Social Inequalities in Response to Antidepressant Treatment in Older Adults

Alex Cohen, PhD; Patricia R. Houck, MSH; Katalin Szanto, MD; Mary Amanda Dew, PhD; Stephen E. Gilman, ScD; Charles F. Reynolds III, MD

Context: We examined the relationship between socioeconomic status and response to treatment for depression among older adults.

Methods: Secondary analysis of pooled data from the open-label phase of 2 National Institute of Mental Health–funded clinical trials of nortriptyline hydrochloride or paroxetine combined with interpersonal psychotherapy (N = 248). We used Cox proportional hazards regression analyses to examine the association between socioeconomic status, indexed by census tract median annual household income and the subject’s educational attainment, and treatment response and remission according to the Hamilton Depression Rating Scale. The association between socioeconomic status and suicidality or depressed mood reported at each week of treatment was examined using repeated-measures generalized logit models.

Results: Subjects residing in middle-income census tracts were significantly more likely to respond to antidepressant treatment than subjects residing in low-income census tracts (adjusted hazard ratio, 1.80; 95% confidence interval [CI], 1.18-2.75). Throughout the course of antidepressant treatment, subjects in the middle- and high-income census tracts were significantly less likely to report suicidal ideation (adjusted odds ratios, 0.48 [95% CI, 0.27-0.94] and 0.39 [95% CI, 0.16-0.94], respectively). No association was found between socioeconomic status and remission.

Conclusion: Residence in a low-income census tract is associated with a less favorable course of depression among older adults receiving a combination of pharmacologic and psychosocial treatment.

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Socioeconomic inequalities in health have been observed for nearly 200 years1,2; on average, persons with lower socioeconomic status (SES) have elevated rates of morbidity and mortality relative to persons of higher SES.3,4 These inequalities have been demonstrated at all stages of life, from early childhood5 through old age,6 and for physical7 and mental disorders.8 An extensive literature exists about the influence of the components of SES—income,9 education,10 and occupation11—and the factors that mediate the association (eg, psychosocial environments,12-14 biological processes,15 and ethnicity16,17). A number of studies have demonstrated the association between indicators of low SES and prevalence of depression.18-20 These social differentials, as demonstrated in a meta-analysis by Lorant et al,21 may be attributable to the tendency of individuals with lower SES to be at increased risk for onset of first depression and the likelihood of these individuals to have a more severe course of depression (in terms of episode duration and recurrence) compared with individuals with higher SES. Given the factors that are associated with these inequalities (eg, low income, lack of education, and stressful social environments), it seems reasonable to assume that these same factors may also vitiate the effects of pharmacologic and psychosocial interventions and produce social inequalities in response to treatment.22,23 However, research on social factors and treatment response has been inconclusive. In a series of studies published in the late 1960s and early 1970s, Rickels et al22,24 and Downing and Rickels25 found that low SES was associated with poorer response to pharmacotherapy. In contrast, another study26 found no association between SES and treatment outcomes. Although some research has suggested that high educational status is associated with positive clinical outcomes27,28 and improved social adjustment,29 other work did not.30 Findings about the effects of employment have also been inconsistent. One study28 found that employment was associated with improved outcomes, whereas other studies29,30 found no such association. Although low income is predictive of increased rates and persistence of depression,31 its association with treatment outcome is less clear.31

Author Affiliations:
Department of Social Medicine, Harvard Medical School (Dr Cohen), and Departments of Society, Human Development and Health and Epidemiology, Harvard School of Public Health (Dr Gilman), Boston, Mass; and Department of Psychiatry, Intervention Research Center for the Study of Late-Life Mood Disorders, University of Pittsburgh School of Medicine, Pittsburgh, Pa (Ms Houck and Drs Szanto, Dew, and Reynolds).
Integrating the findings of previous research on SES and antidepressant response is difficult in view of inconsistencies in the measures of SES used and differences in treatment modalities and settings across studies. For example, only 1 of these studies collected direct information on family income, whereas measures of educational status were variously based on number of years in school or whether an individual had graduated from high school or college. The findings of Rickels et al. and others were based on treatments administered in multiple settings (ie, outpatient clinic, general medical practice, private psychiatric practices, and primary care clinics), with possible differences in the quality of care offered in particular practices or by particular physicians.

