

Missed Diagnosis of Psychotic Depression at 4 Academic Medical Centers

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Background: Major depressive disorder with psychotic features (psychotic depression), though occurring relatively frequently in the general population, is a commonly missed psychiatric diagnosis.

Objective: To ascertain accuracy of diagnosis of psychotic depression among inpatients at 4 academic medical centers and explore whether presenting symptoms, treatment setting, and physician's level of training affect the accuracy of diagnosis.

Method: The medical records of 65 patients who met DSM-IV criteria for psychotic depression following systematic assessment were analyzed to ascertain the concordance between chart diagnoses and research diagnoses arrived at using the Structured Clinical Interview for DSM-IV. The patients were participants in the National Institute of Mental Health Study of Pharmacotherapy of Psychotic Depression, conducted from December 28, 2002, through June 18, 2004, at 4 academic medical centers. For each patient's hospital visit, separate standardized data forms were completed on the basis of each physician's assessment of the patient prior to screening for the study. Hospital records from the emergency room and from admission to psychiatric units were reviewed. Among these 65 patients, 130 chart diagnoses had been made.

Results: Psychotic depression had not been diagnosed prior to research assessments for 27% of the 130 diagnoses in our sample. The 3 most common diagnoses assigned to patients meeting research criteria for psychotic depression were major depressive disorder without psychotic features, depression not otherwise specified, and mood disorder not otherwise specified. Failure to identify psychotic depression was more likely when symptoms of depressed mood, hallucinations, or delusions were not noted in the medical record (all $p < .005$). The accuracy of diagnoses was greater on inpatient units than in emergency rooms ($\chi^2 = 7.64$, $p < .01$).

Conclusion: The diagnosis of psychotic depression is frequently missed in emergency room and inpatient settings. The findings of this study

are sobering given the serious morbidity and mortality of psychotic depression and the implications for treatment if an inaccurate diagnosis is made.

Trial Registration: clinicaltrials.gov
Identifier: NCT00056472

(*J Clin Psychiatry* 2008;69:1293–1296)

Received Sept. 25, 2007; accepted Nov. 16, 2007. From the Department of Psychiatry, University of Massachusetts Medical School, and UMass Memorial Healthcare, Worcester (Drs. Rothschild and Winer and Ms. Fratoni); the Department of Psychiatry, University of Toronto (Drs. Flint and Mulsant and Ms. Kasapinovic); the University Health Network, Toronto; the Geriatric Program and Research Institute, Toronto Rehabilitation Institute; and the Toronto General Research Institute (Dr. Flint and Ms. Kasapinovic); and the Centre for Addiction and Mental Health, Toronto (Dr. Mulsant), Ontario, Canada; the Department of Psychiatry, University of Pittsburgh School of Medicine, and Western Psychiatric Institute and Clinic, Pittsburgh, Pa. (Drs. Mulsant and Whyte); and the Department of Psychiatry, Weill Medical College of Cornell University, New York, N.Y., and New York Presbyterian Hospital–Westchester, White Plains (Drs. Heo and Meyers and Ms. Gabriele).

Supported by U.S. Public Health Service grants MH62446, MH62518, MH62565, MH62624, MH67710, UL1 RR000056, and MO1 RR024153 from the National Institute of Mental Health. Eli Lilly and Company and Pfizer Inc provided study medication free of charge.

Presented as a poster at the 158th annual meeting of the American Psychiatric Association; May 21–26, 2005; Atlanta, Ga.

Acknowledgment and financial disclosure appear at the end of the article.

