ORIGINAL ARTICLE

The Relationship Between Antidepressant Medication Use and Rate of Suicide

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Background: Approximately 30 000 people die annually by suicide in the United States. Although 60% of suicides occur during a mood disorder, mostly untreated, little is known about the relationship between antidepressant medication use and the rate of suicide in the United States.

Objective: To examine the association between antidepressant medication prescription and suicide rate by analyzing associations at the county level across the United States.

Design: Analysis of National Vital Statistics from the Centers for Disease Control and Prevention.

Setting: All US counties.

Participants: All US individuals who committed suicide between 1996 and 1998.

Main Outcome Measures: National county-level suicide rate data are broken down by age, sex, income, and race for the period of 1996 to 1998. National county-level antidepressant prescription data are expressed as number of pills prescribed. The primary outcome measure is the suicide rate in each county expressed as the number of suicides for a given population size.

Results: The overall relationship between antidepressant medication prescription and suicide rate was not significant. Within individual classes of antidepressants, prescriptions for selective serotonin reuptake inhibitors (SSRIs) and other new-generation non-SSRI antidepressants (eg, nefazodone hydrochloride, mirtazapine, bupropion hydrochloride, and venlafaxine hydrochloride) are associated with lower suicide rates (both within and between counties). A positive association between tricyclic antidepressant (TCA) prescription and suicide rate was observed. Results are adjusted for age, sex, race, income, and county-to-county variability in suicide rates. Higher suicide rates in rural areas are associated with fewer antidepressant prescriptions, lower income, and relatively more prescriptions for TCAs.

Conclusions: The aggregate nature of these observational data preclude a direct causal interpretation of the results. A high number of TCA prescriptions may be a marker for those counties with more limited access to quality mental health care and inadequate treatment and detection of depression, which in turn lead to increased suicide rates. By contrast, increases in prescriptions for SSRIs and other new-generation non-SSRIs are associated with lower suicide rates both between and within counties over time and may reflect antidepressant efficacy, compliance, a better quality of mental health care, and low toxicity in the event of a suicide attempt by overdose.

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THE ENORMOUS HUMAN COST of suicide makes research and prevention a national priority. Worldwide, there are approximately 1 million suicides annually. In the last 25 years, approximately 750 000 people died by suicide in the United States, and suicides outnumber homicides by at least 3 to 2. Deaths from suicide exceeded deaths from AIDS by 200 000 in the past 20 years.[1] The estimated cost to the nation in lost income alone is $11.8 billion annually.[1] Biological, psychological, social, and cultural factors all have a significant impact on the risk of suicide; however, more than 90% of suicides in the United States are associated with psychiatric illness.[2-6] The most common psychiatric illness associated with suicide is a mood disorder,[2-7] and although most seek professional help within 1 month before death,[8] most are untreated at the time of death.[9-11]

The latter observation suggests that lack of treatment contributes to suicide risk and that more widespread antidepressant treatment may reduce suicide rates. At the same time, concerns have been raised about the capability of some medications, such as selective serotonin reuptake inhibitors (SSRIs), to reduce the risk of suicide in mood disorders, especially in youth (see http://www.fda.gov/cder/drug/advisory/mdd.htm). There is a paucity of random-

ized, controlled clinical trials that evaluate the safety and efficacy of any antidepressant medication in depressed patients at risk for suicide because of a history of suicidal behavior. In the absence of such data and the huge number of participants such studies would require to have adequate statistical power owing to the low base rate of suicide, alternative approaches are needed to provide an indication of the relationship between antidepressant treatment and suicide.