The present study builds on previous research by providing an examination of whether 2 core components of SES, income and education, have an effect on re-}

**METHODS**

**SUBJECTS**

Subjects were participants in 1 of 2 studies funded by the National Institute of Mental Health and conducted at the University of Pittsburgh, Pittsburgh, Pa, on the maintenance treatment of late-life depression. The first of these studies investigated the efficacy of combined nortriptyline hydrochloride and interpersonal psychotherapy in 169 subjects 59 years and older. The second study evaluated the efficacy of combined paroxetine and interpersonal psychotherapy among 116 subjects 69 years and older. Both studies began with open-label (ie, nonblinded and standardized treatments within each study) short-term and continuation treatments for major depressive disorder before randomization to 1 of several maintenance treatment conditions. The present analyses are based on data from the short-term and continuation phases, which together lasted up to 26 weeks. Combining data from the 2 studies resulted in a demographically and clinically diverse sample.

The analysis sample for the current study included 248 subjects (145 from study 1 and 103 from study 2) whose census tract median annual household incomes were available from the US Census Bureau.

**MEASURES**

Depressive symptoms were measured weekly with the 17-item Hamilton Rating Scale for Depression (HRSD). Scores on the HRSD were used to generate indicators of treatment efficacy for the present study as follows. Response to treatment was defined as HRSD scores of 10 or less for at least 3 consecutive weeks; remission of major depressive disorder was defined as HRSD scores of 6 or less for at least 3 consecutive weeks. The depressed mood and suicide items from the HRSD were used in analyses of differential treatment response at the symptom level. As core symptoms of depression, we believed these 2 items would give the best indication of whether response to treatment was associated with SES. For depressed mood (HRSD item 1), a rating of 0 (subject denies any feelings of sadness, hopelessness, helplessness, or worthlessness) was coded as not depressed. Subjects were coded as depressed if they reported gloomy attitude, pessimism, or hopelessness on questioning (rating of 1); reported these feelings spontaneously (rating of 2); or communicated them nonverbally (rating of 3). For suicidality (HRSD item 3), a rating of 0 (subject denied any degree of suicidality) or of 1 (subject said life is empty or not worth living) was coded as nonsuicidal. Subjects who reported recurrent thoughts of death or wishes to be dead (rating of 2), had active suicidal ideation (rating of 3), or had attempted suicide (rating of 4) were classified as suicidal.

Income and years of education were used as the 2 measures of SES in the current study. Income was based on the median annual household income of the census tracts in which subjects lived, categorized as less than $25,000 (reference category), $25,000 to $50,000, and more than $50,000. The income groups correspond to tertiles of median household income in Allegheny County, Pennsylvania, the county of residence of 88% of the subjects. Census tract data have been used in many investigations of social inequalities in health in the United States. Information on subjects’ years of education was collected at baseline.

Demographic variables included in the analyses have been shown to be associated with depression, including age in years, sex, race/ethnicity (nonwhite vs white), and marital status (married, widowed, and separated/divorced/never married). The baseline clinical characteristics included in the analyses were first vs recurrent episode of depression, age at first lifetime onset of depression, duration in weeks of the current episode, the subject’s concurrent medical burden as measured by the Cumulative Illness Rating Scale–Geriatric, and the total 17-item HRSD score.

**DATA ANALYSES**

Cox proportional hazards regression analyses were used to evaluate the association of SES with time to response and time to remission. Data from nonresponders were censored at 26 weeks or at the time of nonresponse, ie, when they were in need of nonprotocol treatment. We modeled the association between SES and the presence of depressed mood and suicidality at each clinical assessment during the first 20 weeks of the trial using repeated-measures generalized logit regression. For these analyses, we used data from the first 20 weeks of the trial only because, after that point, the number of observations fell off sharply.

