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Antidepressants and Youth: Healing or Harmful?

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Abstract

A series of drug innovations that began in 1987, including the introduction of several Selective Serotonin Reuptake Inhibitors (SSRIs) has led to a tremendous growth in the use of antidepressants in the United States. This growth, however, has been accompanied by a growing concern about the risks of prescribing antidepressants, particularly to children. Indeed, research linking the use of antidepressant drugs to an increased risk of suicidal behaviors in youth motivated the U.S. Food and Drug Administration to direct antidepressant drug manufacturers to include warning labels about the potential dangers. This paper examines the relationship between antidepressants and suicide among youth in the USA. Using state-level data on youth suicides and age-specific prescriptions for antidepressants, we find no relationships between suicides for adolescents ages 15 to 19 and prescriptions for Selective Serotonin Reuptake Inhibitors/Serotonin-Norepinephrine Reuptake Inhibitors or tricyclic and tetracyclic antidepressants. In contrast, we find that newer generation antidepressants are associated with lower numbers of suicides for this age group. For younger children, ages 10 to 14 we find no relationship with suicides for any type of antidepressant.

Keywords

United States; antidepressants; suicides; youth

INTRODUCTION

During the last two decades the use of antidepressants has become increasingly common, even among children and adolescents. The increased use of antidepressants is partly due to a series of drug innovations that began in 1987, including the introduction of several selective serotonin reuptake inhibitors (SSRIs). Compared to earlier antidepressants such as tricyclic and tetracyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs), SSRIs are easier to administer, reduce the likelihood of overdose, and offer fewer negative side effects (USDHHS 1999). Subsequently, the late 1990s ushered in another set of new medications, including venlafaxine (*Effexor*) and nefazadone (*Serzone*) which affect both norepinephrine and serotonin (SNRIs), as well as chemically unrelated antidepressants, such as the sedating mirtazepine (*Remeron*) and the more activating bupropion (*Wellbutrin*).

Zito, Safer, DosReis, Gardner, Soeken, Boles, & Lynch (2002) show that antidepressant use increased tremendously among youth between 1988 and 1994. For example, in one mid-Atlantic state's Medicaid program, the rate of antidepressant use among 2–19 year olds rose

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from 3.9 per 1000 to 17.18. The authors find that TCAa were the most commonly used antidepressant in 1988, but this was equaled by SSRIs by 1994. In a more recent study, claims data from a private insurance company in the U.S. showed an antidepressant medication rate of 16.3 per 1000 for children ages 0–19, which is much higher than that found in three Western European Countries (Zito, Tobi, de Jong-van den Berg, Fegert, Safer, Janhsen et al. 2006). Yet another study found that youths ages 10–19 enrolled in a mid-Atlantic state's SCHIP program had higher rates of SSRI use than similar children in private insurance companies (2.7 percent vs. 2.2 percent). The discrepancy may be due to differences in provider payment arrangements, copayments, or health or racial disparities (Safer, Zito, & Gardner 2004).

As the use of antidepressant drugs in children has become more widespread, concern has grown about their risks. In 2003 a safety commission in the United Kingdom reviewed results from antidepressant drug trials and concluded that *Effexor* should not be used for depression treatment in children ages 6 to 17 due to the lack of demonstrated efficacy in treating depressive illness and a risk of harmful outcomes, such as hostility and suicidal ideation (Vitiello & Swedo, 2004). In 2004 the U.K. warning was broadened to include other SSRIs. Similarly, in October 2004 the United States Food and Drug Administration (FDA) issued a black box warning for inclusion in all antidepressants, stating that they increased the risk of suicidal thinking and behavior in studies of children with major depressive and other psychiatric disorders. The European Medicines Agency followed in April 2005 with a warning regarding the increased risk of suicide attempt and suicidal thoughts in children and adolescents. Its warning was targeted specifically at SSRIs and SNRIs.

The recommendations by these safety agencies are based on data from controlled drug trial results. For example, the recommendation by the FDA is based on a review of twenty-four placebo-controlled trials ranging from 4 to 16 weeks and involving nine antidepressant drugs. In total 4,100 subjects were included in the pediatric trials of SSRIs (Vitiello & Swedo, 2004). The FDA concludes, "the analysis showed a greater risk of suicidality during the first few months of treatment in those receiving antidepressants. The average risk of such events on drug was 4%, twice the placebo risk of 2%. No suicides occurred in these trials" (FDA, 2004). As with many randomized trials, these clinical studies suffer from small sample sizes and limited scope. Small sample sizes are particularly problematic in the current context, because completed suicides among children and adolescents are rare. In addition, depression itself increases the risk for suicide, and persons with a history of suicide attempt or with suicidal ideation are typically excluded from the trials. Furthermore, the trial results may not generalize from their controlled trial environments to more typical practice settings. Lastly, given the short duration of the studies, it is not clear if the increased risk occurs only at the onset of using the drugs or if it persists. Given these uncertainties it is not surprising that the FDA conclusion is being debated in the academic literature.