One approach involves large-scale naturalistic studies of at-risk populations, such as those with mood disorders. Lithium treatment of bipolar illness appears to reduce suicide rates,[12-17] although results vary across studies.[18-20] Another approach involves analyses of national population data sets. A decrease in suicide rate correlates with increased antidepressant use in Europe,[21-25] Scandinavia,[26] the United States,[27] and Australia.[28] Doubling of prescriptions for SSRIs correlated with a 25% decrease in the suicide rate in Sweden.[26] A study[29] in Italy found a 36% increase in prescription rates to correlate with an 18% decline in suicide rates in female individuals only. An educational intervention study[30] in a province in Sweden that targeted primary care physicians' recognition and treatment of depression had a disproportionate benefit for female suicide rates because of better help-seeking behavior in women. We found that antidepressant prescription rates have risen faster and the decrease in suicide rates has been greater in women in the United States.[31] Suicide and suicide attempts in patients with depression are associated with no treatment or inadequate prescription or consumption of antidepressants.[8,10,11,32,33]

Population-based changes in suicide rates may have explanations other than increased use of antidepressant medications.[1] Suicide rates have risen in Japan in the last 4 years, and so has the use of SSRIs.[34] Iceland has had no meaningful change in suicide rates despite a 4-fold increase in antidepressant prescriptions.[35] To better understand the association between antidepressant medication use and suicide completion, we obtained county-level data on suicide rates for 1996 to 1998 in the United States from the Centers for Disease Control and Prevention (CDC), Atlanta, Ga. These suicide rates vary enormously among counties; therefore, combining them with trends over time in county-level prescription levels in a single integrated analysis offers a more powerful tool for delineating suicidal risk factors than analyses over time. We analyzed the relationship between antidepressant pharmacy prescription volumes and suicide rate overall at the county level, adjusted for case mix (ie, sex, race, age, and income).

METHODS

The National Center for Health Statistics of the CDC maintains the National Vital Statistics,[36] including suicide rate data that are derived from state vital record systems based on local death certificate registries. Suicide rates for 1996 to 1998 were obtained from the CDC for each US county broken down by sex, race (African American vs other), and age (5-14, 15-24, 25-44, 45-64, and 65 years and older). County-level antidepressant medication prescription rate data designed to provide estimates of national and local prescription volumes (IMS Health Inc, Plymouth Meeting, Pa) came from a random sample of 20 000 pharmacies (stratified by type, size, and region) from the 36 000 pharmacies in the IMS Health Inc database, representing more than half of all retail pharmacies in the continental United States. The data do not include hospital prescriptions. Statistical methods are used to extrapolate these data to provide national figures. For each county, prescription rates (number of pills per county from 1996 to 1998) were obtained for 3 antidepressant subclasses: tricyclic antidepressants (TCAs), SSRIs (citalopram hydrobromide, paroxetine hydrochloride, fluoxetine hydrochloride, fluvoxamine maleate, and sertraline), and other non-SSRI antidepressants (nefazodone hydrochloride, mirtazapine, bupropion hydrochloride, and venlafaxine hydrochloride).

To relate antidepressant prescription use to suicide rate, adjusting for county-specific case mix (age, sex, and race), we used a mixed-effects Poisson regression model.[37-41] The mixed-effects Poisson regression model is suitable for rare-event data in which the observed number of suicides in a given county may be small (including zero) and the number at risk (ie, population size) may vary from county to county. The model estimates overall suicide rate conditional on age, sex, race, and antidepressant prescription and can also be used to estimate covariate-adjusted county-specific estimates of suicide rates. In terms of antidepressant drug prescription, we used the natural logarithm of number of pills per person per year to adjust for differential population size of counties and to eliminate excessive influence of counties with extremely high or low antidepressant prescription rates. In the model, age, sex, and race were considered fixed effects, and the intercept and antidepressant drug prescription effects were treated as random effects. This model specification allows both the suicide rate and the relationship between antidepressant drug prescription and suicide to vary from county to county. As such, we can estimate county-specific changes in suicide rates attributable to changes in antidepressant drug prescription, adjusted for the age, sex, and race composition of each county. The effect of policy changes (eg, adding or eliminating a particular type of antidepressant medication) can be estimated by accumulating the county-specific estimates across all counties. To test the possibility that the observed associations are simply due to access to quality health care, we included the effects of median county-level income as a covariate in a second model. To decompose the overall relationship between suicide rate and antidepressant drug prescription into intracounty and intercounty components, a third model was fitted using the county mean drug prescription and yearly deviation from the mean for each class of drugs as covariates in the model. The estimated coefficient for the mean drug use corresponds to between-county effect, and the estimated coefficient for the yearly deviations from the county mean corresponds to the within-county effect.

