THE FDA AND ABCS:
THE UNINTENDED CONSEQUENCES OF ANTIDEPRESSANT WARNINGS ON HUMAN CAPITAL

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## **ABSTRACT**

Using annual cross-sectional data on over 100,000 adolescents aged 12-17, we studied academic and
behavioral outcomes among those who were and were not likely affected by FDA warnings regarding
the safety of antidepressants. Just before the FDA warnings, adolescents with probable depression
had grade point averages 0.14 points higher than adolescents with depression just after the warnings.
The FDA warnings also coincided with increased delinquency, use of tobacco and illicit drugs.  Together,
our results stress the importance of mental health and its treatment as an input into cognitive and non-cognitive
aspects of human capital.

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A burgeoning theoretical and empirical literature argues that compared with cognitive aspects of human capital, "non-cognitive" aspects of human capital are equally important. Empirical evidence links varied non-cognitive characteristics, ranging from measured hyperactivity, anxiety, locus of control, and self esteem in childhood to later wages, income, and social outcomes (Jo Blanden et al., 2006, Lex Borghans et al., 2008, Samuel Bowles et al., 2001, Janet Currie and Mark Stabile, 2009, James J. Heckman et al., 2006). A universally agreed upon construct of non-cognitive dimensions of human capital is not yet available, and researchers currently describe these in a variety of ways. For example, Currie and Stabile (2009), argue that non-cognitive aspects of human capital "are likely to capture some aspects of mental health as well as innate character traits" (e.g., being extroverted).

An important gap in this promising strand of literature is a full understanding of whether the deleterious effects of mental disorders on human capital are malleable when addressed through policy or clinical intervention. In the last several decades, innovations in pharmaceutical and behavioral treatments for mental health conditions have drastically altered the treatment of emotional and behavioral problems in children. This paper exploits a dramatic change in treatment of a common condition during adolescence -- depression -- that is often linked with poor productivity in early and later adulthood, to examine how depression and its treatment affect a broad set of human capital measures including academic outcomes, delinquency, and substance use.

By age 18, an estimated 15 percent of US children, or around 3 million, will have experienced some type of depression (K. R. Merikangas et al., 2010). Each year, nearly 9 percent of adolescents have suffered major depression, defined as either depressed mood or loss of interest or pleasure and four or more other depression symptoms continuously for at least two weeks (Substance Abuse and Mental Health Services Administration (SAMHSA), 2007).[1] The same sources estimate that under half of these children receive treatment for depression in a given year. In adults, depression has been associated with lower productivity. Adults with depression have lower rates of employment and lower earnings among individuals who do work

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[1] In addition to mood and suicidal thoughts/actions symptoms used in the DSM-IV diagnosis of depression focus on changes in: sleep, eating, energy, concentration, and self-image.

(Susan L. Ettner et al., 1997). There is some suggestion that depression during adolescence affects life cycle productivity, by affecting human capital investment (Ernst R. Berndt et al., 2000, Weili Ding et al., 2009, Jason M. Fletcher, 2008). In addition to its effect on mood, depression causes restlessness, anxiety, difficulty with concentration, and feelings of worthlessness, all of which may inhibit academic performance or other aspects of human capital. However, depression's effect on human capital is difficult to measure due to omitted variable biases, described in more detail below. Hence, a policy action which significantly alters the use of antidepressants offers a unique opportunity to learn about depression and its treatment.

In May of 2003, the manufacturer of Paxil, a popular antidepressant generically known as paroxetine, notified the Food and Drug Administration (FDA) that paroxetine increased suicidal thoughts and actions in some pediatric clinical trial participants. This report launched a series of FDA actions including public communications regarding the safety of paroxetine, public hearings regarding evidence on the safety of *all* antidepressants, and ultimately, the October 2004 decision to require black-box warnings regarding the safety of pediatric antidepressant use on virtually all antidepressant product labels and packaging.

The evidence to date demonstrates that the FDA's actions (and the public response to these actions) had a profound effect on treatment patterns for adolescent patients with depression. The release of this new safety information was widely covered in the popular press (Colleen L Barry and Susan H Busch, 2010), and accompanied abrupt declines in pediatric antidepressant use of 20-30 percent following years of steady increases in the number and share of youth treated with antidepressants (Susan H Busch et al., 2010, Robert D. Gibbons et al., 2007, Anne M. Libby et al., 2007, Charles B. Nemeroff et al., 2007, Mark Olfson et al., 2008, Jim Rosack, 2005). Critics of the FDA warnings expressed concerns regarding the impact of the warnings on clinical outcomes. These concerns increased when youth suicide rates climbed abruptly in 2004 and 2005, following a decade of relatively steady decline (Jeffrey A. Bridge et al., 2008, Robert D. Gibbons, C. Hendricks Brown, Kwan Hur, Sue M. Marcus, Dsulal K. Bhaumik, Joelle A. Erkens, Ron M.C. Herings and J. John Mann, 2007). To examine the effects of treated and untreated adolescent depression on human capital outcomes, we exploit the abrupt change in pediatric antidepressant use induced by FDA warnings to compare outcomes of adolescents who sought professional help for depression problems just before and just after the release of the FDA advisories in 2004.

This unique natural experiment permits us to examine several questions with relevance for the economics of human capital, for health policy, and for clinical practice. First, it allows us to study potential unintended consequences of a regulatory policy designed to protect pediatric patients from safety risks of a widely used class of pharmaceuticals. Second, the FDA's actions permit us to estimate effects of reducing the pharmaceutical treatment of depression on human capital development in adolescents. Third, we compare the effects of depression problems among adolescents more and less likely to receive antidepressants, in a real world setting, rather than the more pristine setting of clinical trial research. During the period immediately before and after the FDA warnings on antidepressants, the extensive margin of treatment (seeking any treatment versus none) did not change measurably, as we describe below. However, the intensive margin of treatment fell as patients were less likely to receive antidepressants. Throughout the paper, we refer to a decline in treatment to describe this movement along the intensive margin from treatments that include an antidepressant to those that do not. Such evidence can provide information on whether policies expected to improve access to mental health treatment such as *The Mental Health Parity and Addiction Equity Act of 2008* and the 2010 *Patient Protection and Affordable Care Act*, have the potential to influence economic outcomes for adolescents with depression.

Using seven years of the annual cross-sectional National Survey on Drug Use and Health (2001-2007), we use a difference-in-difference design to study academic and behavioral outcomes in over 100,000 adolescents aged 12-17, comparing outcomes for adolescents with and without a recent episode of probable depression. Throughout the paper, we define adolescents as having a recent episode of probable depression if they report having sought any professional help for depression problems in the past 12 months. We find that in 2002 and 2003 adolescents with probable depression had grade point averages .14 to .20 points higher than adolescents with depression in the latter half of 2004 and 2005. Consistent with prior literature on mental health and academic outcomes in adolescence, changes in average GPA for depressed adolescents were driven entirely by declines in the grades of adolescent girls (Janet Currie and Mark Stabile, 2006, Weili Ding, Steven F. Lehrer, J. Neils Rosenquist and Janet Audrain-McGovern, 2009, Jason M. Fletcher, 2008). We find no change in average grades among adolescents with no recent episodes of probable depression. We also find similar patterns for substance use and delinquency outcomes for adolescents with probable depression, relative to other adolescents.