Recent research with a one-year community follow-up by the Treatment for Adolescents With Depression Study Team (TADS) compares rates of suicide ideation, attempts, and deaths based on treatment type. Specifically, this clinical trial compares outcomes among depressed youth receiving different combinations of cognitive-behavioral therapy (CBT) and the SSRI, fluoxetine (TADS 2004). The results show that teens receiving a combination of fluoxetine and CBT had the largest reduction in suicide thoughts. However, receiving fluoxetine alone yields the same reduction as a placebo. The numbers of suicide attempts in the sample were too small to provide meaningful statistical results, and no suicide deaths occurred during the study.

PREVIOUS RESEARCH

The existing non-experimental literature on antidepressants and suicide spans three types of studies. The first set of studies we identify compares aggregate national trends in suicides and antidepressant use within a given country. For many countries, the early 1990s were a time period when SSRIs rapidly entered the market. An examination of suicide rates before and after the introduction of SSRIs provides a natural experiment to attribute changes in the suicide rates to the introduction of certain drugs. Among adults, three studies observe a negative relationship between antidepressants and suicides (Hall, Mant, Mitchell, Rendle, Hickie & McManus, 2003; Carlsten, Waern, Ekedahl & Ranstam, 2001; Isacson 2000) while one study observes a negative relationship for females but a positive relationship for males (Barbui, Campomori, D'Avanzo, Negri & Garattini, 1998). Only the Carlsten et al. (2001) study examines the correlation between antidepressant use and suicides by age. Using data from Sweden the authors find a negative relationship between antidepressant sales and suicides for youth ages 15–24. The common flaw among these trend studies is that they rely on simple correlational analyses and for the most part do not control for other factors that may have changed concurrently with the suicide rate.

The next set of studies also use aggregate data on suicides and antidepressant use, but use multivariate regression to account for observed and unobserved covariates. Olfson, Shaffer, Marcus & Greenberg (2003) uses data on filled antidepressant prescriptions by age from two cross-sections in the late 1980s and the late 1990s. The study finds a negative relationship between antidepressant use and suicides. Dahlberg & Lundin (2004) analyze suicides by age group in Sweden from 1990 to 2000. They show there is no statistically significant effect of increased antidepressant sales on the suicide rate, but that there may be an increase in suicides among young persons under age 25 concurrent with increased antidepressant sales. Ludwig & Marcotte (2005) also incorporate observed covariate and unobserved covariates through the use of country fixed effects in their analysis of suicides and antidepressant sales in 27 countries. They find that suicides fall more sharply in countries with the greatest increase in antidepressant sales. However, they are not able to separate antidepressant sales by age group. Gibbons, Hur, Bhaumik & Mann (2005) study U.S. county level suicides and prescriptions from 1996 to 1998. They find a negative relationship between SSRI use and suicides and a positive relationship between TCA use and suicides. However, the Gibbons et al. (2005) study has only three years of data and is not able to separate prescription drugs by age group.

A third set of studies use patient-level data that includes both antidepressant use and suicide attempts. A study by Jick, Kaye & Jick (2004) uses a matched case control study of 300 patients in the UK. This study finds no statistical difference in the risk of suicidal behaviors among children ages 10 to 19 using SSRIs, compared to dothiepin, a commonly prescribed tricyclic antidepressant. However, if both types of antidepressants are associated with increased suicidal behavior then the study will find no effect by design. Valuck, Libby, Sills, Giese & Allen (2004) examine patient claims data from adolescents age 12 to 18 in the US. Among adolescents in treatment for major depression, they compare those receiving medication to those receiving therapy only. Adjusting for selection into treatment type (i.e., class of antidepressant medicine or no medicine), the authors find no statistical relationship between use and suicide attempts.

Our approach is similar to the second set of studies in that we link aggregate prescription data to aggregate suicide rates over several years. Consequently, we are able to construct a panel of state-level observations and control for a number of observed and unobserved covariates. The advantage of our study is that we observe antidepressant use for children and adolescents specifically and we observe suicides and prescriptions quarterly instead of annually.

METHODS AND DATA

The empirical model is shown in equation (1):

$$S_{ijt} = \delta_0 + \delta_1 A_{ijt} + \delta_2 X_{jt} + \delta_3 \gamma_j + \delta_4 \mu_t + \delta_5 (\mu * \tau)_{jt} + \epsilon_{ijt}. \quad (1)$$

Equation (1) specifies that suicides (S) for an age group (i) in a state (j) for a given year and quarter (t) is a function of antidepressant prescriptions (A_{ijt}), other determinants of suicides (X_{jt}), quarter-year effects (γ_t), state effects (μ_j), state*time interactions ($\mu * \tau$) and an error term. The principal hypothesis tested is whether or not antidepressants are associated with suicides and if so, in which direction.

Given that suicides are counts, we use the Fixed Effects Poisson (FEP) estimator to estimate the models (Wooldridge, 2002; Cameron & Trivedi, 1998). This estimator is a quasi-maximum likelihood estimator that includes parameters or “fixed effects” to account for unobserved heterogeneity across the units of observation (states, in our case). Estimates are consistent regardless of whether the counts actually have a Poisson distribution (Wooldridge 2002). To permit overdispersion, a common feature of count data that is not accommodated by the Poisson MLE, standard errors are adjusted for heteroskedasticity of unknown form (Cameron & Trivedi 2005). Each model includes the log of the relevant population as a right hand side variable to normalize for exposure. The coefficient on log population is constrained to equal one.