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Major depressive disorder with psychotic features (psychotic depression) (MD-Psy), a disorder with considerable morbidity and mortality,^{1,2} is more common than is generally realized and is encountered frequently in clinical practice.^{3–5} Although studies done in both inpatient and outpatient settings have estimated that 16% to 54% of depressed adults are psychotic,⁶ MD-Psy is often not diagnosed accurately because the psychosis may be subtle, intermittent, or concealed, leading to a misdiagnosis of nonpsychotic depression.⁷

The American Psychiatric Association's practice guidelines⁸ for the treatment of MD-Psy recommend either the combination of an antidepressant and an antipsychotic or the use of electroconvulsive therapy. Yet, in order to effectively treat a patient with MD-Psy, a correct diagnosis must be made. Improperly diagnosing a patient as having a psychotic disorder such as schizophrenia or failing to recognize psychotic features of a major depressive episode will defer the use of effective treatment modalities. Recent data from the National Institute of Mental Health (NIMH) Study of Pharmacotherapy of Psychotic Depression (STOP-PD)⁹ suggest that suboptimal treatment of MD-Psy may be happening at an alarming rate.¹⁰ By delaying the start of effective therapeutics, morbidity and mortality, as well as health care costs, may be increased.

The purpose of the present study was to ascertain the accuracy of the diagnosis of MD-Psy among inpatients at 4 academic medical centers and to explore whether the symptoms with which each patient presents, the setting of the patient's presentation for treatment, and the level of training of the physician affect the accuracy of diagnosis and, furthermore, whether these patterns differ in younger adults with MD-Psy as compared to older adults with MD-Psy.

METHOD

Of the first 103 subjects randomly assigned in the NIMH STOP-PD study,⁹ conducted from December 28, 2002, through June 18, 2004, 66 subjects recruited through inpatient settings were included in the present study (the 37 outpatients were not included). This study focused on inpatients to facilitate the location of previous diagnoses. Written informed consent was obtained from all participants (or substitute decision makers, when applicable) using procedures approved by local institutional review boards prior to the initiation of any research assessments. All participants were diagnosed as suffering from MD-Psy after assessment with the Structured Clinical Interview for DSM-IV (SCID).¹¹ The diagnostic process in the STOP-PD study was more rigorous than just a SCID interview, as the diagnosis was arrived at by a meticulous process that included a review by the principal investigator of a narrative of the patient's psychotic symptoms, a score of 3 or higher on the delusion item of the Schedule for Affective Disorders and Schizophrenia,¹² and a score of 2 or higher on at least 1 of the conviction items of the Delusion Assessment Scale.¹³

To assess the concordance between the STOP-PD diagnoses and the clinical diagnoses assigned prior to recruitment into the study, patient charts were reviewed by research assistants at each of 4 sites, and initial clinical diagnosis notes that were completed by physicians who had seen the patients on the units or in the emergency

rooms prior to study enrollment were extracted. Collected information included level of training of the physician, patient location (emergency room or inpatient unit), presenting symptoms of the patient, and medical and psychiatric clinical diagnoses the physician made. If the subject had been seen by both a resident and an attending psychiatrist, both physicians' diagnoses were collected. In addition to chart review, data collected during the baseline visit of the STOP-PD study⁹ were included in the analysis.