The paper proceeds as follows: section I provides background on the FDA actions surrounding antidepressant use in pediatric patients and media coverage of FDA announcements, advisories and warnings; section II describes changes in prescribing patterns and youth suicides surrounding the 2003 and 2004 FDA actions; section III explains the data and methods in detail; section IV presents our regression analyses for academic outcomes, substance use, and delinquency; section V discusses potential threats to our approach; and section VI concludes.

## I. FDA ACTIVITY ON THE SAFETY OF PEDIATRIC ANTIDEPRESSANT USE

Antidepressant use among adolescents rose steadily and substantially during the 1990's through 2000 (Mark Olfson, Steven C. Marcus and Benjamin G. Druss, 2008, Mark Olfson et al., 2002). This increase likely stemmed from several sources. First, the development of Selective Serotonin Reuptake Inhibitors (SSRIs) shifted the balance between the risks and benefits of using antidepressants to treat patients with depression; earlier generation antidepressants were lethal in overdose. FDA approval of the SSRI Prozac (fluoxetine) for depression treatment in children further increased the willingness of clinicians, including general practitioners, to prescribe antidepressants to children. Of the antidepressants available to treat depression today, fluoxetine has the most evidence supporting its use. In the latter part of 2004, a landmark multisite randomized trial of fluoxetine alone and with cognitive behavioral therapy (CBT) showed significant improvements in depression symptoms compared with a placebo (John March et al., 2004). The most beneficial effects occurred in adolescents randomized to receive fluoxetine (either in combination with CBT, or alone). Greater attention to mental health problems in youth, as evidenced by the 2003 Surgeon General's report, also may have resulted in increases in treatment. This was also a time when antidepressants were heavily marketed to health care professionals – in 1999 the pharmaceutical industry spent just under $1 billion dollars on marketing (Meredith B. Rosenthal et al., 2002). At the same time, marked increases in direct-to-consumer advertising raised awareness of the availability of pharmaceutical treatments for depression and accompanied greater social acceptance of psycho-pharmaceutical treatment generally (Cindy Parks Thomas et al., 2006). However, the growth of child and adolescent antidepressant use reversed abruptly with the disclosure of possible new safety risks, disseminated by the FDA in a series of public advisories and warnings.

Figure 1 shows the dates of major FDA activity and media coverage of the concerns regarding pediatric use of antidepressants.  The FDA's five specific public communications on pediatric antidepressant use began in June 2003 with a one-page warning about potential risks of increased suicidal thoughts or actions for a single SSRI, Paxil (generically known as paroxetine). Subsequent risk communications increased the scope of the warnings. After considering evidence from hearings, and evidence presented in an FDA-sponsored meta-analysis of 24 randomized controlled trials, an FDA joint advisory committee voted to recommend a black box warning, although 8 of the 23 members dissented.[2] Suicide is a rare event; the meta-analysis findings reported an increase in suicidal thoughts and actions (suicidality), but did not include any child who had completed suicide. A black box warning, or a required warning in the packaging of a prescription drug warning of serious or life threatening adverse side effects, is the strongest warning required by the FDA.  In October 2004, the FDA issued a public health advisory directing drug manufacturers to include a black box warning of increased suicidality risk for children and adolescents on a broad range of antidepressants beginning January 1, 2005. These warnings strongly urged providers to increase monitoring of pediatric patients using antidepressants. As shown in Figure 1, media coverage of FDA activity was moderate in response to the June 2003 warning regarding Paxil, but it was heavier in March of 2004 in response to FDA public hearings and a broad advisory, as well as in the latter half of 2004 when the FDA announced its decision regarding black box warnings.  Barry and Busch (2010) further document that media coverage was more negative in early 2004, focusing on the possible safety risks of antidepressants, rather than potential benefits.  Later in 2004, there was more attention given to the controversy regarding the FDA's decision to require black box warnings.

## II. CHANGES IN ANTIDEPRESSANT USE AND YOUTH SUICIDES

In the last five years, multiple studies have documented large declines in pediatric antidepressant use coincident with the 2004 FDA advisories and warnings, with most estimates suggesting that antidepressant use fell by 20% to 30% relative to the peak levels of antidepressant use in the 12

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[2] The FDA commissioned meta-analysis found a two fold increase in risk of suicidality in youth taking antidepressants, compared to placebo groups (4 versus 2 %).  This evidence has been criticized because it considered suicidality (no child in any of the trials considered committed suicide) and many trials excluded youth who were suicidal at baseline.

to 24 months surrounding the warnings (Susan H Busch, Richard G Frank, Douglas L. Leslie, Andres Martin, Robert A. Rosenheck, Erika G. Martin and Colleen L Barry, 2010, Susan H. Busch et al., 2011, Robert D. Gibbons, C. Hendricks Brown, Kwan Hur, Sue M. Marcus, Dsulal K. Bhaumik, Joelle A. Erkens, Ron M.C. Herings and J. John Mann, 2007, Benji T Kurian et al., 2007, Anne M. Libby, David A. Brent, Elaine H. Morrato, Heather D. Orton, Richard Allen and Robert J. Valuck, 2007, Charles B. Nemeroff, Amir Kalali, Martin B. Keller, Dennis S. Charney, Susan E. Lenderts, Elisa F. Cascade, Hugo Stephenson and Alan F. Schatzberg, 2007, Mark Olfson, Steven C. Marcus and Benjamin G. Druss, 2008, Satish Valluri et al., 2010). The most often cited of these studies are summarized briefly in Appendix Table I.

Studies that focus on monthly antidepressant sales demonstrate an initial abrupt decline in prescribing of antidepressants in pediatric populations beginning in January-March of 2004, the time of public hearings on the safety of pediatric antidepressant use (Benji T Kurian, Wayne A. Ray, Patrick G. Arbogast, D. Catherine Fuchs, Judith A. Dudley and William O. Cooper, 2007, Charles B. Nemeroff, Amir Kalali, Martin B. Keller, Dennis S. Charney, Susan E. Lenderts, Elisa F. Cascade, Hugo Stephenson and Alan F. Schatzberg, 2007). One study of all-payer data representing about half of all prescription activity in the U.S., shows the precipitous drop in the number of prescriptions for children under age 18 that occurred in January-June 2004 coincident with intense media coverage of FDA's hearings and its second advisory on safety risks of pediatric antidepressant use (Charles B. Nemeroff, Amir Kalali, Martin B. Keller, Dennis S. Charney, Susan E. Lenderts, Elisa F. Cascade, Hugo Stephenson and Alan F. Schatzberg, 2007).