Data on completed suicides come from the Multiple Cause of Death public use files, provided by the Centers for Disease Control. From this data we calculate quarterly counts of suicides for 10–14 year olds and 15–19 year olds for each state in the years 1997–2003. We caution that the counts of suicides are probably underreported (Mohler and Earls 2001). However, so long as the underreporting is uncorrelated with our measures of antidepressant use, the underreporting will not bias the coefficients of interest. The only effect might be to raise the standard errors of the coefficients.

Data on antidepressants prescriptions come from IMS’s National Disease and Therapeutic Index (NDTI). The NDTI is a nationally representative sample of office based physicians in private practice drawn from a universe of all physicians in the United States. The sample is a randomly drawn, two-stage stratified cluster, where the stages are doctors and workdays. The sample of doctors is selected by primary specialty and the 9 census divisions. All primary specialties involved in direct patient care are included. Each physician reports information on all patients seen during two consecutive workdays in each calendar quarter. From the patient data, we create state-level quarterly counts of “drug appearances” (defined below) and prescriptions for antidepressants. We separate these into “new therapies” only and new and continued therapies combined (termed “all therapies”). New therapies mean that the drug therapy was started in the current visit. Continued therapies mean that the drugs were previously ordered and are continued. We examine new therapies separately from continued because research has shown that the risk of suicidal behaviors is the highest during the first few days of therapy (Jick et al., 2004).

A drug appearance is a mention of a drug during a patient visit. In the NDTI data, drug appearances include prescriptions, samples, drugs sold or given to the patient from their stock, hospital orders, drug recommendations that were not accompanied by a prescription, and drugs that were not issued during the current visit (i.e. no prescription, no sample and no medication sold, but drugs were issued on a previous visit). Non-issues only appear for continued therapies. We exclude drug recommendations from the counts so that our count total represents patients who have obtained or can obtain the drug with a prescription. We also use a separate variable for each antidepressant that counts only the actual prescriptions.¹ Actual prescriptions

represent a range of 66–91 percent of the drug appearances, depending on the year and drug under consideration.

We generate drug appearance counts for new therapies and all therapies for patients aged 10–14 and 15–19. The counts are then divided by the number of total patient visits for the relevant age group in each state, year and quarter and multiplied by 1000. Therefore, our measures of antidepressant use are the number of drug appearances per 1000 patient visits (in the relevant age group) in a state for a specific year and quarter for 1997–2003. We also create similar rate for new therapies that take the form of prescriptions only. Means for these and all other variables are shown in Table 1.

The NDTI identifies four groups of antidepressants: 1) Tricyclics and Tetracyclics (TCAs), 2) MAO Inhibitors (MAOIs), 3) SSRIs/SNRIs, 4) newer generation antidepressants (NGAs). Examples of TCAs include *Elavil*, *Amitriptyline* and *Imipramine*. Common SSRI/SNRIs include *Zoloft*, *Lexapro*, and *Prozac*. *Wellbutrin* is the most popular newer generation antidepressant. MAOIs are rarely prescribed to children. In the seven years of NDTI sample data, there is only one prescription of a MAOI for a child, therefore we exclude MAOIs as a separate category of antidepressants from this analysis. Annual trends in the three categories of antidepressants and suicides are shown in Figures 1 and 2 for ages 15–19 and Figures 3 and 4 for ages 10–14.

The NDTI data has two limitations worth noting. First, the prescription data are from office based physicians so any prescriptions from in-patient facilities are not included. Second, we have no way of knowing whether or not a prescription was filled or if a prescription was written after a sample was given.

In generating the drug appearance rate, we do not distinguish among visits to different types of physicians. However, the doctors in the NDTI data can be identified by specialty and we use this information to create a variable representing the percent of antidepressant drug appearances that come from a psychiatrist. This variable is included in all models and will help to capture some of the characteristics of our sample of patient cases that may be correlated with suicides and with the drug appearance counts in the data, such as illness severity. For example, Burns, Costello, Angold, Tweed, Stangl, Farmer et al. (1995) show that children with the most severe symptoms of mental illness are much more likely to visit a mental health specialist than any other source. These authors conclude, “For children with a diagnosis and/or impairment, the general health care system was rarely the sole source of mental health care.” p. 152. A study of adults found that individuals with more severe symptoms of major depressive disorder (MDD) were more likely to see psychiatrists than those with less severe symptoms (Kessler, Berglund, Demler, Jin, Koretz, Merikangas et al. 2003). Further, adequacy of treatment for MDD, defined as either pharmacotherapy or psychotherapy visits above specific thresholds, was greater in the specialty mental health sector than other sectors.