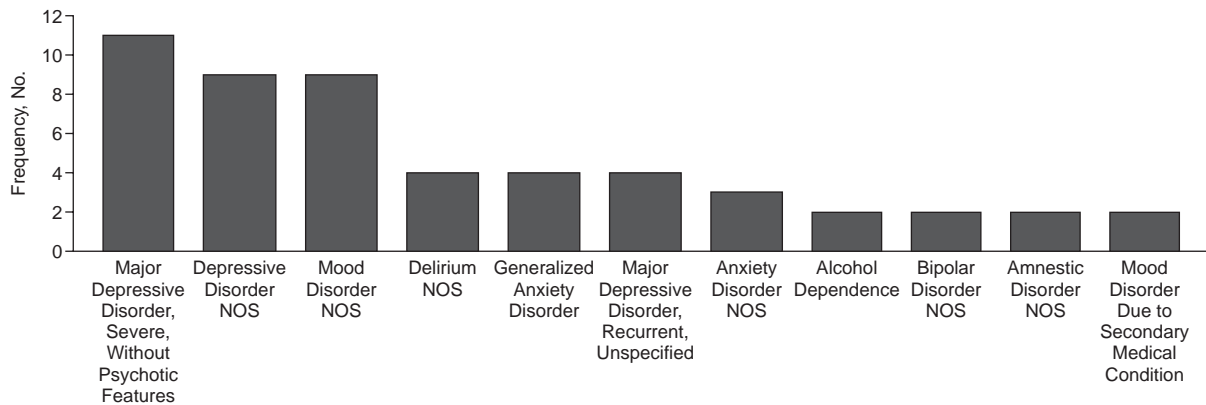
Of these subjects, 66 patients had been recruited from an inpatient setting, all but 1 with identifiable clinical diagnoses as found by the raters. Data from these 65 patients included clinical diagnoses, recorded symptoms, and age group (young or old). Among these 65 patients, 130 clinical diagnoses were made by physicians, ranging from 1 to 3 diagnoses per patient. Younger patients were defined as those between the ages of 18 and 59 years, and older patients were those over the age of 60 years.

Clinical diagnostic accuracy was coded as "correct," "rule out," or "incorrect" on the basis of information from physicians' notes. A correct clinical diagnosis included a diagnosis of MD-Psy or a primary diagnosis of MD-Psy within a differential diagnosis. A rule-out clinical diagnosis was specifically stated as "rule out" in the physician's note. A missed clinical diagnosis was the absence of any mention of MD-Psy in the physician's note. Interrater reliability was demonstrated as follows for the process of coding clinical diagnoses: raters at each of the 4 sites classified clinical diagnoses in 2 charts (1 from an emergency room and 1 from an inpatient unit) from each of the other 3 sites. The weighted κ coefficient was 0.90. Chi-square analyses were based on the total number of clinical diagnoses.

RESULTS

Eighty-five (65%) of the possible 130 clinical diagnoses were accurate, 10 (8%) indicated MD-Psy as a rule-out, and 35 (27%) failed to consider MD-Psy. The rate of missed diagnoses of MD-Psy in the emergency room setting (22/56, 39%) was significantly higher than the rate of missed diagnoses on the inpatient units (13/74, 18%) ($\chi^2 = 7.64$, $p < .01$). The rate of missed diagnoses of MD-Psy was significantly higher among attending psychiatrists (31/90, 34%) than among psychiatry residents (4/40, 10%) ($\chi^2 = 8.61$, $p < .005$). There was no statistically significant difference in the rate of missed diagnosis in younger patients (< 60 years of age) compared with older patients (≥ 60 years of age).

The 3 most common misdiagnoses of MD-Psy were major depressive disorder without psychotic features, depression not otherwise specified (NOS), and mood disorder NOS (Figure 1). Missing the diagnosis of MD-Psy was more likely to occur if the psychiatrist failed to note

Figure 1. Most Common Diagnoses Given When Diagnosis of Psychotic Depression Was Missed^a

^aSince some patients received more than 1 misdiagnosis, the figure shows 52 missed diagnoses. Abbreviation: NOS = not otherwise specified.

in the medical record the presence of depressed mood ($\chi^2 = 11.48$, $p < .005$), delusions ($\chi^2 = 19.48$, $p < .005$), or hallucinations ($\chi^2 = 11.69$, $p < .005$).

DISCUSSION

The results of this study indicate that 27% of 130 diagnoses among a well-characterized sample of patients with a research diagnosis of MD-Psy were initially incorrectly diagnosed at 4 academic medical centers. It is likely that the missed diagnosis rate observed in this study is a conservative estimate of the rate in the general clinical population, as patients with comorbid conditions such as a history of substance abuse in the past 3 months or unstable medical conditions were excluded.