Based on clinical trial evidence, one may view treatments for pediatric depression on a continuum regarding their efficacy. Combination treatment, or antidepressants in conjunction with evidence-based psychotherapy, reduced symptoms of depression most in randomized clinical trials, followed by antidepressants alone, and then evidence-based psychotherapy alone (John March, Susan Silva, Stephen Petrycki, John Curry, Karen Wells, John Fairbank, Barbara Burns, Marisa Domino, Steven McNulty, Benedetto Vitiello and Joanne Severe, 2004).[3] In

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[3] This widely cited multisite randomized trial found combination treatment to be superior to fluoxetine alone or cognitive behavioral therapy alone. Rates of response (i.e. a significant decline in depression symptoms) for the four treatments studied were Combination, or fluoxetine with cognitive behavioral therapy (71 percent) fluoxetine alone (62 percent), cognitive behavioral therapy alone (43 percent), and placebo (35 percent). This study provided 15 psychotherapy visits in 12 weeks to children in the therapy arms of the trial.

effect, the FDA warnings moved adolescents along this continuum toward less effective treatments. This is particularly true given that most adolescents receiving "psychotherapy alone" in real-world clinical settings receive far fewer psychotherapy visits and lower quality therapy than what was received by trial participants. Some children who previously would have received combination treatment received psychotherapy alone. Others moved from antidepressant treatment alone to no evidence-based treatment. The literature is mixed on whether or not the receipt of psychotherapy increased after the warnings. One study suggests there was a slight increase in receipt of any psychotherapy – among treated adolesents, the percent receiving at least one psychotherapy visit rose less than 5 percent in the period after the warnings ((Susan H Busch, Richard G Frank, Douglas L. Leslie, Andres Martin, Robert A. Rosenheck, Erika G. Martin and Colleen L Barry, 2010, Anne M. Libby, David A. Brent, Elaine H. Morrato, Heather D. Orton, Richard Allen and Robert J. Valuck, 2007, Satish Valluri, Julie M. Zito, Daniel J. Safer, Ilene H. Zuckerman, C. Daniel Mullins and James J. Korelitz, 2010). In contrast, another study found no such increase (Susan H Busch, Richard G Frank, Douglas L. Leslie, Andres Martin, Robert A. Rosenheck, Erika G. Martin and Colleen L Barry, 2010, Anne M. Libby, David A. Brent, Elaine H. Morrato, Heather D. Orton, Richard Allen and Robert J. Valuck, 2007, Satish Valluri, Julie M. Zito, Daniel J. Safer, Ilene H. Zuckerman, C. Daniel Mullins and James J. Korelitz, 2010). In addition, the types of providers who prescribed antidepressants shifted, with primary care physicians writing a smaller share of total antidepressant prescriptions compared with psychiatrists after the FDA warnings (Charles B. Nemeroff, Amir Kalali, Martin B. Keller, Dennis S. Charney, Susan E. Lenderts, Elisa F. Cascade, Hugo Stephenson and Alan F. Schatzberg, 2007, Mark Olfson, Steven C. Marcus and Benjamin G. Druss, 2008).

Because our study design relies on the timing of the abrupt shift in antidepressant use among adolescent patients with depression, we present additional evidence on antidepressant patterns for 12-17 year olds from two complementary sources, Florida Medicaid claims data and Marketscan data, a large administrative database of pharmaceutical claims for privately insured individuals. The Marketscan data include all individuals with diagnoses of depression in a given quarter based on *International Classification of Diseases, Ninth Revision* (ICD-9) Codes 296.2, 296.3, 300.4, and 311. Antidepressant use is defined as one or more claims for any of 36 antidepressants covered by the FDA black box warning in that quarter. In the Florida Medicaid data, these include only pediatric patients with new diagnoses of depression using the same

codes above.  We defined new diagnoses of depression as those without any code for depression in the 120 days prior to an initial diagnosis of depression. In the Florida data, antidepressant use is defined as one or more claims for any of 36 antidepressants covered by the FDA black box warning within 30 days of diagnosed depression.[4]  Figure 2 plots the antidepressant prescription fills from both of these data sets.  Despite slightly different definitions and time periods, the prescribing patterns are remarkably similar in the Marketscan and Florida Medicaid data. Prescriptions fall abruptly beginning in the first quarter of 2004 (although girls in the Marketscan data show a drop starting one quarter earlier).  Also of note, the prescribing patterns are similar across sexes.  Comparing 2003 to 2005, the relative declines were smaller in the Marketscan data (about 10 to 15 percent relative decline) compared with the Medicaid data (about 25 to 30 percent relative decline).  The greater drop in a sample made up exclusively of pediatric depression patients with new episodes of depression is consistent with the notion that changes in prescribing in response to FDA advisories and warnings affected new depression episodes more than existing episodes (Susan H. Busch, Richard G. Frank, A. Martin and Colleen L. Barry, 2011, Benji T Kurian, Wayne A. Ray, Patrick G. Arbogast, D. Catherine Fuchs, Judith A. Dudley and William O. Cooper, 2007).

Figure 2 depicts the timing of drops in antidepressant use in two populations, but it is important to understand how the FDA activity on antidepressants affected prescribing patterns in a broader national population.  Using adolescents aged 12 to 17 in the nationally representative Medical Expenditure Panel Surveys (2002-2006), we estimate the share with any antidepressant use (use of an antidepressant in a calendar year) among those with one or more medical encounters for depression. The MEPS sample is considerably smaller than the samples depicted in Figure 2, and the diagnoses are a little less precise than those in actual claims data.[5]  In addition, data are not available by quarter.  Nonetheless, Figure 3 shows a dramatic absolute decline of over 20 percentage points (24 for boys and 22 for girls) in antidepressant use between 2003 and 2005, or a relative decline of over 30 percent.  We note that this graph suggests little

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[4] We also examined trends in use of antidepressants within 60 days or 90 days of diagnosed depression.  Although the levels are higher in the 60-day and 90-day windows, the trends in antidepressant use are very similar.

[5] The MEPS reports 3-character International Classification of Disease-9th Revision codes.  We defined a cohort of depressed children using code 296 (affective psychoses), 300 (neurotic disorders), and 311 (depression Not Elsewhere Classified).  This category is necessarily broader than that defined in administrative data from Florida Medicaid, for example, but more specific than what is available in the NSDUH based on seeking treatment.

decline in 2004; this is likely due to the use of calendar year prevalence – data from 2004 include months where rates of antidepressant use were still increasing.

To establish a link between declines in antidepressant use and human capital among depressed adolescents, one also needs to examine whether symptoms of depression changed after changes in treatment (reductions in antidepressant use).  Suicide represents the most extreme consequence of depression, and one that depression treatments target. To better understand how the FDA activity around pediatric antidepressant use may have affected symptoms in the population of adolescents with depression, Figure 4 presents information regarding suicides in the United States over the period from 1999 to 2007.  These data are drawn from the Centers for Disease Control and Prevention's publicly available information on deaths by cause and selected demographic characteristics.  Because of dramatically different levels of suicides by age and gender (males commit suicide more often, and between ages 10 and 24, suicide rates rise with age), the figure presents the natural log of suicide deaths per 100,000 population, separately for two age groups (10-19 and 20-24), and by sex.  Because the 2004 FDA warnings applied to pediatric antidepressant use, they did not directly affect 20-24 year olds. Youth suicides had been flat or declining among 10-19 year olds in the years preceding the warnings, but in 2004, 10-19 year old girls experienced a sharp increase in suicides, of over 30 percent.  There was no abrupt rise among older ages (20-24) as expected, given that these early warnings focused on pediatric populations.  These results echo those presented by Gibbons and colleagues (2007), but include three additional years of data (through 2007).  Gibbons and colleagues also note that since 1988, U.S. youth suicide rates have declined in all but two years (1994 and 2000), and these increases were much smaller than the increase in suicides in 2004.  Taken together, we interpret the trends in antidepressant use and the concomitant rise in youth suicide as evidence that symptoms of depression rose in the adolescent population in 2004 and 2005 in response to the FDA advisories and warnings on the safety of pediatric antidepressant use.  We use this abrupt change in treatment and symptoms of depression to identify human capital effects of depression treatment.