Regression models for time to response/remission, depressed mood, and suicidality were estimated sequentially. The first regression model included 2 indicator variables for income (middle and high income vs low income) and 3 indicator variables for education (12, 13-15, and ≥16 years vs <12 years). In addition to the income and education variables the second model included sociodemographic variables, and the third model included baseline clinical characteristics. Results of the unadjusted and adjusted models of treatment response are shown; for the remaining outcomes, only the final adjusted models are shown because the effects of SES did not vary substantively between models.

The demographic and baseline clinical characteristics of subjects in the 2 studies are presented in Table 1. On average, subjects in study 2 were older and had higher levels of education. Severity of depression was more pro-

The present study builds on previous research by providing an examination of whether 2 core components of SES, income and education, have an effect on re-
nounced among study 1 subjects, as indicated by higher levels of recurrent depression (an inclusion criterion for study 1), higher HRSD scores, and a higher prevalence of suicidality. Controls for demographic and baseline clinical characteristics in the multivariate models serve to adjust the effect estimates for SES differences in the samples enrolled in the 2 studies. In the pooled sample, the only significant difference in the demographic and baseline clinical characteristics of subjects in the different income groups was that the low-income group had a greater proportion of nonwhite subjects ($\chi^2 = 10.42; P = .005$).

Treatment response rates among study subjects in the low-, middle-, and high-income groups were 80% (32 subjects), 77% (122 subjects), and 78% (39 subjects), respectively. Median times to response (HRSD score of ≤10 for 3 weeks) were 9.1, 7.0, and 7.4 weeks in the low-, middle-, and high-income groups, respectively.

Unadjusted and adjusted hazard ratios (HRs) comparing the likelihood of treatment response among individuals in the middle- and high-income groups relative to those in the low-income group are shown in Table 2. Unadjusted HRs were obtained from separate models containing only income or education. These effects were then entered into a model together (adjusted model 1); subsequently, the effects of income and education were adjusted for demographic factors (adjusted model 2) and baseline clinical characteristics (adjusted model 3). In the unadjusted models and in adjusted model 1, income and education were not significantly associated with response to combined pharmacologic and psychosocial treatment. However, after accounting for demographic factors (model 2) and baseline clinical characteristics (model 3), we observed a significant difference in the likelihood of treatment response between subjects in the middle-income category relative to those in the low-income category. Model 3, which included baseline clinical characteristics in addition to the SES and demographic variables, revealed that middle-income subjects were significantly more likely to respond to treatment than were low-income subjects (HR, 1.80; 95% confidence interval [CI], 1.18-2.75) and that high-income subjects were marginally although not significantly more likely to respond to treatment (HR, 1.25; 95% CI, 0.76-2.05). Combining middle- and high-income subjects into a single category demonstrated that, in the aggregate, they were significantly more likely to respond to treatment than were low-income subjects (HR, 1.61; 95% CI, 1.07-2.42).

Other results included were that (1) years of education was not a significant covariate in any of the models and (2) in model 3, nonwhite race/ethnicity was significantly associated with greater likelihood of treatment response (HR, 2.02; 95% CI, 1.16-3.54). Remission rates in the low-, middle-, and high-income groups were 48% (19 subjects), 47% (74 subjects),
and 44% (22 subjects), respectively. As in the analyses for response, unadjusted and adjusted Cox proportional hazards models were estimated to examine the relationship between SES and remission of depressive symptoms (HRSD score of ≤6 for 3 consecutive weeks). Census tract income and education were not significantly associated with remission.

