medications, particularly the newer antidepressants, are now routinely used, even in deployed environments, as long as they do not require blood-level monitoring and have wide safety margins.

We agree with Dr. George Brown that service use does not equate with treatment need. The Epidemiologic Catchment Area Survey (5) and the National Comorbidity Survey (6) have shown that in the general population only 25%–30% of people with diagnosable mental disorders receive professional help. This figure is probably lower in the military, given the stigma and the predominantly male population. Additional research is needed to understand the reasons for attrition related to mental disorders in the military and to design prevention and intervention strategies that will reduce the barriers to care for patients, encourage earlier treatment, and reduce the occupational impact of these disorders.

Finally, research on veterans' health issues has been widely published and accepted, even though the population is highly selected and the health care system is unique. Just as we have learned from veterans about trauma, health, and aging, we believe the military offers a rich and largely untapped environment for achieving new insights into the epidemiology of mental disorders and their impact on occupational functioning in younger adults.

The views expressed are those of the authors and do not reflect the official position of the Department of Defense or the Department of the Army.

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Suicide and Major Depression

TO THE EDITOR: I wish to offer some comments on the article by Maria A. Oquendo, M.D., et al. (1). The topic of their study is important—how to reduce the occurrence of suicidal acts in people suffering from major depression. However, the present study contains some flaws in methods and logic that deserve comment.

In this naturalistic, prospective study, the authors wanted to demonstrate an association between antidepressant treatment and reduced acts of suicide. They did not find one and concluded that the reason was inadequate doses of antidepressant medication. However, their article did not support this conclusion. Their Discussion section stated, "We were unable to demonstrate that pharmacotherapy of major depression protected patients against suicide attempts," and then went on to note that "nine (43%) of the 21 follow-up suicide attempts occurred while patients were receiving adequate treatment" (p. 1748). This is indeed the authors' important finding. The problems with this article are in the first sentence of the discussion: "Relapse of recurrence of major depression increased the risk of suicide attempt during the 2 years after discharge from the hospital, *underlining the importance of optimal maintenance antidepressant treatment as a suicide prevention strategy* [italics added]" (p. 1748). But this association is precisely what their article does *not* show.

We know that the authors believe that there is a significant association here, as witnessed by their ample citations of European studies to support it. But their own study does not support it, and the authors think they know why—inadequate antidepressant dosing of the subjects during the study period. But even this case is not made convincingly. In their Method section, they asserted (without apparent reference) minimum adequate daily doses for 25 antidepressants. They did not state their basis for assigning these standards, by which they then measured adequacy of treatment. I do not disagree with the doses themselves (except for the authors' recommendation of 400 mg/day of trazodone) but only with their treating these "guidelines" as if they were universally accepted and clinically meaningful. The act of using something as a premise that is in fact a conclusion to be proven is a form of begging the question, an error in the logic of question framing.

This problem is compounded in the Results section, where the authors attempted to show that over one-half of their study group was underdosed. They cited mean daily doses of fluoxetine (32.9 mg/day), paroxetine (42.5 mg/day), sertraline (120.7 mg/day), and citalopram (38.3 mg/day) as apparent evidence of underdosing. Yet these doses met the authors' own standards! I work in a large group practice and know that these four antidepressants together constitute about 90% of all antidepressants in our setting. So were the patients in this study actually underdosed?

The authors can certainly be excused for following the common belief that antidepressants treat both depression and suicidality. But the inability of their study to support this belief should serve to make us cautious about our assumptions and careful about our questions. If the 43% of the authors' study group receiving adequate antidepressant medication showed significant suicidal behavior after treatment, then something else must be at work. One cannot ascribe this to treatment resistance, as some authors do. Suicidality is not synonymous with depression, and treatment does not equal medication. An article such as this does not suffer so much from poor science as from a (common) failure in psychopharmacology research to "think outside the bottle." At this time in

our field, we still have not proven that selective serotonin reuptake inhibitors are clinically better than placebo (2). We all know that depression and acts of suicide are mentally complex phenomena. Until we begin studying them in sufficient depth, we will only get articles that raise more questions than they answer.