## III. EMPIRICAL METHODS AND DATA

*Contribution to the Literature and Overview of Identification Strategy*

Researchers have attempted to quantify the impact of depression on measures of academic achievement, but even the most rigorous evidence to date makes causal inference regarding the

effect of depression difficult.  More importantly, there is no evidence from real world settings (as opposed to randomized clinical trials) that treating adolescent depression can improve academic outcomes.  Fletcher (2008) estimates the relationship between adolescent depression status and educational attainment, identifying the effect of depression based on fixed effect models, which effectively compare adolescent siblings with and without symptoms of depression.  His analysis documents a correlation between depression and poorer educational attainment for girls, but not for boys.  The interpretation of this analysis relies on the assumption that only differences in depression cause the observed differences in academic outcomes, rather than some fixed trait like motivation or ability that might be correlated with depression, yet differs across siblings.

Another study uses genetic markers as identifying instruments for adolescent depression and finds a significant negative effect of depression on grade point average, but again these significant effects are only observed for girls (Weili Ding, Steven F. Lehrer, J. Neils Rosenquist and Janet Audrain-McGovern, 2009).   This approach requires the assumption that the genetic marker relates only to depression, and not other unmeasured traits that could influence grade point averages.  Other research using person-level fixed effects models for a sample of a somewhat older age group (college students) does not find gender differences in the relationship between depression and grade point average (Daniel Eisenberg et al., 2009).  These three studies mark significant progress toward the goal of understanding human capital effects of depression during the crucial period of adolescence, but each relies on relatively strong, and somewhat similar assumptions that depression, and not related unmeasured traits, drives academic differences within families, according to genetic markers, or within an individual over time.  None of these studies provides information regarding the treatment of depression and academic achievement.

Researchers have also attempted to quantify the effect of adolescent depression on other outcomes that represent non-cognitive dimensions of human capital including substance use and delinquency.  For example, recent literature showed that state-level rates of antidepressant use are correlated with violent crime rates, but not with property crime rates (Dave E. Marcotte and Sara Markowitz, 2010).  When these researchers focusing specifically on prescription rates and crime rates for teenagers, they find little evidence that psychiatric drugs, and antidepressants in particular, are associated with either homicide rates or arrest rates for violent and property

crimes. A 10-year longitudinal follow-up of the National Comorbidity Survey confirmed that individuals with major depression at baseline (1990-92) were much more likely to initiate the use of illicit drugs in the subsequent decade compared to individuals without major depression (J. Swendsen et al., 2010). Adolescents aged 12-17 with a major depressive episode in the past year were twice as likely to initiate illicit drug use compared with those without depression (16.1 versus 6.9 percent) (Substance Abuse and Mental Health Services Administration (SAMHSA), 2007)

Despite ample research on depression and substance use, causal evidence on the effect of depression treatment on these outcomes is rare. Epidemiologic studies that present correlations between depression and substance use disorders cannot distinguish a causal role for depression from a case in which substance use disorders cause depression or a case in which a third factor contributes to both depression and substance use disorders (N. Breslau et al., 1998, Meyer D. Glantz, 2002, Eva Jane-Llopis and Irina Matytsina, 2006, J. Swendsen et al., 2008). Experimental studies on the effects of depression treatment target a narrow range of pediatric patients (excluding, for example, patients with a history of substance abuse), and focus on a limited set of clinical outcomes.

To augment existing literature on adolescent depression and academic outcomes with a complementary and stronger identification strategy, and to answer the clinical and policy relevant question of whether treating depression can improve human capital outcomes, we take advantage of a powerful natural experiment: the sudden decline in use of antidepressants for treating pediatric depression induced by the Food and Drug Administration's (FDA's) 2003-2004 warnings on the risks of suicidality associated with pediatric antidepressant use. We compare academic and behavioral outcomes for adolescents who sought treatment for depression just before and just after the sharp drop in adolescent antidepressant use in the first quarter of 2004. Adolescents without recent episodes of depression serve as a comparison group. Our identification relies on the assumption that any difference in prescribing patterns and outcomes immediately before versus immediately after the first quarter of 2004 relate only to FDA hearings and advisories, and thus mimics random variation.

*National Survey on Drug Use and Health*

The data for our analyses come from the National Surveys on Drug Use and Health (NSDUH).[6]
The NSDUH is an annual survey conducted by the Substance Abuse and Mental Health Services
Administration that collects data from approximately 70,000 individuals aged 12 and older who
are representative of the U.S. population.  Several features of the NSDUH are particularly salient
for our analyses.  The NSDUH is in the field year-round and the public-use version of the dataset
includes a variable indicating the quarter in which the interview occurred.  The NSDUH has a
large sample of adolescents, as 12-17 year olds comprise approximately one third of the total
samples.  In addition, although the NSDUH focuses on substance use issues, it also collects
survey data on mental health, education, and delinquency.  In our main analyses, we use the
2001-2007 years of the NSDUH. After restricting to adolescents, that yields a sample size of
126,355 observations during all 28 quarters from 2001-2007.  Our analyses have slightly smaller
samples of adolescents for two reasons.  All analyses exclude the first quarter of 2004, due to the
fact that it straddles months that can be thought of as pre- or post- period.  This exclusion,
combined with missing information on academic outcomes leaves 106,635(121,785)
observations in models of academic(substance use) outcomes.[7]  Finally, outcome variables
related to stealing and fights cover the 12 month period before the survey, so we exclude the first
two quarters of 2004 to have a cleaner pre- and post- period, leaving 116,371 observations with
complete information on delinquent behaviors.

*Depression Measure*

As described above, our key comparison is in academic outcomes for adolescents with probable
depression before and after the FDA warnings about antidepressant risks. A more ideal measure
of depression status  based on a validated diagnostic instrument was not asked of adolescents in
the NSDUH until 2004.  Instead, we proxy for probable depression status by using information
collected from adolescents about whether they received any treatment or counseling services for
emotional or behavioral problems from a diverse set of sources over the past 12 months.  This

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[6] Prior to 2002, the survey was called the National Household Survey on Drug Abuse.
[7] We explored the large number of missing observations for academic outcomes.  About 2.5 % of respondents have
missing grade point information because their schools do not report letter grades and another 6% report that they did
not attend school in the past year.   One might expect drop out rates to increase if adolescents receive less treatment
of depression following changes in prescribing patterns.  This would bias us against finding adverse effects on
school outcomes.  We confirmed that the probability respondents report attending school at the time of the survey
did not fall coincident with the change in prescribing patterns that occurred with the FDA activity in 2004.  There is
no change in the trend in school attendance over the time period we study.

population reflects those we most expect to be affected by the warning. The NSDUH asks respondents whether they stayed overnight in a hospital, in a residential treatment center, or in therapeutic foster care. Respondents also report whether they received any services for emotional or behavioral problems from a partial day hospital or day treatment program; from a mental health clinic or center; from a private therapist, psychologist, psychiatrist, social worker, or counselor; from an in-home therapist, counselor, or family preservation worker; from a pediatrician or other family doctor; whether they talked to school counselors, school psychologists, or had regular meetings with teachers about emotional or behavioral problems.