MD-Psy was most commonly misdiagnosed as either major depressive disorder without psychotic features, depression NOS, or mood disorder NOS. It is quite striking that none of the patients with missed diagnoses were considered to have a psychotic disorder. This finding suggests that the physicians are missing the psychosis rather than the mood disorder. In many cases, it may be that the physician does not miss the symptom (e.g., guilt, poverty, persecution) but does not recognize that the symptom is a delusion. In particular, the distinction between delusional and nondelusional guilt is frequently difficult. Guilt is a common symptom of depression, and although the guilt may be beyond what is typically expected in depression, the point at which guilt “crosses the line” and becomes delusional is often not clear. This difficulty suggests that better training of physicians is needed to assess and decide when symptoms are delusional, as well as the development of more precise guidelines in DSM-V for making this distinction. A recent analysis¹⁰ in an overlapping sample of patients indicating a low use of antipsychotic medication in patients with MD-Psy in the community is consistent

with the low detection of psychotic features seen in this analysis.

If the psychiatrist noted the presence of depressed mood, delusions, or hallucinations, it increased the likelihood of an accurate clinical diagnosis. Patient age was not a factor in the accuracy of diagnosis.

There were significant differences in the accuracy of diagnosis of MD-Psy based on the setting of the patient interview. The greater accuracy of correctly diagnosing MD-Psy on the inpatient units ($p < .01$) when compared to the emergency room is most likely due to more brief interactions between the patient and clinicians in the emergency room setting.

Psychiatry residents made more accurate diagnoses than attending psychiatrists. The greater accuracy of diagnosis in the smaller subset of subjects seen by residents than attending psychiatrists may result from the fact that the residents were more likely to have heard a lecture from a study physician on the importance of diagnosing MD-Psy than the attending psychiatrists at these 4 medical centers.

Our observations are consistent with a previous study¹⁴ of first-admission psychotic patients in which considerable differences between research and clinical diagnoses were observed in patients with mood disorders and schizophrenia. In future studies, longitudinal follow-up will be critical to ascertain the predictive validity of initial research and clinical diagnoses.¹⁴ Furthermore, the inclusion of minorities will be important as some studies have suggested that African Americans are significantly more likely than Caucasians to be diagnosed with schizophrenia and less likely to be diagnosed with MD-Psy.¹⁵

The findings of this study are sobering given the serious morbidity and mortality of MD-Psy and the implications for treatment if an inaccurate diagnosis is made. As the process for DSM-V is beginning, it will be important to revisit the issue of whether MD-Psy should

be a separate illness in DSM-V, as was recommended (but rejected) for DSM-IV,^{1,16} rather than a specifier of MDD, a position where it can more easily be overlooked. The hope would be that if MD-Psy were a separate illness in DSM-V, it would result in greater awareness and more accurate diagnosis among practitioners.

Acknowledgment: The authors thank Catherine Peasley-Miklus, Ph.D., for her consultation and comments on this study. Dr. Peasley-Miklus is affiliated with the Department of Psychiatry, Weill Medical College of Cornell University, New York, N.Y., and New York Presbyterian Hospital-Westchester, White Plains, and has no competing interests relative to the subject matter of this article.