We include in the models two variables representing the supply of psychiatric care in each state. The variables are 1) the number of psychiatrists per 100,000 population; 2) the number of psychiatric hospital beds per 100,000 population. These variables are important to include because the availability of psychiatric care can affect suicides by influencing the full price of receiving mental health treatment through the availability of services. The full price includes not only the monetary cost of care, but travel and time costs as well. In the case of health care, the latter are likely to be a large part of the full price. We caution that these variable could be endogenous if the observed level of psychiatric care reflects the overall mental health status

¹Prescriptions are shown for new therapies only since prescriptions written under continued therapies represent only the renewals that are written during an office visit. This is not likely to be a good representation of the stock of antidepressant drugs being used by children.

of the state population. For example, holding all else constant, consumer demand theory predicts that there will be more psychiatrists demanded in states with higher rates of mental illness. However, we do not believe that the inclusion of these variables are problematic since models that omit these variables yield extremely similar results to those presented below.

A number of studies have shown that suicide rates are positively associated with higher rates of unemployment, lower income and lower education (Hamermesh and Soss 1974, Huang 1996; Marcotte 2003; Ostamo, Lahelma & Lönnqvist 2001), although these results are not upheld in some studies (Andres 2005; see Rehkopf and Buka 2006 for a comprehensive review). Higher levels of female labor force participation have also been observed to be correlated with suicide rates (Huang 1996; Burr, McCall & Powell-Griner 1997). To represent these factors, we include in all models the state quarterly unemployment rate, quarterly real income per capita, the annual percentage of the population ages 25 years and over that has obtained a bachelor's degree, and the female labor force participation rate. Unemployment and female labor force participation rates come from Department of Labor, Bureau of Labor Statistics. Per capita income comes from the Department of Commerce, Bureau of Economic Analysis, and educational attainment comes from the Department of Commerce, U.S. Census Bureau.

Higher suicide rates are often observed in rural areas (Middleton, Gunnell, Frankel, Whitley & Dorling 2003; Singh and Siahpush 2002; Wilkinson and Israel 1984). A person's religiosity is another factor that may predict suicidality (Huang 1996; Greening and Stoppelbein 2002). To represent these factors, we include the percentage of the state's population living in rural areas and the annual percentage of each state's population identifying with certain religions (Mormon, Southern Baptist, Protestant and Catholic). The rural population comes from the U.S. Census Bureau and the religion data come from Jones, Horsch, Houseal, Lynn, Marcum, Sanchagrin et al. (2002).

Substance use is also believed to be strong predictor of suicidal behaviors (Kelly, Lynch, Donovan & Clark 2002; Cutler, Glaeser, & Norberg. 2001; and Borges, Walters & Kessler 2000) In light of this relationship, state annual per capita beer consumption is included in all models following results from Markowitz, Chatterji & Kaestner (2004) showing a positive relationship between beer consumption and teenage suicides. Data on beer consumption come from the *Brewers Almanac* and are expressed in gallons per capita.

POTENTIAL ENDOGENEITY

The results of this study should be interpreted carefully and should be considered as correlations and not causal relationships. It is likely that the direction of causality runs from antidepressants to suicides, but this cannot be firmly established because of the potential for endogeneity of antidepressant prescriptions in the suicide equation. This endogeneity can come from two sources. The first is a correlation with unobserved factors in the error term. For example, one could argue that the number of suicides reflect the mental health of the population in general and that a change in the underlying mental health status would influence both suicides and treatment or antidepressant use. This is in essence a "third factor" story, where an unobserved third factor, the underlying mental health of the population, is correlated with the two observed variables. We can account for many of these unobserved factors through the use of state fixed effects, which will help to capture any unobserved time-invariant state effects which may influence suicide and may be correlated prescription practices. We also include a linear state-specific time trend in the models to capture quarterly state-specific trends that may coincide with the variables of interest. Finally, all models also include time dummies (representing the unique quarter and year of the observation) to capture secular trends in the suicide rates. In the tables below, we show models with and without the state fixed effects and state-specific trends.

The models without these variables serve as benchmark estimates, and are somewhat comparable to those prior studies that do not include controls for area-level fixed effects. As we will show in the results section, including these variables can make an important differences in the estimates.

The second source of endogeneity comes from the potential reverse causality from suicides to antidepressant prescriptions. For example, a suicide or more commonly, a suicide attempt in a community may lead to media coverage and information about the use and efficacy of antidepressants. The suicide and/or the media coverage could also lead to depression or other mental health problems in individuals. When these factors cause more individuals to seek treatment, antidepressant use could rise in a community as a result of the suicide. Negative publicity about antidepressants following a suicide could cause people to stop using the drugs.

Unfortunately, we do not have valid instruments to use that might allow us to estimate a simultaneous equation system and provide evidence for or against the exogeneity of the antidepressant appearances. However, one argument against the reverse causality story in our models is that suicides are extremely rare. In 2003, only 1,731 suicides occurred nationally among children ages 10–19, out of population of approximately 41.7 million. Also, the media tend to follow strict guidelines about publicizing suicides which include excluding the word “suicide” from headlines, avoiding detailed descriptions of the method, and avoiding dramatizing the suicide with descriptions and pictures of grieving friends and family. The publicity around suicides may simply not be present. Also, we tested models that include a one quarter lead of the antidepressant drug appearance measures instead of the current value. If reverse causality were problematic, we would expect to see a statistically significant correlation between the future antidepressant use and current suicides. However, this is not the case for in all models tested, every measures of antidepressant use is statistically insignificant when the leading value is considered. This exercise provides additional evidence against the reverse causality argument.