The final sets of analyses evaluated the association between SES and the HRSD items for suicide and depressed mood as recorded each week during the first 20 weeks of treatment. The weekly pattern of suicidality by income group is shown in the Figure. Although the percentage of subjects who endorsed the suicide item declined during the treatment period, suicidal ideation was consistently higher in the low-income group than in the middle- and high-income groups. Repeated-measures logistic analyses were used to quantify the average SES differences in suicidality during 20 weeks of treatment. Even after controlling for baseline clinical characteristics, middle- and high-income subjects were significantly less likely to endorse suicidal ideation than were low-income subjects (Table 3). The adjusted odds of suicidality for the middle-income group were 0.48 times that of the low-income group (95% CI, 0.27-0.94) and for the high-income group were 0.39 times that of the low-income group (95% CI, 0.16-0.94). These odds ratios suggest an inverse relationship in the association between income and suicidality during treatment for major depression. When the middle- and high-income groups were combined, the average odds of suicidality were 0.46 times that of the low-income group (95% CI, 0.24-0.87). Years of education was not related to suicidality during treatment.

Szanto et al34 reported that suicidal ideation is associated with a significantly lower likelihood of treatment response in the current sample. In view of this and the present findings that census tract median household income of subjects is associated with both suicidality and likelihood of response during treatment, we conducted several exploratory analyses to evaluate the extent to which suicidal ideation contributes to the link between census tract median household income and treatment response. We performed these analyses by adding indicators to model 3 (Table 2) for suicidal ideation at baseline (HR, 1.04; 95% CI, 0.71-1.52) and at any time during the

### Table 2. SES and Times to Treatment Response With Multiple Cox Proportional Hazards Regression Analyses

<table>
<thead>
<tr>
<th>SES</th>
<th>Median household income</th>
<th>HR (95% CI)</th>
<th>Adjusted Model 1</th>
<th>Adjusted Model 2*</th>
<th>Adjusted Model 3†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (Reference)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>1.37 (0.92-2.02)</td>
<td>1.38 (0.92-2.05)</td>
<td>1.70 (1.12-2.58)</td>
<td>1.80 (1.18-2.75)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>1.14 (0.71-1.82)</td>
<td>1.13 (0.70-1.82)</td>
<td>1.33 (0.81-2.16)</td>
<td>1.25 (0.76-2.05)</td>
<td></td>
</tr>
<tr>
<td>Education, y</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>0.94 (0.64-1.38)</td>
<td>0.91 (0.62-1.33)</td>
<td>0.88 (0.59-1.29)</td>
<td>0.98 (0.66-1.45)</td>
<td></td>
</tr>
<tr>
<td>13-15</td>
<td>1.04 (0.67-1.63)</td>
<td>1.03 (0.65-1.61)</td>
<td>1.02 (0.64-1.61)</td>
<td>1.03 (0.65-1.65)</td>
<td></td>
</tr>
<tr>
<td>≥16</td>
<td>0.91 (0.58-1.43)</td>
<td>0.94 (0.60-1.48)</td>
<td>1.12 (0.70-1.78)</td>
<td>1.09 (0.67-1.60)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio; SES, socioeconomic status.

*Model 2 included the demographic factors age, sex, race/ethnicity, and marital status.
†Model 3 included the demographic factors and baseline clinical characteristics recurrent depression, age at first onset, number of weeks of current episode, Cumulative Illness Rating Scale–Geriatric score, and total 17-item Hamilton Rating Scale for Depression score.

Figure. Endorsement of the Hamilton Rating Scale for Depression suicide item. The percentage of subjects endorsing suicidal ideation (recurrent thoughts of death or active suicidal thoughts) is shown across 20 weeks of treatment by census tract median household income level. Higher percentages of the low-income group endorsed suicidality than the middle- and high-income groups.

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treatment period (HR, 0.75; 95% CI, 0.55-1.04). However, the HRs for income remained statistically significant and virtually unchanged. Together, these findings indicate that the association between income group and treatment response is not attributable to suicidal ideation, but rather both SES and suicidality independently predict the likelihood of responding to antidepressant therapy.

