Dr. Warner is employed by Novartis Pharmaceuticals, Inc.

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Dr. Alexopoulos Replies

To the Editor: Dr. Warner's letter highlights critical issues in elderly suicide prevention. Despite efforts in prevention at a national level, one American is lost to suicide every 16 minutes. The toll is particularly high for men over the age of 75 years, who have a suicide rate 3.3 times higher than that of the general population, reaching 35.7 per 100,000 individuals (1). However, these numbers are underestimates because of underreporting.

Despite the alarming statistics, little is directly known about prevention interventions in later life. Dr. Warner points out several risk factors for suicide. However, there is limited direct evidence that addressing these factors (e.g., treating depression and pain, enriching the social network of persons at risk, removing firearms) reduces the incidence of suicide. The PROSPECT study focused on patients 60 years of age and older (75–84 years: N=155; ≥85: N=30) and used suicidal ideation and depressive symptoms as a proxy for suicide prevention. We selected this strategy for two reasons. First, depression and suicidal ideation are risk factors for suicide. Second, there is face value in ameliorating depressive symptoms and thus reduction of suffering and family disruption and improved outcomes of several comorbid medical disorders. Showing that the PROSPECT intervention works in primary care patients is important because two-thirds of depressed older adults are exclusively treated in the primary care sector. Nonetheless, the PROSPECT study provides no more than indirect evidence of the effectiveness of an intervention for suicide prevention.

Errors in the assessment and treatment planning of elderly suicidal patients can be fatal. Among elderly persons, there are only four suicide attempts for every completed suicide, but there are 100 to 200 attempts per completed suicide in individuals aged 15–24 years (1). Assessment difficulties arise, to a large measure, from the older patients' reluctance to share thoughts on suicide and from poor acceptance of suicide risk by patients' families. Much of the difficulty in treatment planning arises from the absence of direct knowledge of the effectiveness of clinical interventions specific to elderly suicide prevention. Another reason is the expectation by clinicians and families that suicide can be prevented in most, if not all, cases. This unrealistic expectation is in part generated by an emotional reaction caused by stigmatization of suicide and often leads to treatment measures that are either idiosyncratic, overly restrictive, or both.

We believe that direct studies of interventions for elderly suicide prevention and systematic efforts to destigmatize suicide are two initiatives likely to make a difference. Currently, our approach in the reduction of suicide risk must rely on indirect findings of factors associated with high suicide rates. However, definitive guidance to clinicians can only come from effectiveness studies of specific interventions targeting reduction of suicide itself rather than reduction of suicide risk factors. Destigmatization of suicide and mental illness at the community level and during clinical interactions with patients and families is critical. It can increase the accuracy and promptness of reporting suicide thoughts and related symptoms by patients and families, set appropriate outcome expectations, and allow clinicians to make informed and rational treatment plans.

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Limitations of the Hamilton Anxiety Rating Scale as a Primary Outcome Measure in Randomized, Controlled Trials of Treatments for Generalized Anxiety Disorder

To the Editor: In the August 2009 issue of the *Journal*, Falk Leichsenring, D.Sc., et al. (1) presented findings from a randomized, controlled trial comparing short-term psychodynamic psychotherapy and cognitive-behavioral therapy (CBT) in patients with generalized anxiety disorder. We are pleased to see a trial assessing the efficacy of short-term psychodynamic psychotherapy, a form of psychotherapy that has not been adequately studied in the treatment of anxiety disorders. However, despite the importance of the questions addressed in this study, there is a serious methodological concern that limits the conclusions that can be drawn.

The issue is the primary outcome measure. In randomized, controlled trials, the primary outcome measure is the principal indicator by which the efficacy of an intervention is evaluated. It measures the outcome of greatest importance in a trial. The principal indicator of treatment efficacy in this study was the Hamilton Anxiety Rating Scale (HAM-A), a clinician-administered scale that assesses the severity of 14 broad categories of symptoms, presumed to be associated with anxiety. HAM-A has been used as an outcome measure in numerous generalized anxiety disorder treatment studies and has long been the standard primary outcome measure in pharmacological randomized, controlled trials.

At one time, when generalized anxiety disorder was a nonspecific disorder characterized by diffuse anxiety symptoms, the use of HAM-A was appropriate. However, with the introduction of DSM-III-R in 1987, generalized anxiety disorder became a disorder of worry. The central symptom of DSM-IV-TR-defined generalized anxiety disorder is excessive and uncontrollable worry. HAM-A does not adequately measure the central symptom of DSM-IV-TR generalized anxiety disorder (2). Furthermore, most of the symptoms assessed by HAM-A (e.g., cardiovascular, respiratory, and gastrointestinal symptoms) are not among the DSM-IV-TR-associated symptoms of generalized anxiety disorder. HAM-A has been in existence for one-half century and remains a popular instrument for assessing anxiety despite these limitations. However, the scale is poor at discriminating between generalized anxiety disor-

der and depression (3), and there are several newer measures that are more appropriate for assessing generalized anxiety disorder symptoms and worry in particular. Of note, in the randomized, controlled trial conducted by Leichsenring et al., short-term psychodynamic psychotherapy and CBT led to comparable decreases in HAM-A scores. However, CBT was superior to short-term psychodynamic psychotherapy in the secondary outcome measure, which was the Penn State Worry Questionnaire, a well-established measure of excessive and uncontrollable worry.