RESULTS

The results of the Poisson regression models are presented in Table 2 for suicides among teens ages 15–19 and in Table 3 for suicides among those ages 10–14. These two tables include the drug appearance rate as the independent variable of interest. Recall that drug appearances include prescriptions, samples, physician stock and hospital orders. Models that include only new prescriptions are presented in Table 4. Four models are presented in Tables 2 and 3. The first and second columns include drug appearances for new therapies, that is, the number of antidepressants per 1000 visits that were started in the current visit. The third and fourth columns include rates of all therapies, which includes new therapies and therapies that were previously ordered and are continued. These measures of antidepressant therapies reflect alternatively new starts and the stock of use. The first and third models exclude the state fixed effects and linear time trends, while the second and fourth models include these variables. Even though the latter models are our preferred specifications, we present the former as a benchmark to show how the coefficients may change by accounting for the unobserved state characteristics.

All models include the drug appearance rate for NGAs, SSRI/SNRIs and TCAs. Including all three simultaneously is not problematic because the correlations between the rates are very low. For all therapies, the simple correlation is 0.02 for TCAs and NGAs and 0.06 for TCAs and SSRI/SNRIs, and 0.22 for SSRI/SNRIs and NGAs. The correlations are even lower among new therapies: 0.02 for SSRI/SNRIs and NGAs, –0.01 for TCAs and NGAs and 0.02 for TCAs and SSRI/SNRIs.

Among 15–19 year olds, NGAs appear to have a negative relationship with the state-level suicide count. This holds for new therapies and all therapies. The coefficients are statistically significant in three of the four models at at least the 10 percent level in a two-tailed test. Only when state fixed effects and linear trends are excluded for new therapies is the coefficient on NGAs insignificant. Using the more inclusive specification that includes state fixed effects and state linear trends, the results indicate that every additional NGA drug appearance per 1,000 visits is associated with a 0.4 percent decrease in suicides per quarter for new therapies and a 0.2 percent reduction in suicides per quarter for each for new and continuing therapies. Note that each additional drug appearance per 1000 visits represents a large increase (60.35%) over the mean of 1.66. In percentage terms, a 10 percent increase in new NGA appearances is associated with an average reduction in suicides of 0.066 percent per quarter, while a 10 percent increase in new and continued NGA appearances is associated with an average reduction in suicides of 0.116 percent per quarter.²

The results for the SSRIs/SNRIs are interesting in that new therapies of these drugs are not statistically associated with changes in the suicide counts. For all therapies, the coefficient on the SSRI/SNRI appearances is positive and statistically significant at the 10 percent level in the model when state fixed effects and linear trends are excluded. This is the result that worries the US Food and Drug Administration, the UK Committee on Safety of Medicines and the European Medicines Agency. However, the positive relationship between SSRIs/SNRIs and suicides disappears once unmeasured state effects are included. TCAs tell a similar story to the SSRIs/SNRIs in that there appears to be no statistical relationship between TCAs and suicides among teenagers ages 15–19.

Table 3 shows the results for suicides among children ages 10–14. Here, none of the coefficients on the antidepressants are statistically significant implying that there is no discernable relationship between the mention of the drugs and suicides among young teenagers. We caution that suicides among this age group are extremely rare and we may simply not have the power to detect any effects.

Table 4 shows results from models that consider new prescriptions only (i.e., excluding visits with drug mentions that are samples, hospital orders, or similar). For brevity, only the coefficients on the antidepressant rates are listed. Columns 1 and 2 presents results for suicides among children ages 15–19 and columns 3 and 4 presents results for suicides among children ages 10–14. The results in Table 4 are consistent with the results of the previous tables. Newer generation antidepressants are negatively associated with the suicide count for 15–19 year olds but have no association with the suicide count of younger children. None of the other antidepressants have a statistically significant relationship with suicides for either age group.

The results of the other included variables show that once the state dummies and trends are added, few other factors are associated with suicide. In these models, for the older teens, Table 2 shows that higher state unemployment rates are positively associated with suicides. This results confirms results found by Hamermesh & Soss (1974), Huang (1996), and Ostamo et al. (2003). We also find that in our preferred models, beer consumption is negatively related to suicide. This last result is in stark contrast to the positive and significant beer consumption coefficients in the models without the fixed effects. This result also does not confirm previous findings by Kelly et al. 2002, Cutler et al. 2001, and others. The discrepancy in our results may

²To put our results for newer generation antidepressants into context, the Goldsmith, Pellmar, Kleinman & Bunney (2002) estimates the total value of lost productivity due to suicides in the United States at \$11.8 billion in 1998, or approximately \$386,000 per death. This number excludes the costs of medical and funeral expenses, and the costs to the victim's family. This number also applies to victims of all ages, and would be much higher for youth since they face a longer time frame of lost wages. This can be compared to estimates of lifetime medical treatment costs for antidepressants of different classes, including newer generation drugs, ranging from approximately \$15,000 to \$17,000 (Revicki, Brown, Keller, Gonzales, Culpepper, & Hales 1997).

arise from different samples, time periods and estimation techniques. Our results for beer consumption should be considered with skepticism, particularly since we are using the consumption levels of the entire population to predict youth suicide. Data on youth consumption would be more appropriate, however, to the best of our knowledge such data is not available on a state level.