The repeated-measures analyses showed that the depressed mood item from the HRSD was not differentially endorsed by subjects in the 3 income groups (Table 3).

### Table 3. SES and Suicidality and Depressed Mood

<table>
<thead>
<tr>
<th>SES</th>
<th>Suicidality†</th>
<th>Depressed Mood†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median household income</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Low</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Middle</td>
<td>0.48 (0.27-0.94)</td>
<td>0.81 (0.54-1.22)</td>
</tr>
<tr>
<td>High</td>
<td>0.39 (0.16-0.94)</td>
<td>1.43 (0.90-2.28)</td>
</tr>
<tr>
<td>Education, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>12</td>
<td>0.97 (0.48-1.99)</td>
<td>0.83 (0.54-1.29)</td>
</tr>
<tr>
<td>13-15</td>
<td>0.72 (0.36-1.47)</td>
<td>0.83 (0.51-1.36)</td>
</tr>
<tr>
<td>≥16</td>
<td>0.93 (0.42-2.15)</td>
<td>0.95 (0.58-1.55)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; OR, odds ratio; SES, socioeconomic status.
*Includes results of fully adjusted regression models controlling for all demographic factors (age, sex, race/ethnicity, and marital status) and baseline clinical characteristics (recurrent depression, age at depression onset, number of weeks of current episode, Cumulative Illness Rating Scale–Geriatric score, and total 17-item Hamilton Rating Scale for Depression [HRSD] score).
†We used repeated-measures generalized logit models for the HRSD suicide and depressed mood items recorded at each week of treatment.

The analyses revealed 2 significant associations between SES (as indicated by census tract median household income) and response to treatment for major depressive disorder in older adults. First, subjects who resided in low-income census tracts were less likely than other subjects to respond to treatment. This effect was strongest for the comparison of low- and middle-income subjects. One possible explanation for this finding comes from research that demonstrated that the persistence of depressive episodes was more pronounced among individuals with lower SES. That is, if individuals with lower SES tend to have depressive episodes of greater duration, rates of difficult-to-treat depression may also be elevated in this population.

Although subjects who lived in middle- and high-income census tracts were, in the aggregate, more likely to respond to treatment than subjects who lived in low-income census tracts, we must note that the nonlinearity of the results contradicts our expectation that subjects who lived in high-income census tracts would be the most likely to respond. We are not able to provide a definitive explanation for this but can offer possible reasons. First, the imprecise correspondence between the census tract and individual measures of SES may have weakened the dose-response relationship. For example, some subjects of modest means may have become home owners before their neighborhoods underwent significant increases in property values and became characterized as high-income census tracts. In contrast, home ownership in a high-income neighborhood might reflect past SES but not present circumstances. Under either of these conditions, census tract information would not accurately reflect individual measures of SES and, thus, would weaken the association between household income and treatment response.

Census tract income was a significant predictor of response to treatment only when accounting for individual demographic and baseline clinical characteristics. Ultimately, data on individual and neighborhood-level SES will be needed to correctly distinguish the effects of neighborhoods from those of individual characteristics when considering predictors of response to antidepressant treatment.

The second association between SES and treatment outcomes was that, compared with subjects who lived in low-income census tracts, subjects who lived in middle- and high-income census tracts had significantly lower levels of suicidality during the clinical trials. Low-income subjects were about twice as likely as middle-income subjects and about 2.5 times as likely as high-income subjects to report suicidal ideation during treatment, suggesting an inverse relationship between the median household income of the neighborhoods in which subjects resided and suicidality. Furthermore, an exploratory analysis provided no evidence that suicidal ideation mediated the association between residence in a low-income census tract and treatment response. Rather, income and suicidality were independently related to treatment response.

