimentally controlled treatment outcome in MDD.[15,17]

Even though our study is not a controlled treatment study, data on the course of MDD offer important information for clinicians as well as suggest factors to include in future treatment studies. Clinically, our findings highlight the importance of assessing PDs, as they provide important prognostic information and may provide a useful signal regarding patients that may require additional therapeutic attention. The presence of a PD in patients experiencing a current MDD episode not only prospectively predicted slowed remission, but also prospectively significantly moderated eventual time to MDD relapse following the remission from that episode. Our findings highlighted the specific effects of BPD and OCPD in moderating MDD relapse. These 2 PDs have affective (in the case of BPD) and cognitive (in the case of OCPD) features related to depressed mood, and such features may suggest the possibility of more specific vulnerability markers for MDD than the PD diagnoses per se. Moreover, as we have reported elsewhere,[47] the presence of BPD prospectively predicts new onsets of MDD in patients without lifetime histories of MDD. These findings raise the possibility that effective treatments may need to address underlying PD psychopathology or psychosocial deficits associated with PDs, not just Axis I symptom relief, in order to maximize outcome.[48] We have reported elsewhere prospective analyses showing that reductions in PD psychopathology temporally precede reductions in MDD psychopathology[48,49] as well as improvements in psychosocial functioning.[49]

Our clinical suggestion that effective treatments of MDD should address associated personality psychopathology and psychosocial deficits in addition to symptom relief appears potentially consistent with the more general maintenance treatment literature. The increasing emphasis by clinicians on longer-term or "maintenance" pharmacotherapy does not appear to have influenced the high rates of relapses and recurrences in MDD.[9] Kennedy and colleagues[9] note that their long-term MDD recurrence patterns in a recent cohort (ie, during the "maintenance era" of MDD treatment) do not differ from their earlier cohort long-term findings in the Cambridge follow-up study. Although reviews of longer-term treatment studies generally conclude that maintenance antidepressant treatments reduce risk of MDD relapse relative to

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placebo,[50] high relapse rates remain a concern.[51,52] Emerging evidence from RCTs suggest psychological treatments such as interpersonal psychotherapy as possible alternatives to medication for preventing MDD relapse.[53,54] Maintenance interpersonal psychotherapy for recurrent MDD was associated with improvements in PD pathology over 2 years.[21] Moreover, cognitive therapy appears to have superior and specific effects on preventing relapse.[55] For example, treatment studies have found that cognitive therapy is superior to antidepressant medication for preventing relapse in moderate-to-severe MDD cases[56] and especially in patients with residual[57] and recurrent forms of MDD.[58] These benefits are sustained after treatment completion on the basis of 4.5-year follow-ups.[57] Bockting and colleagues[58] reported that the strength of the protective effect of cognitive therapy in preventing MDD relapse intensified in those patients with more than 5 prior MDD episodes. In the present study, we found support for both prior MDD episodes and presence of PD as significant moderators of MDD relapse. Perhaps some of the positive relapse prevention findings for cognitive therapy reflect the focus on addressing cognitive features along with improving coping and psychosocial functioning rather than just symptom relief. Future research should test the potential moderating effects of PD on such psychosocial interventions for MDD.

In summary, we found that PDs predict prospectively and robustly a pattern of slowed remission from MDD, and patients who remitted from MDD who had coexisting PDs had a significantly shorter time to relapse than those without any PD. Future research should attempt to delineate dynamic factors that might further influence the timing of relapses in MDD such as more proximal factors (eg, life events) and associated changes or fluctuations in psychosocial functioning or PD psychopathology.[40,48,59]

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