Parameters of the models were estimated using maximum marginal likelihood, whereas county-specific rates were obtained with empirical Bayes estimation using the method of Hedeker and Gibbons.[42] The computer program MIXPREG (http://www.uic.edu/labs/biostat) was used for these analyses. Complete statistical details are presented in the Institute of Medicine report *Reducing Suicide: A National Imperative*.[41]

RESULTS

To establish goodness of fit of the mixed-effects Poisson regression model to the observed data, observed and estimated (adjusted for age, sex, and race) suicide rates are given in **Table 1**. In general, suicide rate increases with age, is higher in male individuals, and is lower in Afri-

Table 1. Observed and Expected Suicide Rates by Age, Race, and Sex, 1996-1998

Individuals by Age Group, y	No. of Suicides	Population	Observed Rate	Expected Rate
5-14				
Black males	79	9 256 227	0.9	1.0
Black females	28	8 978 221	0.3	0.3
Other males	620	50 356 003	1.2	1.4
Other females	206	47 847 778	0.4	0.5
15-24				
Black males	1333	8 389 386	15.9	17.7
Black females	191	8 352 196	2.3	2.4
Other males	9482	47 906 710	19.8	22.2
Other females	1673	45 396 608	3.7	4.2
25-44				
Black males	2546	15 274 935	16.7	18.4
Black females	474	17 191 095	2.8	3.3
Other males	27 209	109 106 670	24.9	28.3
Other females	6977	108 864 081	6.4	7.2
45-64				
Black males	861	7 741 680	11.1	12.4
Black females	224	9 633 227	2.3	2.6
Other males	17 358	72 740 945	23.9	26.7
Other females	5307	76 289 629	7.0	7.8
≥65				
Black males	415	3 295 133	12.6	14.2
Black females	83	5 140 632	1.6	1.4
Other males	14 074	38 889 596	36.2	39.8
Other females	2814	55 229 051	5.1	5.7

can American individuals. Black female individuals have the lowest suicide rates across the age range. In white male individuals, the suicide rate increases with age, whereas in all other groups, the suicide rate is either constant or decreases after age 65 years. Comparison of the observed and expected frequencies reveals that the mixed-effects Poisson regression model fits the observed data extremely well. The observed number of suicides from 1996 to 1998 was 91 673, and the estimated rate (based on actual drug use) was 90 973, a difference of only 233 suicides per year (0.76%). Maximum marginal likelihood estimates (MMLEs), standard errors, and associated probability values for all main effects and 2-way interactions are presented in **Table 2**. The estimated marginal rates in Table 1 were obtained by exponentiating the MMLEs in Table 2, corresponding to each cell and integrating over the random-effects distribution.

Bayes estimates of county-level suicide rates adjusted for effects of race, sex, and age were obtained. A Bayes estimate of 1.0 represents an adjusted rate equal to the national rate, a Bayes estimate of 2.0 represents a doubling of the national rate, and a Bayes estimate of 0.5 represents half the national rate. Inspection of a map of the Bayes estimates (**Figure 1**), which are divided into quartiles, namely, 0.75 or less (at least 25% less than the national rate), 0.76 to 1.25 (equal to the national rate), 1.26 to 1.75 (25% to 75% greater than the national rate), and 1.76 or more (at least 75% greater than the national rate), reveals that even after accounting for these important demographic variables, considerable spatial or geographic variability remains. Highest adjusted rates are typically found in less densely populated areas of the western United States and Alaska.

Table 2. Maximum Marginal Likelihood Estimates, Standard Errors, and Probability Values for the Clustered Poisson Regression Model

Effect	MMLE	SE	*P* Value*
Intercept	−4.331	0.040	<.001
Female	−1.009	0.076	<.001
Black vs other	−0.292	0.103	.005
Age 15-24 vs 5-14 y	2.788	0.041	<.001
Age 25-44 vs 5-14 y	3.030	0.040	<.001
Age 45-64 vs 5-14 y	2.971	0.041	<.001
Age ≥65 vs 5-14 y	3.371	0.041	<.001
Female × black	−0.345	0.036	<.001
Female × age 15-24 y	−0.664	0.080	<.001
Female × age 25-44 y	−0.355	0.077	<.001
Female × age 45-64 y	−0.223	0.077	.004
Female × age ≥65 y	−0.938	0.078	<.001
Black × age 15-24 y	0.065	0.106	.54
Black × age 25-44 y	−0.139	0.105	.18
Black × age 45-64 y	−0.473	0.107	<.001
Black × age ≥65 y	−0.740	0.112	<.001
County variance	0.280	0.003	<.001

Abbreviations: MMLE, maximum marginal likelihood estimate.
**P* values for clustered Poisson regression model.