For each of the services that a respondent reported using in the past 12 months, the respondent is asked a series of closed-ended questions to determine why they used that service. Two of those follow-up questions are used to identify probable depression: Whether the services were because the respondent thought about or tried to kill themselves, or because the respondent felt depressed.[8] All of the questions related to mental health treatment were asked in a consistent manner in the 2001-2007 surveys. We code someone as having probable depression if they respond that they used any of the above services (excluding services from school counselors, psychologists, and teachers since they would not be prescribers of antidepressants) and if that service was used because of suicidality or depression.[9] As shown in Table 1, 6.6% of the sample is classified as having probable depression.

Table 1 shows sample characteristics separately by gender and whether an adolescent was depressed, according to the definition above. As expected, probable depression is more common among females (8.5 percent depressed) than males (4.8 percent depressed). Compared with non-depressed adolescents, the depressed respondents are slightly older, more likely to be white, and more likely to live in families with moderate or low-income levels.

*Outcome Measures*
We examine three types of outcomes: academic achievement, substance use, and delinquency. We measure academic achievement using the respondents' self report of their average grades in the most recent grading period. In the NSDUH, respondents select one of four choices: A+/A/A-

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[8] The other possible explanations were because the respondent felt afraid or tense, because of breaking rules or acting out, because of eating problems, or because of some other reason.
[9] For brevity, throughout the paper, we refer to those classified as having probable depression as "depressed".

, B+/B/B-, C+/C/C-, or D or lower.  When treated as a cardinal measure, this variable has an interpretation that is similar to GPA, with 4.0 indicating the highest grades.[10] We also evaluated a set of intermediate schooling measures regarding school attendance and adolescent attitudes toward school, but these results were imprecisely estimated, and for brevity, we omit them here.

Next we examine outcomes relating to substance use in the past 30 days.  Respondents were asked, "In the last 30 days on how many days did you…" have 5 or more drinks on the same occasion?; smoke part or all of a cigarette?; use _____(an illicit drug or in the case of prescription drugs, use____non-medically)?[11] We used these questions to form indicator variables for binge drinking, cigarette use, illicit drug use, and nonmedical prescription drug use in the past 30 days.  Finally, we examined measures of delinquency.  Respondents were asked, "During the past 12 months, how many times have you… stolen or tried to steal anything worth more than $50?; gotten into a serious fight at school or work? Attacked someone with the intent to seriously hurt them?"  We used these responses to create indicator variables regarding fighting, stealing, and attacking.

All of our outcome measures are summarized in Table 2.   Our sample characteristics match the literature on academic outcomes. Grades are slightly higher on average for females than males, and depressed adolescents fare slightly worse than their non-depressed peers. Our delinquency measures suggest that a significant minority of children engaged in fighting and stealing.  About 42 percent of boys and 34 percent of girls with a recent episode of depression reported one or more fights in the past 12 months, compared with 25 percent of boys and 17 percent of girls in the non-depressed group.  Stealing and "attacking" with the intent to hurt someone was less common.  Less than 10 percent of non-depressed kids reported this behavior, while 23 percent of boys and 15 percent of girls in the depressed group had attacked someone in the prior 12 months.

Substance use was not uncommon, especially among the depressed adolescents.  In this group, 16(19) percent of boys(girls) reported binge drinking, 21(26) percent of boys(girls)

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[10] We also estimate ordered probit models for this outcome, but our results are unchanged.
[11] Respondents were prompted individually about an exhaustive list of drugs in the following categories (marijuana, heroin, cocaine, crack, LSD, PCP, ecstacy, methamphetamine, hallucinogens, inhalants, sedatives, stimulants, tranquilizers, pain relivers, and oxycontin), and the NSDUH recodes responses to reflect any positive response to an illicit drug, or any response that indicates inappropriate prescription drug use).

reported using cigarettes, 22(21) percent of boys(girls) had used an illicit drug, and 8(9) percent of boys(girls) had used prescription drugs inappropriately in the prior 30 days. In all cases but binge drinking, substance use was twice as common in the depressed adolescents compared with their non-depressed peers.

*Empirical models*

Our basic regression specification employs the model described in Equation (1).

$$Y_{it} = \alpha + \beta_1 * t + \beta_2 PostFDA + \beta_3 PostFDA * t + \beta_4 D +$$
$$\beta_5 D * t + \beta_6 D * PostFDA + \delta X_i + Q_t + \varepsilon_{it} \qquad (1)$$

*Y* denotes any one of our outcome variables. Our time variable *t*, is a linear time trend over the 28 quarters of our study period.[12] The variable *PostFDA* is 0 until the first quarter of 2004 and 1 after that. The variable *D* indicates whether a respondent falls into the depressed group. The vector *X* includes a set of sociodemographic variables. These variables include a dummy variable for sex, a linear age trend, and a set of dummy variables for race/ethnicity (white, black, native American, native Hawaiian/Pacific islander, Asian, more than one race, or Hispanic). *X* also includes a set of dummy variables for family income (<$10,000, $10-29,999, $20-29,999, $30-39,999, $40-49,999, $50-74,999, $75,000 or more). *Q* represents a set of quarter dummies to adjust for seasonality. In these models, the key coefficient that identifies the effect of the FDA warnings on human capital outcomes for adolescents with probable depression after controlling for underlying trends in academic achievement is $\beta_6$.

We estimate our main models of academic achievement using OLS. For our other outcome variables, which are dichotomous, we estimate probit models. In the tables, we present probit coefficients, and for our main variables of interest, we provide the marginal effects as well as bootstrapped standard errors of the marginal effects (based on 500 replications of samples drawn with replacement). All of our regression models utilize the NSDUH sampling weights to be representative of the U.S. population. We estimate our models with heteroskedasticity-robust standard errors clustered on the time period (defined by quarter of measurement).

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[12] Adding a quadratic term or higher-order polynomials did not improve the model fit, nor did they affect our main coefficients of interest.

**IV. RESULTS**

*Academic achievement*

We first present graphical evidence of the trends in academic achievement for adolescents with probable depression. Figure 5 shows the average grades for adolescents with probable depression, where each point indicates average grades in a quarter. In the periods before the FDA warnings, there are no discernable trends in average grades for adolescents with and without probable depression. After the FDA warnings, the average grades dropped abruptly for depressed girls, though not for depressed boys. In addition, Figure 5 also shows the trend in average grades for adolescents without probable depression. As expected, the average grades for adolescents without probable depression are higher than those for depressed adolescents. Average grades for adolescents without depression were flat throughout the study period, with no apparent change around the time of the 2004 FDA advisories and warnings.