We did not observe an association between SES and the likelihood of remission. The relatively small proportion of subjects who achieved remission (48%, 47%, and 44% in the low-, middle-, and high-income groups, respectively) might account for this, but it is also possible that predictors of remission and response (as defined in this study) are not the same. Further research is necessary to answer this question.

To the extent that educational status usually serves as a principal component of SES, is generally correlated with income, and has been shown to be a predictor of response to treatment, we had expected it to be a significant covariate in our analyses. However, in our models, educational status was not a predictor of response to treatment or of endorsement of the HRSD suicide item. This might be explained by a cohort effect. It is only in recent decades that the economy of the Pittsburgh region has shifted from heavy industry to higher education, medicine, and services. However, when the older subjects in our study came of age, economic and social success in the industrial economy was not so dependent on education. Thus, we speculate that years of education is a less accurate measure of SES in this sample.

Racial/ethnic disparities in health have garnered a great deal of attention. Given that some of the worst disparities in health are seen as being embedded in the close re-
relationship between minority status and low SES, we would have welcomed the opportunity to examine this relationship and its influence on treatment response. However, the small number (n = 19) of minority-status subjects in our sample did not permit this. The analyses did suggest that race/ethnicity and SES are not synonymous. To the contrary, being nonwhite appeared to be associated with a greater likelihood of response. This may reflect lower lifetime rates of depression among nonwhite subjects, as has been observed in national epidemiology surveys, or it may reflect that, although minority persons generally lack adequate care for depression, once they receive it, they respond well. Further research, with more representative samples, is needed to disentangle the independent and interdependent effects of SES and race/ethnicity on depression and response to treatment.

Although the research reported herein is broadly consistent with results of previous work, there are several limitations. First, the use of census tract data on median household incomes is potentially problematic insofar as this may not be an accurate representation of an individual's own income. Without data on individuals' incomes, we cannot determine whether the associations between census tract median household income and response to treatment are due to the nature of the census tracts in which subjects lived, to the influence of subjects' actual household incomes, or to factors correlated with both. However, area-based measures of SES have been shown to be fairly stable over time, and have been shown to predict a range of health outcomes in general and for older adults in particular, and have been argued to provide valid approximations of social inequalities in health when individual data are not available. In particular, results from the Hampshire Depression Project are suggestive of neighborhood-level variation in antidepressant treatment. In that study, attendees of primary care practices that were located in low-SES neighborhoods were more likely to have depressive symptoms at baseline and 6 months.

Second, inferences about SES differences in response to treatment are constrained by the lack of a placebo arm. Thus, we cannot replicate the work of Rickels et al., who found relatively small differences between responses to antidepressant medication or placebo among low-SES patients in an outpatient clinic and relatively large medication-placebo differences among middle-SES general practice patients. However, given that their findings may have been biased by unknown factors in the different treatment settings, the question of whether SES patterns in response to active interventions are different from or simply mirror the “natural” course of depression more generally must await further investigation.

Third, one must be cautious in generalizing the results of these analyses. The psychological, biological, and social worlds of children, adolescents, and adults, and middle, and older adults are different, and, thus, we would expect that the relationship between SES and response to treatment, as well as the relative contributions of neighborhood effects and the characteristics of individuals, are likely to vary across age groups.

Despite its limitations, this study suggests that social worlds, in interaction with the demographic and clinical characteristics of individuals, may affect response to antidepressant treatment, even in clinical trials when subjects receive optimal pharmacologic and psychosocial treatments. Therefore, we suggest that future clinical trials routinely gather data on individual income, educational degrees earned, occupation, and aspects of the broader social environment such as social capital. However, to transform evidence into knowledge that will inform the treatment of depression, it is essential that future research examines all of the factors (eg, neighborhoods, stress, social support, race/ethnicity, income inequalities) that may mediate the association between SES and clinical outcomes.

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Correspondence: Alex Cohen, PhD, Department of Social Medicine, Harvard Medical School, 641 Huntington Ave, Boston, MA 02115 (alex_cohen@hms.harvard.edu).

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