The overall relationship between all prescribed antidepressant drugs and suicide rate was not statistically significant ($z=-1.46$, $P=.14$). To determine whether antidepressant class-specific associations exist, a model with TCAs and SSRIs plus non-SSRIs was fitted to the data. The combination of SSRIs and non-SSRIs was used to avoid multicollinearity because these 2 drug classes were highly correlated ($r=0.98$).

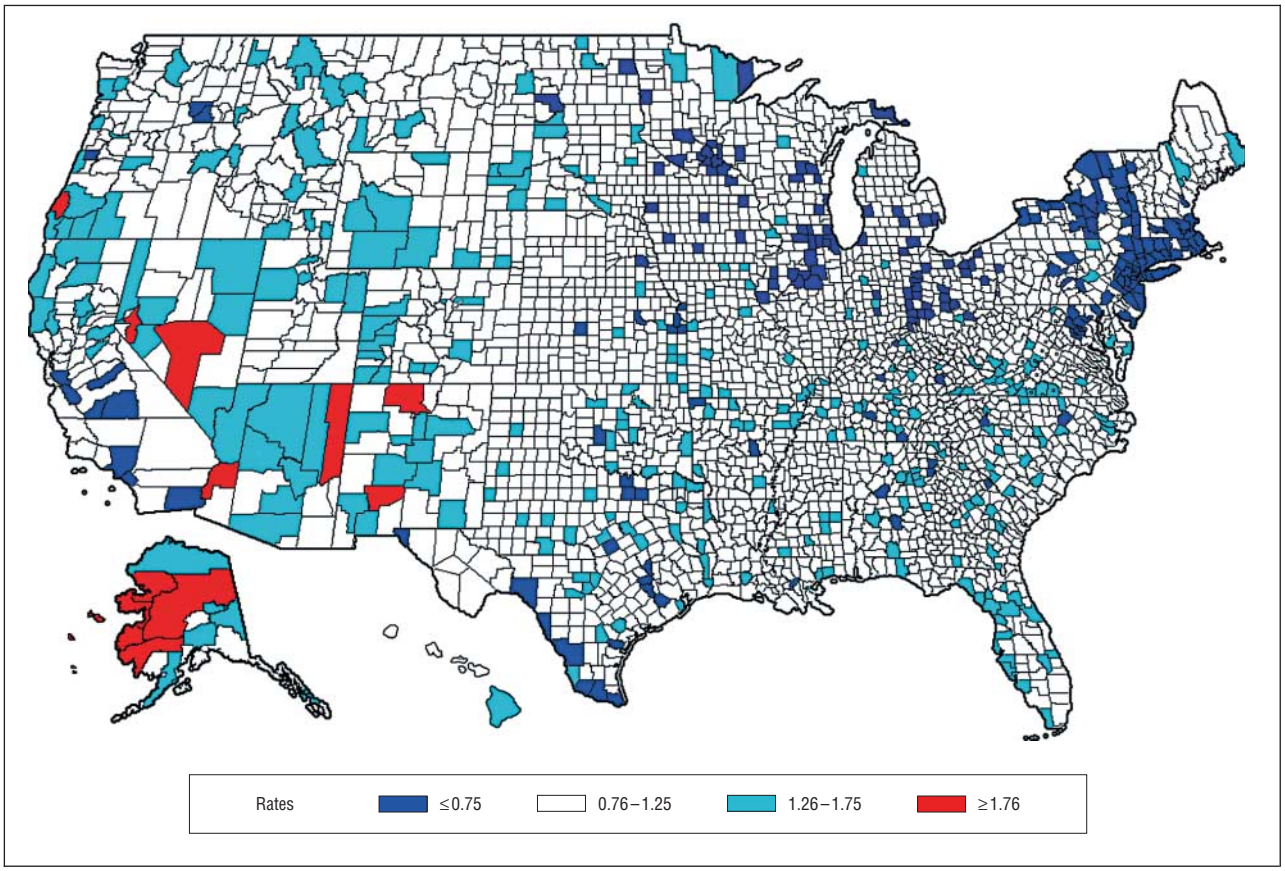

Figure 1. Statistical (empirical Bayes) estimates of county-specific adjusted annual suicide rates in the United States. A Bayes estimate of 1.0 indicates that the rate for the county was equal to the national rate of 12 per 100 000 population, a Bayes estimate of 2.0 represents a doubling of the national rate, and a Bayes estimate of 0.5 represents half the national rate. The estimates are based on all data from 1996 to 1998, adjusted for age, sex, and race.

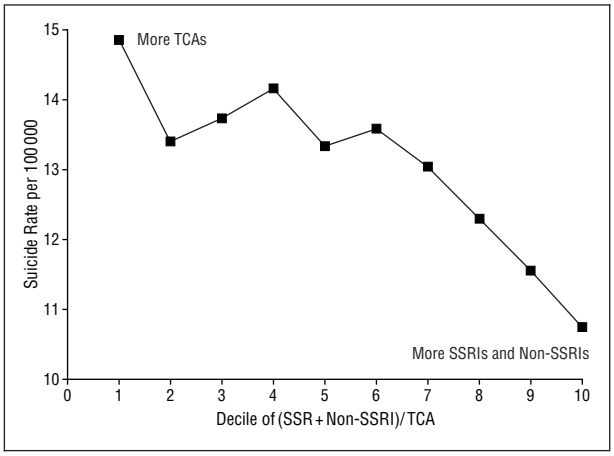

Figure 2. The relationship between the ratio of prescriptions for selective serotonin reuptake inhibitors (SSRIs) plus non-SSRIs to tricyclic antidepressants (TCAs) and observed suicide rate per 100 000 population in the United States, 1996-1998.

The MMLEs indicate that the combination of SSRI and non-SSRI or non-TCA prescriptions had a significant negative association with suicide rate (MMLE = –0.15, $P<.001$). Prescribed TCAs had a significant positive association with suicide rate (MMLE = 0.20, $P<.001$), meaning increases in prescribed TCAs are associated with increases in the suicide rate, whereas increases in prescribed SSRIs and non-SSRIs or non-TCAs are associated with decreases in the suicide rate. Because we have expressed prescribed TCAs and non-TCAs on logarithmic scales and the estimated coefficients are of opposite sign (prescribed TCAs had a positive association and non-TCAs had a negative association), this is mathematically equivalent to stating that the ratio of prescribed SSRIs plus non-SSRIs to TCAs is related to suicide rate. When this ratio is large (more SSRI and non-SSRI or non-TCA prescriptions), the suicide rate is lower, such as in Michigan, and when it is smaller (greater relative TCA prescription), the suicide rate is higher, such as in central and southern states.