Table 3 shows the results of the regression models of our main outcome variable, average grades. The results for column 1 are for the full sample. The key coefficient of interest, $\beta_6$, is estimated to be -0.142, implying that average grades dropped significantly after the FDA warnings. The regression results also confirm the graphical evidence. The key coefficient for females (column 2) is larger in magnitude ($\beta_6$= -0.203) and more precise than the coefficient for males, which is not significantly different from zero ($\beta_6$=-0.030). Table 4 examines whether these effects occurred throughout the grade distribution by estimating models of whether respondents report having an A average or better, a B average or better, or a C average or better. Adolescents with a recent episode of probable depression were 8.6 percentage points less likely to earn a B or better and 3.5 percentage points less likely to earn a C or better after the FDA advisories in early 2004. This was driven by the depressed girls, who were 11 percentage points less likely to earn a B or better and 6 percentage points less likely to earn a C or better following the FDA advisories. There appears to be little effect of FDA advisories and the decline in depression treatment on the likelihood of reporting an A average.

Table 5 shows key coefficients and marginal effects of the FDA warnings on substance use. Smoking increased in the full sample by 4.6 percentage points. Although depressed

adolescents are much more likely to binge drink than their peers, the FDA advisories appear to have little effect on binge drinking. Among girls, the FDA advisories and decline in the treatment of depression increased the use of illicit drugs by 5.4 percentage points and increased nonmedical prescription drug use by 4.3 percentage points. As with academic outcomes, the effects on illegal drug use and nonmedical prescription drug use are driven mainly by girls rather than boys, although the effects on cigarette use are similar across gender.

Table 6 shows key coefficients and marginal effects of the FDA warnings on delinquency outcomes. Fighting and stealing both rose disproportionately among depressed adolescents in the post period. Fighting rose by 6.5 percentage points and stealing rose by 4.6 percentage points in the full sample, although the effects on stealing were driven entirely by depressed girls. There was no significant effect of the FDA warnings on attacks in the last 12 months. Taken together, our results suggest there were important adverse consequences of the FDA advisories on grades, substance use, and other delinquent behavior. Depressed girls seem to have been affected most by these unintended consequences, since we measured no significant changes in grades or behavior among boys with likely depression. Next we consider several alternative interpretations of our findings.

## V. ALTERNATIVE INTERPRETATION OF THE RESULTS

In this section, we address several potential threats to our interpretation of the results. The most obvious concern is that with so much change in the treatment of depression, the composition of the "depressed" group is changing in ways that could bias us towards the conclusion that the FDA warnings had an adverse impact on depressed adolescents. If, for example, the marginal depression patient, in terms of severity, was less likely to seek treatment following the FDA warnings, we would worry that the remaining set of depression patients might be sicker and have worse human capital outcomes than those patients who opted not to seek treatment. To explore this concern, we examined both the trend in and the composition of our sample of adolescents with probable depression. Figure 6 plots the share of adolescents with probable depression throughout our study period, and we report the results of tests for significant changes in the level or trend of depressed adolescents in the post-period of our analysis. There

are no abrupt changes in the share of adolescents who report seeking treatment for depression. In models of depression status as a function of time, there was no decline in the share of adolescents aged 12 to 17 seeking treatment for depression after the FDA warnings.[13]

In Table 7, we estimated models like those in equation 1, using each of the covariates included in *X* as our outcome variable (controlling only for quarter of survey). We tested whether the coefficient on *Depress\*Post-FDA* was significant, indicating that characteristics of adolescents in the depressed group changed substantially with the change in prescribing patterns. Table 7 shows that there were no significant changes in race, ethnicity, gender, income or age of adolescents seeking treatment for depression. This suggests that our estimated effects of the FDA warnings are not explained by compositional changes in who is depressed.

A second factor to consider during this time period is whether we might be measuring a broader concern about all psychotropic medication. Several studies have examined whether there were changes in use of antipsychotics or other psychotropic drugs (i.e. stimulants or benzodiazapines) (A. Libby et al. 2007; C. Nemeroff et al. 2007). None of these studies found changes in use of other psychotropic medications. We examined this possibility by computing the annual prevalence rate of stimulants in the MEPS and find no changes in use.

Finally, one may question how reasonable it is to find effects for girls but not for boys. We turn to this next. One reason we might observe such a result could be that antidepressants are less effective to treat depression in males versus females. The clinical literature has evaluated the effects of various antidepressants by gender with mixed results. For example, a recent review of studies on sex differences in effects of antidepressants summarizes evidence both supporting and refuting differential efficacy of antidepressants by sex (Wendy K. Marsh and Kristina M. Deligiannidis, 2010). However, studies focused on SSRIs in larger patient populations, such as a study of citalopram in the Sequenced Treatment Alternatives to Relieve Depression, or STAR\*D trial, document significantly larger treatment effects among women relative to men (Elizabeth A. Young et al., 2009). Furthermore, differential effects of antidepressants by gender have been concentrated among patients under age 50, leading some to

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[13] Data from the nationally representative MEPS (not shown) corroborate the NSDUH trends. There are no statistically significant differences in annual rates of depression treatment among 12-17 year olds for any of the years between 2002 and 2006.

hypothesize that hormonal activity affects the efficacy of antidepressants (Michael E. Thase et al., 2005). These differences are too small to explain the dramatic effects for girls versus boys, though.  Our results are consistent with other observational studies comparing the outcomes of depressed adolescents to non-depressed adolescents.  Papers by Fletcher and Ding and colleagues (Weili Ding, Steven F. Lehrer, J. Neils Rosenquist and Janet Audrain-McGovern, 2009, Jason M. Fletcher, 2008), as well as earlier work (Ernst R. Berndt, Lorrin M. Koran, Stan N. Finkelstein, Alan J. Gelenberg, Susan G. Kornstein, Ivan M. Miller, Michael E. Thase, George A. Trapp and Martin B. Keller, 2000) found that high school graduation rates and grades were lower for girls with depression compared to girls without, but they did not find similar results for boys.  One piece of evidence that supports the notion that the FDA warnings were more important for girls than for boys is the evidence on suicides.  The relative rise was  large for girls, about 33 percent, and trivial among boys.  This relationship merits further study.

*Magnitude of Response to Antidepressants*

Our analysis offers a reduced form estimate of the overall effect of the FDA advisories and warnings on human capital for adolescents with recent episodes of depression.  However, an important back of the envelope calculation to better understand the clinical and policy implications of our results is to convert our estimates into an estimated effect of antidepressants on human capital outcomes among adolescents seeking care for depression.  This computation requires an estimate of the absolute decline in antidepressant use for a population like that in the NSDUH data. The MEPS data presented in Figure 3 most closely mirror the NSDUH sample, although one should note that the diagnoses used to define the MEPS sample are slightly different than those used to characterize probable depression in the NSDUH.  However, the absolute decline in antidepressant use of 22 to 24 percentage points, or about one fifth in the MEPS data suggest that when multiplied by a factor of five, our estimated effects of changes in outcomes in response to the FDA induced decline in antidepressant use yield a crude estimate of the magnitude of the effect of antidepressants on grades, substance use, and delinquency, among adolescents aged 12 to 17 with probable depression.

In other words, among depressed girls, where the effects are concentrated, treatment with antidepressants increases grades by a full point (from a C to a B, for example), reduces the chance of smoking and illicit drug use by 20 to 25 percentage points, and reduces the chance of

stealing or fighting by even greater magnitudes (about 30 to 35 percentage points).  These suggest both large effects of untreated or undertreated depression, as well as an impressive treatment effect of antidepressants in the community during the period leading up to advisories and warnings regarding antidepressants.