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Drs. Oquendo and Mann Reply

TO THE EDITOR: We found that 43% of the patients who attempted suicide during the follow-up period of our study met minimum standards for adequate pharmacotherapy for depression. Therefore, we do not believe that this finding means that optimal aggressive pharmacotherapy for depression does not reduce the occurrence of suicidal acts in those with major depressive episodes. Rather, we think that it reflects the problem of undertreatment more than treatment-resistant depression contributing to suicidal behavior and, in some cases, the effect of comorbidity with axis II cluster B personality disorder. As Dr. Wright points out, our literature review supported this interpretation of our data.

Dr. Wright objects to the choice of minimum adequate daily doses. He is referred to Sackeim et al. (1) as the basis for the medication standards used in our study. Dr. Wright also objects to our statement that most of our subjects received suboptimal antidepressant treatment. However, adequacy of treatment is related to dose *and* duration of treatment. Therefore, without both pieces of information, a complete judgment about the adequacy of the treatment cannot be made.

We agree with Dr. Wright that suicidality and depression are not synonymous. It is our opinion that in those at risk for suicidal acts, the presence of an episode of depression increases the risk for acting on suicidal thoughts. This view is supported by the increased odds (by sevenfold) of making a suicide attempt when a major depressive episode occurs during a follow-up period.

Of course, psychotropic interventions are not the only tool in the clinician's armamentarium. However, they are a critical element in the continuation treatment of severe major depression in inpatients.

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Sensitivity of the D8/17 Assay

TO THE EDITOR: Mae S. Sokol, M.D., and colleagues (1) recently reported a significantly higher rate of D8/17 positivity among 16 adolescents with anorexia nervosa (81%) than among 17 psychiatric comparison subjects (12%). The mean percentage of D8/17 positivity might "be useful in identifying PANDAS [pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections] anorexia nervosa" (p. 1431). The results of that investigation are similar to findings in two previous studies (2, 3) demonstrating excellent performance of the D8/17 assay in distinguishing patients with obsessive-compulsive disorder (OCD) from healthy comparison subjects—85% to 100% of OCD patients were D8/17 positive in comparison with 5% to 15% of healthy comparison subjects. However, our subsequent experience has been less satisfactory and suggests that the assay is not yet reliable enough to be used as a diagnostic tool.

In our work, a total of 216 samples were gathered over a 4-year period from 26 subjects with Sydenham's chorea, 42 subjects with OCD and/or tic disorders (PANDAS subgroup), and 19 healthy comparison subjects. Samples were obtained at the National Institute for Mental Health (NIMH) by workers blind to patient diagnosis and sent to Rockefeller University, where assays were performed by immunofluorescent microscopy before August 1998 and subsequently by flow cyometry, according to methods previously reported (4). Written informed consent or assent was obtained from all subjects, who were participating in studies of Sydenham's chorea and OCD that were approved by NIMH institutional review boards.

Overall, the sensitivity of the D8/17 assay for the 68 patients with Sydenham's chorea or OCD/tics was 61.8% (42 assays were positive). Of concern, only 12 assays (46.2%) obtained from the 26 Sydenham's chorea patients were positive, which is significantly lower ($z=5.2$, $p<0.001$) than that previously reported for patients with rheumatic fever (89%–100% were D8/17 positive) (5, 6). Thus, the D8/17 assay failed to "diagnose" the majority of the patients with Sydenham's chorea. Furthermore, the reliability of the assay was suboptimal. Longitudinal observations of 54 subjects tested at random intervals over the study period demonstrated test-retest agreement of 61.1% (N=132) for the 216 samples assayed (kappa=0.18). Of particular concern, agreement was observed in only 48 of 61 split samples (78.7%, kappa=0.48).

In conclusion, the sensitivity of the D8/17 assay decreased to unacceptably low levels during the period of observation. The declining sensitivity may have been due to changes in methods or the characteristics of the monoclonal antibody. If so, the performance might be improved by reversion to earlier techniques. Meanwhile, it appears premature to include the D8/17 assay in the diagnostic workup of patients with neuropsychiatric disorders such as OCD, tics, and anorexia nervosa.

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