Regarding magnitude of the case mix–adjusted effects, the mean population from 1996 to 1998 was 248 060 988, and the number of suicides during this 3-year period was 91 673, making an annual rate of 12.32 suicides per 100 000 population. Going from actual TCA prescription at that time to hypothetically no TCA prescription at that time (adjusted for age, sex, race, and SSRI plus non-SSRI or non-TCA prescriptions), the model estimates 10 237 fewer suicides per year (33%) or 4.12 per 100 000 population as the annual suicide rate. By contrast, if SSRI plus non-SSRI or non-TCA prescriptions were hypothetically eliminated, the estimated number of suicides would be predicted to increase by 15 202 suicides per year or the rate would increase by 6.13 per 100 000 population (a 50% increase). These effects are apparent in the raw data (ie, unadjusted for the effects of sex, age, and race) (**Figure 2**). For the lowest decile (high rela-

tive TCA prescription), the overall observed suicide rate is approximately 15 per 100 000 population, whereas for the highest decile (low relative TCA prescription), the suicide rate is approximately 10 per 100 000 population. Note that the finding of an association between TCA prescription and suicide rate does not necessarily imply that it is a causal association in which, for example, sometimes patients attempt suicide by an overdose of their antidepressant medication and TCA prescription leads to suicide or that overdoses of TCAs are much more commonly lethal compared with overdoses of other antidepressants. Prescriptions for TCAs may also be an indicator of one of many possible problems in the health care provision system, such as limited access to quality mental health care.