None of the other included variables are statistically related to suicides in our preferred models for children ages 15–19. In addition, only one variable is statistically related to suicides among younger children ages 10–14 in our preferred models. Table 3 shows that states having a higher percentage of residents identifying themselves as Southern Baptist also have higher suicide rates among this age group. In addition to the potential power problems discussed previously for this age group, the inclusion of the state fixed effects and linear trends may eliminate all the independent variation in many of these included variables. Note that many of the variables do predict suicides for both age groups when the fixed effects and trends are excluded. Factors such as per capita income, education level, beer consumption, percent rural, and certain religions are all statistically associated with suicides among youth ages 10–14 and 15–19.

CONCLUSION

This study uses seven years of quarterly data on aggregate trends in suicides and antidepressants among children and youth. Ultimately, we do not find evidence that would support the concerns of the international drug safety authorities. We should note that our study examines completed suicides rather than suicide ideation or attempts. Nevertheless, we find no statistically significant relationship between SSRI/SSNRIs or TCAs and suicides for adolescents ages 15–19. In contrast, we find that newer generation antidepressants are associated with lower numbers of suicides. For younger children, ages 10 to 14 we find no relationship for any type of antidepressant (NGA, SSRI/SNRI, or TCA), but our conclusions are more tenuous for this age group as our study may be underpowered. Further research, particularly on this youngest age group, is warranted.

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Sources: Drug Appearances: National Disease Therapeutic Index, IMS Health, 1997-2003
 Suicides: Multiple Cause of Death public use files, Centers for Disease Control, 1997-2003

Figure 1.
 Antidepressant Appearances, New Therapies, Ages 15–19

Sources: Drug Appearances: National Disease Therapeutic Index, IMS Health, 1997-2003
 Suicides: Multiple Cause of Death public use files, Centers for Disease Control, 1997-2003

Figure 2.
 Antidepressant Appearances, All Therapies, Ages 15–19

Sources: Drug Appearances: National Disease Therapeutic Index, IMS Health, 1997-2003
 Suicides: Multiple Cause of Death public use files, Centers for Disease Control, 1997-2003

Figure 3.
 Antidepressant Appearances, New Therapies, Ages 10–14

Sources: Drug Appearances: National Disease Therapeutic Index, IMS Health, 1997-2003
 Suicides: Multiple Cause of Death public use files, Centers for Disease Control, 1997-2003

Figure 4.
 Antidepressant Appearances, All Therapies, Ages 10–14

Table 1**Means and Standard Deviations**

Variable name	Definition	Age 15–19 Mean, SD	Age 10–14 Mean, SD
Suicides	State-level suicide count, by year and quarter	8.19, 7.69	1.42, 1.73
New therapies: NGAs	Number of new NGA appearances (prescriptions, samples, physician stock, and hospital orders) per 1000 patient visits. Number of NGA prescriptions per 1000 patient visits for the age group.	1.66, 7.28 1.16, 6.26	0.95, 5.29 0.69, 4.69
New therapies: SSRIs/SSNIs	Number of new SSRI or SNRI appearances (prescriptions, samples, physician stock, and hospital orders) per 1000 patient visits. Number of new SSRI or SNRI prescriptions per 1000 patient visits for the age group.	8.78, 20.13 4.70, 13.75	3.85, 11.48 2.88, 10.01
New therapies: TCAs	Number of new TCA appearances (prescriptions, samples, physician stock, and hospital orders) per 1000 patient visits. Number of new TCA prescriptions per 1000 patient visits for the age group.	1.78, 8.49 1.63, 8.25	1.76, 11.91 1.66, 11.81
All therapies: NGAs	Number of new and continuing NGA appearances (prescriptions, samples, physician stock, hospital orders, and non-issues) per 1000 patient visits.	7.49, 16.64	5.27, 14.49
All therapies: SSRIs/SSNIs	Number of new and continuing SSRI or SNRI appearances (prescriptions, samples, physician stock, hospital orders, and non-issues) per 1000 patient visits.	31.31, 41.55	16.64, 28.70
All therapies: TCAs	Number of TCA appearances (prescriptions, samples, physician stock, hospital orders, and non-issues) per 1000 patient visits.	4.33, 11.85	6.36, 18.05
% drug appearances from psychiatrists	Percent of all types of antidepressant drug appearances from psychiatrists in NDTI data.	0.32, 0.39	0.25, 0.39
State psychiatrists	Number of psychiatrist in the state per 100,000 residents	12.96, 8.68	12.77, 8.21
State psychiatric beds	Number of psychiatric beds in the state per 100,000 residents	35.82, 27.46	35.77, 27.50
Unemployment rate	Quarterly state unemployment rate	4.57, 1.21	4.56, 1.21
Real income	Quarterly state real income per capita (in \$1000s)	16.23, 2.65	16.19, 2.60
Percent college	Percent of the state population with a college education	25.17, 5.11	25.10, 5.00
Female labor force participation	State female labor force participation rate	61.14, 4.24	61.13, 4.25
Beer consumption	State per capita beer consumption in gallons	22.68, 3.70	22.66, 3.70
Percent rural	Percent of the state population living in rural areas	28.08, 15.16	28.24, 15.07
Percent Mormon	Percent of the state population Mormon	2.94, 9.83	2.95, 9.86
Percent Southern Baptist	Percent of the state population Southern Baptist	7.09, 9.69	7.09, 9.72
Percent Catholic	Percent of the state population Catholic	19.98, 12.38	19.94, 12.40
Percent Protestant	Percent of the state population Protestant	19.01, 8.95	19.01, 8.97