## VI. CONCLUSION

Few topics engender as much concern and controversy as treating children and adolescents with psychotropic drugs and academic achievement in the middle and high school years.  Following the FDA's 2004 decision to issue black box warnings on virtually all antidepressants based on safety concerns in children and adolescents, both of these changed.  Prior evidence documents a decline in antidepressant use of 20 to 30 percent following the FDA warnings.  We find that academic achievement among depressed adolescent girls declined after the FDA warnings, falling roughly from a B to B- grade point average.  This decline in grade point average did not occur among adolescents without a recent episode of probable depression.  Academic outcomes were just one aspect of human capital affected by the warnings.  Substance use and other delinquency measures increased among girls seeking treatment for depression as well.

These findings have several implications.  They suggest that the unintended consequences of policies designed to protect consumer safety extend well beyond the clinical considerations that typically contribute to decisions about the costs and benefits of regulatory actions.  The FDA's decision to issue the warning on antidepressants rested on evidence of suicidal thoughts and actions, but not suicide itself.  Indeed, the FDA panel of experts convened to make the decision about a black box warning was divided regarding the relative costs and benefits of issuing the warning for public health. The "costs" of issuing the warning considered were clinical in nature, with potential suicide among depressed patients being the most extreme of these.  However, the discussion did not consider the broader non-clinical costs (and benefits) of treating depression with antidepressants.  Second, our findings also confirm research in very different settings suggesting that depression interferes with academic outcomes, especially for girls.

The third and most significant innovation of this empirical work is that it suggests that treatment of depression can mitigate adverse effects of depression on both cognitive and non-

cognitive aspects of human capital among adolescents. Families, schools, and clinicians devote significant effort to help students with behavioral health issues because they interfere with academic outcomes. These findings suggest that treatment of depression can improve both cognitive outcomes such as grades, as well as delinquent behaviors and the initiation of substance use, all of which are important aspects of human capital.

Our paper focuses on outcomes that occurred within 1 to 12 months of being surveyed, and thus they should be viewed as relatively short-run outcomes. Given controversy over the risks and benefits of antidepressants in the long run, our findings do not suggest we should abandon other forms of treating depression, but rather as evidence that depression affects economic outcomes, and thus successful treatments of depression yields potential benefits that reach far beyond the clinical outcomes typically measured.

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Table 1: Sample Characteristics by Sex and Depression Status

| | All | Males | | Females | |
|---|---|---|---|---|---|
| Not depressed | 0.934 | 0.952 | | 0.915 | |
| Depressed | 0.066 | 0.048 | | 0.085 | |

| | | Males | | Females | |
|---|---|---|---|---|---|
| | **All** n=126,355 | **depressed** n=3,203 | **non-depressed** n=61,292 | **depressed** n=5,686 | **non-depressed** n=56,174 |
| Age | | | | | |
| 12 | 0.159 | 0.145 | 0.158 | 0.083 | 0.169 |
| 13 | 0.169 | 0.169 | 0.172 | 0.131 | 0.169 |
| 14 | 0.170 | 0.159 | 0.171 | 0.168 | 0.171 |
| 15 | 0.171 | 0.174 | 0.170 | 0.209 | 0.169 |
| 16 | 0.167 | 0.165 | 0.167 | 0.208 | 0.165 |
| 17 | 0.163 | 0.188 | 0.163 | 0.201 | 0.158 |
| Quarter | | | | | |
| 1 | 0.244 | 0.244 | 0.243 | 0.264 | 0.244 |
| 2 | 0.253 | 0.270 | 0.251 | 0.255 | 0.253 |
| 3 | 0.253 | 0.247 | 0.254 | 0.240 | 0.253 |
| 4 | 0.250 | 0.239 | 0.252 | 0.240 | 0.250 |
| Race/ethnicity | | | | | |
| White | 0.617 | 0.683 | 0.616 | 0.688 | 0.607 |
| Black | 0.150 | 0.141 | 0.148 | 0.117 | 0.155 |
| Native American | 0.007 | 0.007 | 0.007 | 0.011 | 0.006 |
| Hawaiian/Pacific Islander | 0.003 | 0.002 | 0.003 | 0.002 | 0.004 |
| Asian | 0.040 | 0.020 | 0.041 | 0.017 | 0.042 |
| Multiple | 0.016 | 0.019 | 0.015 | 0.021 | 0.017 |
| Hispanic | 0.168 | 0.127 | 0.170 | 0.144 | 0.169 |
| Family income | | | | | |
| under $10,000 | 0.058 | 0.075 | 0.056 | 0.064 | 0.060 |
| $10,000 - $19,999 | 0.117 | 0.125 | 0.113 | 0.132 | 0.121 |
| $20,000 - $29,999 | 0.113 | 0.117 | 0.112 | 0.109 | 0.114 |
| $30,000 - $39,999 | 0.113 | 0.108 | 0.114 | 0.115 | 0.113 |
| $40,000 - $49,999 | 0.113 | 0.112 | 0.114 | 0.108 | 0.114 |
| $50,000 - $75,000 | 0.192 | 0.189 | 0.193 | 0.189 | 0.190 |
| over $75,000 | 0.293 | 0.274 | 0.298 | 0.282 | 0.289 |

Notes: All means and proportions are estimated with the NSDUH sampling weights and include all non-missing observations in the 2001-2007 NSDUH.

Table 2: Outcome Variables by Sex & Depression Status

| | | Males | | Females | |
|---|---|---|---|---|---|
| | **All** | **Depressed** | **Non-depressed** | **Depressed** | **Non-depressed** |
| GPA | 2.9241 | 2.5337 | 2.8147 | 2.7556 | 3.0799 |
| | (0.878) | (0.944) | (0.887) | (0.904) | (0.834) |
| Grades=A | 0.2848 | 0.1652 | 0.2392 | 0.2155 | 0.3474 |
| Grades=B | 0.2293 | 0.3206 | 0.2672 | 0.2584 | 0.1805 |
| Grades=C | 0.4202 | 0.3588 | 0.4150 | 0.4254 | 0.4286 |
| Grades=D/F | 0.0657 | 0.1555 | 0.0786 | 0.1008 | 0.0435 |
| | | | | | |
| Fights in past 12 months | | | | | |
| 0 times | 0.7780 | 0.5763 | 0.7492 | 0.6621 | 0.8312 |
| 1-2 times | 0.1708 | 0.2899 | 0.1919 | 0.2415 | 0.1347 |
| 3-5 times | 0.0336 | 0.0833 | 0.0382 | 0.0599 | 0.0236 |
| 6-9 times | 0.0082 | 0.0230 | 0.0092 | 0.0188 | 0.0053 |
| 10+ times | 0.0094 | 0.0276 | 0.0115 | 0.0178 | 0.0053 |
| | | | | | |
| Stole in past 12 months | | | | | |
| 0 times | 0.9547 | 0.8505 | 0.9472 | 0.8983 | 0.9738 |
| 1-2 times | 0.0321 | 0.0986 | 0.0378 | 0.0669 | 0.0191 |
| 3-5 times | 0.0064 | 0.0222 | 0.0076 | 0.0146 | 0.0035 |
| 6-9 times | 0.0025 | 0.0091 | 0.0023 | 0.0091 | 0.0017 |
| 10+ times | 0.0043 | 0.0195 | 0.0052 | 0.0110 | 0.0019 |
| | | | | | |
| Attacked anyone in past 12 months | | | | | |
| 0 times | 0.9213 | 0.7742 | 0.9087 | 0.8490 | 0.9498 |
| 1-2 times | 0.0636 | 0.1627 | 0.0735 | 0.1147 | 0.0428 |
| 3-5 times | 0.0092 | 0.0349 | 0.0110 | 0.0236 | 0.0046 |
| 6-9 times | 0.0025 | 0.0119 | 0.0026 | 0.0064 | 0.0014 |
| 10+ times | 0.0034 | 0.0163 | 0.0043 | 0.0064 | 0.0014 |
| | | | | | |
| Substance Use in past 30 days | | | | | |
| Any binge drinking | 0.105 | 0.162 | 0.1077 | 0.1888 | 0.0914 |
| Any cigarette use | 0.116 | 0.2139 | 0.1075 | 0.2599 | 0.1071 |
| Any illicit drug use | 0.105 | 0.2197 | 0.09177 | 0.2078 | 0.1015 |
| Any nonmedical Rx drug use | 0.035 | 0.0789 | 0.0294 | 0.0879 | 0.0339 |