Financial disclosure: Dr. Rothschild is a consultant for Forest, Eli Lilly, Pfizer, and GlaxoSmithKline; has received research funds or honoraria from Bristol-Myers Squibb, Eli Lilly, Forest, Cephalon, Wyeth, Novartis, and Pfizer; and has served on speakers or advisory boards for Eli Lilly, Forest, and Bristol-Myers Squibb. Dr. Flint has received research funds or honoraria from Pfizer Canada, Janssen-Ortho, and Lundbeck Canada and has served on speakers or advisory boards for Janssen and Pfizer. Dr. Mulsant has received research support or honoraria from AstraZeneca, Bristol-Myers Squibb, Corcept Therapeutics, Eisai, Eli Lilly, Forest, GlaxoSmithKline, Janssen-Ortho, Lundbeck, the National Institutes of Health, and Pfizer; has been a consultant for AstraZeneca, Bristol-Myers Squibb, Eisai, Eli Lilly, Forest, Fox Learning System, GlaxoSmithKline, Janssen, Lundbeck, and Pfizer; has served on speakers bureaus for Eisai, Forest, GlaxoSmithKline, Janssen, Lundbeck, and Pfizer; and currently owns stocks (less than \$10,000) in Akzo-Nobel, Alkermes, AstraZeneca, Biogen Idec, Celsion, Elan, Eli Lilly, Forest, General Electric, Orchestra Therapeutics, and Pfizer. Dr. Whyte has received grant/research support from Forest, Ortho-McNeil, and NIMH and has received research supplies from Pfizer. Dr. Meyers has received research funds or honoraria from and has served on the speakers or advisory board for Forest during the past 12 months, and he has served as a consultant for Cyberonics and Forest. Drs. Winer and Heo and Mss. Fratoni, Gabriele, and Kasapinovic have no competing interests relative to the subject matter of this article.

REFERENCES

- Schatzberg AF, Rothschild AJ. Psychotic (delusional) major depression: should it be included as a distinct syndrome in DSM-IV?
- Am J Psychiatry 1992;149:733–745
- Vythilingam M, Chen J, Bremner JD, et al. Psychotic depression and mortality. Am J Psychiatry 2003;160:574–576
- Coryell W, Pfohl B, Zimmerman M. The clinical and neuroendocrine features of psychotic depression. J Nerv Ment Dis 1984;172:521–528
- Johnson J, Horwath E, Weissman MM. The validity of major depression with psychotic features based on a community sample. Arch Gen Psychiatry 1991;48:1075–1081
- Ohayon MM, Schatzberg AF. Prevalence of depressive episodes with psychotic features in the general population. Am J Psychiatry 2002;159:1855–1861
- Rothschild AJ, Mulsant BH, Meyers BS, et al. Challenges in differentiating and diagnosing psychotic depression. Psychiatr Ann 2006;36:40–46
- Rothschild AJ, Schatzberg AF. Psychotic depression: a newly recognized subtype. Clin Neurosci 1993;1:75–80
- American Psychiatric Association. Practice Guideline for the Treatment of Patients With Major Depressive Disorder [revision]. Am J Psychiatry 2000;157(suppl 4):1–45
- Flint AJ, Schaffer A, Meyers BS, et al, for the STOP-PD study group. Research assessment of patients with psychotic depression: the STOP-PD approach. Psychiatr Ann 2006;36:48–56
- Andrescu C, Mulsant BH, Peasley-Micklus C, et al, for the STOP-PD Study Group. Persisting low use of antipsychotics in the treatment of major depressive disorder with psychotic features. J Clin Psychiatry 2007;68:194–200
- Spitzer RL, Williams JBW, Gibbon M, et al. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID). Washington, DC: American Psychiatric Press; 1995
- Spitzer RL, Endicott J. Schedule for Affective Disorders and Schizophrenia-Lifetime Version (SADS-L). New York, NY: Biometrics Research, New York State Psychiatric Institute; 1979
- Meyers BS, English J, Gabriele M, et al, for the STOP-PD Study Group. A delusion assessment scale for psychotic major depression: reliability, validity, and utility. Biol Psychiatry 2006;60:1336–1342
- Fennig S, Craig TJ, Tanenberg-Karant M, et al. Comparison of facility and research diagnoses in first-admission psychotic patients. Am J Psychiatry 1994;151:1423–1429
- Strakowski SM, Flaum M, Amador X, et al. Racial differences in the diagnosis of psychosis. Schizophr Res 1996;21:117–124
- Schatzberg AF, Rothschild AJ. Psychotic (delusional) major depression: should it be included as a distinct syndrome in DSM-IV? In: Widiger TA, Frances AJ, Pincus HA, et al, eds. DSM-IV Source Book. Vol. 2. Washington, DC: American Psychiatric Press; 1996:127–180