A Role for Profiles of Patient-Specific Depression Characteristics and Socioeconomic Factors in the Prediction of Antidepressant Treatment Outcome

To the Editor: In their recent article "Prognostic Subgroups for Citalopram Response in the STAR*D Trial," Jakubovski and Bloch[1] conclude that baseline socioeconomic variables "are likely to be more informative than routine clinical variables such as past medication response, duration and severity of illness, and comorbid psychiatric illnesses" in the prediction of citalopram treatment outcome. In particular, their assertion carries the curious implication that demographic factors are more strongly related to treatment response than patient-specific ones. However, their findings are not in agreement with an earlier study we published using the same data and analysis methods.[2]

In our study, we described prognostic subgroups for citalopram remission that included a combination of patient-specific depression characteristics and socioeconomic variables. For example, our analysis of baseline factors suggested that a person making at least $40,000 per year would have markedly different remission rates (12% vs 55%) depending on depression-specific characteristics such as depressed mood, interest in activities, and insomnia. The 12% rate of remission we identified for a subgroup characterized by higher socioeconomic status but worse patient-specific depression symptoms was actually lower than the rate of remission for any subgroup of lower socioeconomic status patients. Jakubovski and Bloch, on the other hand, suggested that depression-specific characteristics at baseline do not have stronger discriminative power than socioeconomic variables.

We believe that Jakubovski and Bloch's results may reflect variations in subject categorization that deviate from established findings. Notably, in Figure 1A, Jakubovski and Bloch identified 1,023 remitters by the Hamilton Depression Rating Scale and thus indicated that 41% of the subjects in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study remitted, whereas the initial STAR*D report[3] identified only 790 remitters and reported a remission rate of 28%. Furthermore, Jakubovski and Bloch included only completers in their analysis (~2,500 subjects), as opposed to the full analyzable sample of 2,876 patients. Finally, they utilized a more limited set of predictors than we in our analysis: specifically, they did not utilize any individual depression symptoms, nor did they utilize the clinically important anxious depression construct.[4] We believe that these variations markedly affected their findings.

We feel that researchers and clinicians should focus attention on subgroups of patients with combinations of specific, severe depression characteristics and socioeconomic variables. Patient-specific depression characteristics, in addition to socioeconomic factors, can help psychiatrists guide their medication choices and provide additional accuracy over reliance on socioeconomic factors.

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Mr Jakubovski and Dr Bloch Reply

To the Editor: We thank Dr Jain and colleagues for their interest in our recent article.[1] The article written by Jain et al[2] represents excellent complementary reading to our article. Although published prior to our article, their article was not MeSH indexed by the National Library of Medicine until February 22, 2014, long after our article was slated for publication. Unfortunately, this delay prevented our having the opportunity to comment on their work in our publication. We thank Jain et al and *JCP* for giving us the opportunity here to comment on the similarities and differences between our findings and their work.

We agree with Jain and colleagues that the likely sources of differences in results between the articles are (1) the inclusion of different baseline predictor variables between studies, (2) the restriction of our sample to those who actually completed 8 weeks of citalopram treatment, and (3) different definitions of remission between the studies. We do not wish to debate Dr Jain's group regarding whose methodology is better, and we agree with them that their analysis of the data is also methodologically sound. Although Jain et al and our group made different choices regarding whether to examine for predictors of outcome in those who actually *completed* the treatment versus those who *received* citalopram treatment, these are both worthwhile questions for exploration.

We also welcome the opportunity to clear up any confusion regarding the relative importance of socioeconomic predictors and traditional clinical predictors in predicting selective serotonin reuptake inhibitor treatment outcome in major depressive disorder. In our article, we wrote, "Socioeconomic measures, such as income, employment status, and education, were the best predictors of treatment response and more discriminative than clinical attributes, such as past medication response, severity and duration of depression, comorbid psychiatric diagnoses, and substance use."[1(p742)] This finding is consistent across both our results (most discriminant predictor for response was income and for remission was employment status) and Jain and colleagues'[2] secondary analysis of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) data, in which income (remission) and education level (response) were the most discriminative predictors of citalopram outcomes.

We also wrote in our discussion, "Our analysis suggests, perhaps surprisingly, that these [socioeconomic] variables are likely to be more informative than routine clinical variables such as past medication response, duration and severity of illness, and comorbid psychiatric illnesses. Nonetheless, the ROC analysis also demonstrates on several occasions that the combination of a poor socioeconomic situation and poor clinical factors appears particularly pernicious."[1(p746)] Jain and colleagues' results add to our findings by suggesting that additional clinical variables that focus on individual depressive symptoms—particularly anxious depression, and possibly insomnia and significant aches and pains—may have better predictive value than other traditional clinical measures that we utilized. That being said, the predictive value of these symptoms is still less discriminate in their analysis than the socioeconomic measures and appears particularly powerful when used in combination with socioeconomic factors.

In conclusion, we thank Jain and colleagues and *JCP* for the opportunity to comment on their important work in relation to ours. Although there are clearly specific differences in the results between the 2 studies, which are well outlined in the letter by Jain et al and in the second paragraph of our response, the gestalt findings from the dataset are remarkably similar: (1) socioeconomic predictors (income, education, and employment status) were the most discriminative predictors of outcome, and (2) their predictive power was enhanced with traditional clinical predictors. There appears to be a particularly pernicious interaction between poor socioeconomic status and poor clinical factors. We would point readers to both articles on this topic, as we believe they are much more complementary than contradictory. Likewise, we encourage other investigators to study the STAR*D trial database to answer further important questions in depression treatment and research. The National Institute of Mental Health limited-access datasets represent a tremendously underutilized and important clinical research tool that was generously made publicly available to scientific investigators by the US government and individual trial investigators. We hope that our investigation, as well that of Jain and coworkers, represents the tip of the iceberg in terms of these efforts.

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