Note: Observations are quarterly for the years 1997–2003, with the fourth quarter of 1999 excluded because of missing IMS data.

Table 2
Drug Appearances Dependent Variable=Suicides, Ages 15–19

	Baseline Model, New Therapies (1)	Expanded Model, New Therapies (2)	Baseline Model, All Therapies (3)	Expanded Model, All Therapies (4)
New therapies: NGAs	−0.003 (−1.28) [0.997]	−0.004 (−2.08) [0.996]		
New therapies: SSRIs/SSNIs	−0.0003 (−0.41) [1.000]	−0.001 (−1.24) [0.999]		
New therapies: TCAs	0.0003 (0.19) [1.000]	0.0003 (0.18) [1.000]		
All therapies: NGAs			−0.002 (−1.92) [0.998]	−0.002 (−1.87) [0.998]
All therapies: SSRIs/SSNIs			0.001 (1.67) [1.001]	0.0001 (0.17) [1.000]
All therapies: TCAs			0.0005 (0.40) [1.000]	0.0005 (0.45) [1.000]
% antidepressant drug appearances from psychiatrists	0.051 (1.48) [1.053]	0.055 (1.52) [1.056]	0.041 (1.10) [1.042]	0.064 (1.76) [1.066]
State psychiatrists	0.001 (0.23) [1.001]	−0.067 (−1.42) [0.935]	0.001 (0.23) [1.001]	−0.063 (−1.33) [0.939]
State psychiatric beds	0.001 (0.77) [1.001]	−0.0003 (−0.18) [1.000]	0.001 (0.76) [1.001]	−0.0003 (−0.22) [1.000]
Unemployment rate	0.004 (0.23) [1.004]	0.066 (1.97) [1.068]	0.002 (0.13) [1.002]	0.067 (1.98) [1.069]
Real income	−0.073 (−4.71) [0.930]	0.003 (0.05) [1.003]	−0.075 (−4.85) [0.928]	−0.0001 (−0.002) [1.000]
Percent college	0.018 (3.45) [1.018]	0.015 (1.41) [1.015]	0.018 (3.36) [1.018]	0.015 (1.41) [1.015]
Female labor force participation rate	0.007 (1.38) [1.007]	−0.009 (−0.66) [0.991]	0.007 (1.40) [1.007]	−0.009 (−0.66) [0.991]
Beer consumption	0.039 (8.04) [1.040]	−0.070 (−1.90) [0.932]	0.039 (8.00) [1.040]	−0.069 (−1.89) [0.933]
Percent rural	0.004 (2.18) [1.004]	−0.051 (−0.73) [0.950]	0.004 (2.02) [1.004]	−0.052 (−0.72) [0.950]
Percent Mormon	0.013 (6.33) [1.013]	−1.002 (−0.95) [0.367]	0.012 (6.03) [1.012]	−1.009 (−0.96) [0.364]
Percent Southern Baptist	−0.007 (−3.72) [0.993]	−0.706 (−1.14) [0.494]	−0.007 (−3.77) [0.993]	−0.678 (−1.09) [0.508]
Percent Catholic	−0.005 (−2.70) [0.995]	0.059 (0.28) [1.061]	−0.005 (−2.66) [0.995]	0.052 (0.24) [1.053]
Percent Protestant	0.006 (2.22) [1.006]	−0.063 (−0.26) [0.939]	0.005 (1.99) [1.005]	−0.076 (−0.32) [0.927]
State fixed effects	No	Yes	No	Yes
State trends	No	Yes	No	Yes

Note: Drug appearances include prescriptions, samples, physician stock, hospital orders and for all therapies, non-issues. All therapies include new and continued therapies. Each cell shows coefficients from the fixed effects Poisson model, z-statistics in parentheses, and incidence rate ratios (exp(b)) in brackets. Intercepts are not shown. N=1,324. All models also include dichotomous indicators for the year and quarter of the observation, and the state population of people ages 15–19. Columns 2 and 4 also include dichotomous indicators for each state and a linear time trend for each state.