To further explore the relationship between antidepressant prescription and suicide, we present tabulations of suicide rates and TCA and non-TCA drug prescription rates stratified by county population size (**Table 3**) and county median income (**Table 4**). Table 3 reveals that suicide rates are highest in those counties with the smallest populations, where there is approximately a 1:1 ratio of non-TCA antidepressant to TCA prescription. In addition, the overall antidepressant prescription rate is lower in less densely populated counties. By contrast, in more densely populated counties, suicide rates are lower, overall prescription rates are higher, and the ratio of non-TCA antidepressant to TCA prescription is approximately 2:1. Rural areas may be poorer, have less access to psychiatrists, and have more undertreatment of depressive illness, perhaps through prescription of subtherapeutic doses of adverse effect–prone, older TCA medications that are more lethal on overdose, elevating suicide rates.

Table 4 reveals that suicide rates are also related to median income, with the wealthier counties having lower suicide rates. Again, the ratio of non-TCA antidepressant prescription to TCA prescription is approximately 1:1 in less affluent counties and approximately 2:1 in more affluent counties.

To shed further light on this hypothesis, median income for each county from the 2000 US census was included as a predictor in the model (in addition to age, sex, race, and antidepressant medication use). Income is related to suicide rate and had a negative coefficient (MMLE = –0.01, $P<.001$). Counties with higher incomes have lower suicide rates (adjusting for age, sex, and race composition). When income was included in the model, the overall magnitude of the antidepressant medication effects was reduced, but both remained statistically significant and in the same direction as those without income adjustment (TCA MMLE = 0.07, $P<.001$; SSRI plus non-SSRI or non-TCA MMLE = –0.04, $P<.001$).

Finally, drug effects were decomposed into between- and within-county effects. This was done by treating both the mean drug use (average for the 3 years) and the yearly deviation from the mean as random effects in the model. The mean drug use effect represents the between-county association between drug use and suicide, and the yearly deviation effect represents associations within counties between changes in drug use and changes in suicide rate. Significant between-county effects were observed as before, namely, a positive association between TCA prescription and suicide ($P<.001$) and a negative association between non-TCA prescription and suicide ($P<.001$). Within-county effects were also significant for non-TCA prescription and suicide ($P<.001$), in which increases in non-TCA prescription during the 3-year interval within counties were associated with lower suicide rates. By contrast, no significant within-county association between suicide rate and TCA prescription was observed, although the estimated coefficient was positive ($P=.39$).

Table 3. Suicide Rate, TCA Use, and SSRI Plus Non-SSRI Use by Population Size in Deciles

Decile of County Population Size	Suicide Rate per 100 000 Population	TCA Use, Pills per Person	SSRI Plus Non-SSRI Use, Pills per Person
52-4915	17.14	5.45	5.71
4916-8294	17.32	7.00	7.81
8295-12 220	15.02	7.65	8.23
12 221-16 476	16.08	8.26	9.09
16 477-22 244	14.66	8.34	9.75
22 245-31 265	14.41	8.56	13.46
31 266-43 610	14.09	9.15	11.36
43 611-73 598	13.68	8.81	12.06
73 599-150 702	12.86	8.98	19.12
150 703-8 351 444	11.51	7.44	13.39

Abbreviations: SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

Table 4. Suicide Rate, TCA Use, and SSRI Plus Non-SSRI Use by County Median Income in Deciles

Decile of County Median Income, $	Suicide Rate per 100 000 Population	TCA Use, Pills per Person	SSRI Plus Non-SSRI Use, Pills per Person
9243-25 399	13.32	8.28	8.18
25 400-28 273	13.38	8.23	8.91
28 274-30 227	14.92	8.87	10.72
30 228-31 774	14.91	8.78	11.41
31 775-33 435	13.47	8.00	10.69
33 436-35 600	13.62	9.40	13.59
35 601-37 737	14.21	9.09	13.26
37 738-40 794	12.93	8.77	18.64
40 795-46 106	12.03	7.23	12.68
46 107-82 929	10.63	7.15	14.16