HAM-A is problematic for a second reason: it is clinician administered. HAM-A may be vulnerable to allegiance effects and other related factors that can influence the way questions are posed and the way responses are scored by the clinician, even if methods are put into place to limit potential interviewer biases. For this reason, it is important to assess primary outcomes using a combination of clinician-administered and self-report measures.

In our opinion, the results of the randomized, controlled trial conducted by Leichsenring et al. are equivocal, largely as the result of the selection of a primary outcome measure that is an unsuitable measure of the central feature of DSM-IV-TR-defined generalized anxiety disorder.

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Drs. Leichsenring, Salzer, and Leibing Reply

TO THE EDITOR: HAM-A is still one of the most frequently used measures to assess anxiety, including symptoms of generalized anxiety disorder in randomized, controlled trials. This is true for studies assessing the effects of psychotherapy and those assessing the effects of psychotropic drugs. For this reason, we chose HAM-A scores as the primary outcome measure of our study. This is consistent with previous research on generalized anxiety disorder (e.g., reference 1). However, we agree with Dr. Koerner et al. that, for several reasons, HAM-A is not an optimal measure of anxiety in general and of generalized anxiety disorder in particular. This is especially true if HAM-A is applied as the only measure of anxiety.

Dr. Koerner et al. regard the Penn State Worry Questionnaire as a more appropriate measure of generalized anxiety disorder, since it utilizes the DSM-IV criterion for worry. In addition to HAM-A as the primary outcome measure, we included the Penn State Worry Questionnaire as a secondary outcome measure, a procedure that is also consistent with previous research on generalized anxiety disorder (e.g., reference 1). In our article, we reported the results for the outcome measures used, including for the Penn State Worry Questionnaire. It is true that the latter results were in favor of CBT, which we noted as well. In addition, we did use a combination of self-rated and observer-rated outcome measures, as suggested by Dr. Koerner et al. The results of HAM-A were supported, for example, by that of the Beck Anxiety Inventory. Significant differences in efficacy between short-term psychodynamic psychotherapy and CBT were not found in either the Beck Anxiety Inventory or HAM-A. In addition, we used the State-Trait Anxiety Inventory-Trait Version as another measure of anxiety. Again, we found and reported an outcome in favor of CBT. Thus, we used several measures of anxiety that appear to draw on different aspects of anxiety. As reported in our article, the Penn State Worry Questionnaire did not show significant correlations to HAM-A ($r=0.16$, $p=0.23$) or to the Beck Anxiety Inventory ($r=0.16$, $p=0.23$) in the total sample of patients with generalized anxiety disorder ($N=57$). In contrast, the questionnaire correlated significantly with the trait anxiety inventory ($r=0.66$, $p<0.0001$). As we noted in the article, several items of the trait anxiety inventory were related to worry. These correlations suggest that the questionnaire and, in part, the trait anxiety inventory utilize other, more cognitive aspects of anxiety than HAM-A and the Beck Anxiety Inventory. The items of HAM-A and the Beck Anxiety Inventory appear to utilize more somatic aspects of anxiety. The correlation between these two measures was 0.58 ($p<0.001$). These somatic symptoms are another main criterion of generalized anxiety disorder according to DSM-IV.

As already stated, the other main DSM-IV criterion of generalized anxiety disorder is extensive and uncontrollable worry. However, the specificity of pathological worry in generalized anxiety disorder has been questioned by several investigators (2, 3). The nosological controversies associated with the criterion of worry were discussed by Weisberg (4). Furthermore, worry may also be associated with other anxiety disorders and especially with depression (2). In another study conducted by our working group (5), the sensitivity and specificity of the Penn State Worry Questionnaire were assessed. Depending on the cut-off score applied, specificity was between 0.51 and 0.68. These results did not indicate a high specificity of worry or a high specificity of the Penn State Worry Questionnaire for generalized anxiety disorder.

Furthermore, Dr. Koerner et al. note that HAM-A does not adequately differentiate between generalized anxiety disorder and depression. This seems to also be the case for worry and generalized anxiety disorder on the worry questionnaire. Fresco et al. (3) reported that worry and rumination were highly correlated with each other ($r=0.46$) and showed equally strong relationships to both anxiety and depression. In our previous study, we found a significant and high correlation between the worry questionnaire and the Beck Depression Inventory ($r=0.51$) (5). After controlling for depression (using the Beck inventory), the worry questionnaire no longer dif-