Table 3
Drug Appearances Dependent Variable=Suicides, Ages 10–14

	Baseline Model, New Therapies (1)	Expanded Model, New Therapies (2)	Baseline Model, All Therapies (3)	Expanded Model, All Therapies (4)
New therapies: NGAs	0.0004 (0.07) [1.000]	0.004 (0.76) [1.004]		
New therapies: SSRIs/SSNIs	−0.002 (−0.75) [0.998]	−0.001 (−0.55) [0.999]		
New therapies: TCAs	−0.003 (−0.85) [0.997]	−0.003 (−1.03) [0.997]		
All therapies: NGAs			0.001 (0.63) [1.001]	0.002 (0.97) [1.002]
All therapies: SSRIs/SSNIs			0.0003 (0.26) [1.000]	−0.0004 (−0.29) [1.000]
All therapies: TCAs			−0.001 (−0.30) [0.999]	−0.001 (−0.39) [0.999]
% antidepressant drug appearances from psychiatrists	0.010 (0.12) [1.000]	−0.052 (−0.56) [0.949]	−0.065 (−0.79) [0.937]	−0.055 (−0.55) [0.946]
State psychiatrists	−0.003 (−0.36) [0.997]	−0.007 (−0.06) [0.993]	−0.004 (−0.42) [0.996]	−0.008 (−0.07) [0.992]
State psychiatric beds	−0.0003 (−0.22) [1.000]	0.001 (0.24) [1.001]	0.000 (−0.17) [1.000]	0.001 (0.22) [1.001]
Unemployment rate	0.010 (0.26) [1.010]	0.047 (0.60) [1.048]	0.008 (0.21) [1.008]	0.043 (0.54) [1.044]
Real income	−0.067 (−1.90) [0.935]	−0.011 (−0.08) [0.989]	−0.068 (−1.92) [0.935]	−0.015 (−0.11) [0.986]
Percent college	0.035 (3.13) [1.036]	−0.023 (−0.91) [0.977]	0.036 (3.21) [1.037]	−0.024 (−0.96) [0.976]
Female labor force participation	0.005 (0.42) [1.005]	−0.031 (−0.89) [0.970]	0.003 (0.30) [1.003]	−0.028 (−0.81) [0.972]
Beer consumption	0.060 (5.20) [1.062]	−0.079 (−0.81) [0.924]	0.060 (5.17) [1.061]	−0.079 (−0.81) [0.924]
Percent rural	0.011 (2.71) [1.011]	0.100 (0.57) [1.105]	0.010 (2.39) [1.010]	0.095 (0.54) [1.100]
Percent Mormon	0.014 (3.05) [1.014]	0.857 (0.37) [2.355]	0.014 (2.96) [1.014]	0.639 (0.28) [1.895]
Percent Southern Baptist	−0.016 (−3.58) [0.984]	6.674 (3.61) [791.8]	−0.015 (−3.43) [0.985]	6.692 (3.63) [805.7]
Percent Catholic	−0.010 (−2.63) [0.990]	−0.742 (−1.31) [0.476]	−0.010 (−2.53) [0.990]	−0.753 (−1.33) [0.471]
Percent Protestant	0.004 (0.63) [1.004]	−0.730 (−1.12) [0.482]	0.004 (0.72) [1.004]	−0.726 (−1.12) [0.484]
State fixed effects	No	Yes	No	Yes
State trends	No	Yes	No	Yes

Note: Drug appearances include prescriptions, samples, physician stock, hospital orders and for all therapies, non-issues. All therapies include new and continued therapies. Each cell shows coefficients from the fixed effects Poisson model, *z*-statistics in parentheses, and incidence rate ratios (exp(*b*)) in brackets. Intercepts are not shown. *N*=1,316. All models also include dichotomous indicators for the year and quarter of the observation and the state population of people ages 10–14. Columns 2 and 4 also include dichotomous indicators for each state and a linear time trend for each state.

Table 4
Select Coefficients, New Prescriptions Only Dependent Variable=Suicides

	Ages 15–19 (N=1,324)		Ages 10–14 (N=1,316)	
	Baseline Model, New Therapies (1)	Expanded Model, New Therapies (2)	Baseline Model, New Therapies (3)	Expanded Model, New Therapies (4)
New therapies: NGAs	−0.005 (−1.87) [0.995]	−0.005 (−1.98) [0.995]	0.001 (0.20) [1.001]	0.005 (0.76) [1.005]
New therapies: SSRIs/SSNIs	−0.0005 (−0.45) [1.000]	−0.001 (−0.81) [0.999]	−0.002 (−0.65) [0.998]	−0.001 (−0.43) [0.999]
New therapies: TCAs	0.001 (0.31) [1.001]	0.001 (0.32) [1.001]	−0.003 (−0.88) [0.997]	−0.003 (−0.91) [0.997]

Note: Drug appearances include prescriptions only. Each cell shows coefficients from the fixed effects Poisson model, z-statistics in parentheses, and incidence rate ratios (exp(b)) in brackets. Intercepts are not shown. All models also include percent of drug appearances from psychiatrists, per capita psychiatrists and psychiatric beds, the state unemployment rate, real income per capita, education, female labor force participation rate, beer consumption, percent in rural areas, religion variables, dichotomous indicators for the year and quarter of the observation, and the relevant age-specific state population. Columns 2 and 4 also include dichotomous indicators for each state and a linear time trend for each state.