Abbreviations: SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

COMMENT

Adjusted for age, sex, race, and county-to-county variability, overall antidepressant prescription and suicide were not associated. For individual classes of antidepressants, prescription of SSRIs and non-SSRIs or non-TCAs was associated with a lower suicide rate. Prescription of TCAs was associated with a higher suicide rate. This relationship persisted following adjustment for median county income, suggesting that a high relative pre-

scription rate of TCAs is not simply an indicator of limited access to quality mental health care but that choice of treatment matters. In that regard, it is notable that more TCA prescriptions are associated with fewer overall antidepressant prescriptions and lower income.

Decomposing the relationship between antidepressant drug prescription and suicide into between-county and within-county effects demonstrated a relationship between greater non-TCA prescription and lower suicide rates, both within counties and between counties. Prescription for SSRIs and non-SSRIs or non-TCAs is associated with decreases in suicide rate that appear unconfounded by other factors that can vary from county to county (eg, rate of depression, health care access, coverage by specialty mental health services, or socioeconomic status). The same cannot be said for TCAs. Within counties, changes in TCA prescriptions over time are not related to suicide rate; however, differences in TCA prescription between counties (averaging over time) are significantly associated with suicide rate, in which counties with higher TCA prescription had higher suicide rates. One possible explanation for this finding is that there is less within-county change in TCA prescription rates relative to the newer antidepressants, leading to less power to detect a within-county association. The statistical power for detecting a within-county effect is limited because it is partly dependent on the magnitude of changes that occur during the relatively short period for which we had data (1996-1998). Alternatively, high TCA prescription rates in a county may be a marker of poorer access to high-quality mental health care, poor detection or recognition of mental disorders, or poorer treatment and compliance, which in turn may be associated with higher suicide rates. As such, elimination of TCA prescriptions may not produce the decreases in suicide rate predicted by the statistical model. Again, caution must be used in deriving causal inference from analysis of data at this level of aggregation.

Our results agree with studies[21-26] in other countries that reported that a decrease in suicide rate correlated with increased antidepressant use over a particular period, including 2 studies[28,31] that linked the greatest decrease in suicide rates to the segment of the population (older men and women) that had the highest exposure to antidepressants. Suicidal behavior correlates with inadequate prescription of antidepressants,[32] and from 1978 to 1997, the proportion of the outpatient US population with depression receiving at least 1 antidepressant prescription increased from 37.3% to 74.5%.[8,10,43] Mood disorders accounted for 45% of all antidepressant prescriptions in 1997 and 59% in 2000,[31] so both the proportion and therefore the impact of more prescriptions on mood disorders are likely to have been sustained over this limited period for which we have data. What these data do not address is the adequacy of treatment and compliance. Given the adverse effects of TCAs, dose and compliance may be less adequately compared with SSRIs and contribute to the difference in relationship to suicide rates. Helgason et al[35] report that a 4-fold increase in antidepressant prescriptions from 1989 to 2000 in Iceland did not alter the suicide rate. They point out that the per capita use of alcohol also increased more than 50% in the same period and that self-reported use of antidepressants in Iceland was approximately half the prescribed rate. In the United States, most antidepressant prescriptions are for female patients and most suicides are committed by male individuals.[31] Most suicides[9] and serious nonfatal suicide attempts[44] are committed by individuals with major depression that is untreated at the time of death. These individuals may have a higher noncompliance rate with prescribed medication, especially antidepressants with more adverse effects, such as TCAs.

Thus, the increase in non-TCA prescriptions in the United States is most likely associated with treatment of more patients for depression and can thereby potentially lower suicide rates insofar as suicide most commonly occurs in patients with untreated depression.[33] The effect is limited because the highest-risk group may have a lower rate of antidepressant prescriptions and poorer compliance than the rest of the patient population with depression. The low base rate of suicide and the exclusion of suicidal patients from antidepressant treatment trials likely explain why randomized, controlled, antidepressant medication trials have failed to show a reduction in suicide rates.[45] In contrast, studies with a priori aims of studying antisuicidal effects of medications in at-risk individuals can show efficacy. For example, clozapine has a superior antisuicidal effect compared with olanzapine in suicidal patients with schizophrenia,[46] and lithium carbonate has antisuicidal superiority in mood disorders.[14]

This study has limitations. Medication estimates are based on outpatient use. There is some uncontrolled variability in the suicide rate data due to regional differences in the (1) definition of suicide; (2) qualifications of the coroner or medical examiner; (3) extent to which cases are investigated; (4) relationship between prescription rates and taking of medication (which may be weaker in high-risk groups); and (5) quality of preparation of official statistics (which can lead to differential underreporting of suicide rates).[1] Despite this potential variability, strong associations between antidepressant prescription rates and suicide rates were observed. Furthermore, since the associations were in opposite directions for TCAs vs SSRIs and newer non-SSRIs, this variability is not producing systematic bias.

We adjusted for county-level case mix using the suicide risk factors of age, sex, race, and income. Other relevant risk factors for suicide that were not included in our analysis are absorbed by the random effects in the model, which accommodates unobservable or unmeasured sources of county-to-county variability. A potentially important unmeasured variable is county-specific rate of depression. Perhaps less attention is paid to mental disorders in areas where TCA prescription is higher, leading to higher rates of suicide. This is consistent with our interpretation of the relationship between TCA prescription and suicide as a between-county effect, in which TCA prescription is related to lower income and may be a marker for less access to quality mental health services, poorer compliance, and/or poorer detection of depression, which in turn may lead to higher suicide rates due to inadequate treatment. Clearly, the findings of this study relate to associations in the data and not to causation. Randomized, controlled clinical trials in high-risk patients are still needed to confirm efficacy

of newer medications; however, it is unlikely that such studies could be adequately powered to detect such a rare event as suicide.

One possible cause of higher mortality due to suicide by individuals taking TCAs relative to SSRIs is that tricyclics are more toxic on overdose and death rates due to TCA overdose are higher relative to prescription volume compared with SSRIs and other new-generation antidepressants.[47] Given earlier concerns about the safety of SSRIs in adults with depression in terms of suicide risk and more recent concerns about the safety of SSRIs in youth with depression, our results and those of Olfson et al,[43] who performed a similar but less sophisticated analysis in youth, indicate that more SSRI prescriptions are associated with fewer suicides in adults and youth. The risk-benefit ratio associated with prescription of these antidepressants must be clearly favorable to explain the relationships observed in our study.

Overall adjusted suicide rates are extremely high in sparsely populated areas of the western United States and Alaska.[1] However, this is not always the case. Further study of factors that lead to low suicide rates in areas of sparse population with otherwise high suicide rates may identify additional risk factors and protective factors for suicide and ultimately enhance prevention efforts. Factors that may vary geographically and affect suicide rates include availability of health care services, marital status, presence of children in the home, levels of drug abuse, availability of guns, and socioeconomic class, which may depend on psychiatric illness and economic conditions.[48] National suicide prevention efforts should consider the impact of availability of health care services and emphasize the need for adequate diagnosis and treatment of psychiatric disorders.

Finally, the statistical methods used herein are particularly useful in the study of rare events obtained from clustered samples. Not only can we adjust for county-specific case mix, but we can also accommodate unobservable factors that account for county-to-county variability in observed rates. The mixed-effects Poisson regression model used herein fits the observed data extremely well both in the aggregate and at the county level. This type of statistical profiling has widespread application in medical research.

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Correction

Error in Text. In the Original Article titled "Sleep in Lifetime Posttraumatic Stress Disorder: A Community-Based Polysomnographic Study," published in the May issue of the ARCHIVES (2004;61:508-516), an error occurred in the text. On page 512, in the subsection titled "Sleep Breathing and Periodic Leg Movement," the first 2 sentences should have appeared as follows: "We used a cutoff of 5 events/h to measure sleep breathing disturbances (apnea-hypopnea). Findings were 5.2% in the first night and 5.1% in the second night (P=.20)." This correction does not change the observation of no significant difference between the first and second night.