Notes: All means and proportions are estimated with the NSDUH sampling weights and include all non-missing observations in the 2001-2007 NSDUH.

Table 3: Difference-in-difference OLS Models of Grades

| | All Coefficient (SE) | Females Coefficient (SE) | Males Coefficient (SE) |
|---|---|---|---|
| Post-FDA*Depressed | -0.142*** | -0.203*** | -0.030 |
| | (0.046) | (0.052) | (0.094) |
| Depressed | -0.284*** | -0.296*** | -0.277*** |
| | (0.023) | (0.024) | (0.060) |
| Post-FDA | -0.026* | 0.003 | -0.055* |
| | (0.014) | (0.026) | (0.027) |
| Time | 0.002 | 0.004 | 0.001 |
| | (0.001) | (0.002) | (0.002) |
| Time*Post-FDA | -0.001 | -0.004 | 0.002 |
| | (0.001) | (0.002) | (0.002) |
| Time*Depressed | 0.006 | 0.008 | 0.002 |
| | (0.003) | (0.003) | (0.006) |
| Female | 0.268 | | |
| | (0.008) | | |
| Quarter=2 | -0.002 | -0.015 | 0.011 |
| | (0.007) | (0.011) | (0.010) |
| Quarter=3 | 0.002 | 0.000 | 0.004 |
| | (0.007) | (0.008) | (0.012) |
| Quarter=4 | 0.067 | 0.046 | 0.088 |
| | (0.008) | (0.011) | (0.013) |
| Age | -0.046 | -0.038 | -0.052 |
| | (0.002) | (0.003) | (0.003) |
| Race/ethnicity | | | |
|   Black | -0.211 | -0.211 | -0.212 |
| | (0.009) | (0.012) | (0.013) |
|     Native American | -0.156 | -0.071 | -0.234 |
| | (0.051) | (0.085) | (0.051) |
|     Hawaiian/Pacific Islander | -0.212 | -0.288 | -0.124 |
| | (0.073) | (0.086) | (0.131) |
|   Asian | 0.292 | 0.299 | 0.284 |
| | (0.025) | (0.026) | (0.041) |
|    Multiple race | -0.135 | -0.150 | -0.120 |
| | (0.032) | (0.045) | (0.039) |
|   Hispanic | -0.156 | -0.172 | -0.141 |
| | (0.009) | (0.014) | (0.013) |

Table 3: Difference-in-difference OLS Models of Grades, Ctd.

| | All Coefficient (SE) | Females Coefficient (SE) | Males Coefficient (SE) |
|---|---|---|---|
| Family Income | | | |
| $10,000-$19,999 | 0.015 | 0.022 | 0.010 |
| | (0.017) | (0.026) | (0.024) |
| $20,000-$29,999 | 0.058 | 0.068 | 0.049 |
| | (0.018) | (0.027) | (0.023) |
| $30,000-$39,999 | 0.112 | 0.156 | 0.068 |
| | (0.018) | (0.025) | (0.024) |
| | | | |
| $40,000-$49,999 | 0.177 | 0.201 | 0.153 |
| | (0.022) | (0.032) | (0.026) |
| $50,000-$75,000 | 0.296 | 0.317 | 0.277 |
| | (0.020) | (0.023) | (0.027) |
| >$75,000 | 0.467 | 0.487 | 0.448 |
| | (0.018) | (0.022) | (0.024) |
| Constant | 2.748 | 2.978 | 2.786 |
| | (0.022) | (0.028) | (0.028) |
| | | | |
| $R^2$ | 0.1049 | 0.0960 | 0.0793 |
| N | 106,639 | 52,287 | 54,352 |

Notes: OLS models estimated with heteroskedasticity-robust standard errors clustered on the time period. Observations from the first quarter of 2004 are excluded from the models.

Table 4: Effects of FDA Warnings at Different Points in the Grade Distribution

| Dependent Variable | All | Females | Males |
|---|---|---|---|
| | | | |
| A average | -0.0199 | -0.01778 | -0.029 |
| | (0.0213) | (0.0269) | (0.0436) |
| B average or better | -0.0838*** | -0.1123*** | -0.0259 |
| | (0.0289) | (0.0366) | (0.0472) |
| C average or better | -0.0352* | -0.05915*** | 0.0265 |
| | (0.0188) | (0.0162) | -(0.0319) |
| | | | |
| N | 106,639 | 52,287 | 54,352 |

Notes: Each cell represents the marginal effect and bootstrapped standard error from a separate probit model. Standard errors estimated from 500 bootstrap replications clustered on time period. All models exclude observations from first quarter of 2004. All models include the same set of covariates as in Table 3.

Table 5: Effects of FDA Warnings on Substance Use

| | Any Binge Drinking, Past 30 days | | |
| --- | --- | --- | --- |
| | **All Coefficient (SE)** | **Females Coefficient (SE)** | **Males Coefficient (SE)** |
| Post-FDA*Depressed | -0.062 | 0.038 | -0.262 |
| | (0.112) | (0.105) | (0.205) |
| Marginal Effect | -0.014 | 0.009 | -0.055 |
| (SE) | (0.025) | (0.023) | (0.043) |
| Depressed | 0.272*** | 0.331*** | 0.184** |
| | (0.045) | (0.039) | (0.087) |
| Marginal Effect | 0.058*** | 0.066*** | 0.046*** |
| (SE) | (0.004) | (0.005) | (0.007) |
| Post-FDA | 0.079** | 0.110** | 0.051 |
| | (0.038) | (0.049) | (0.047) |
| Marginal Effect | 0.000 | 0.003 | -0.003 |
| (SE) | (0.006) | (0.003) | (0.012) |
| N | 121,785 | 59,589 | 62,196 |
| Pseudo-$R^2$ | 0.1321 | 0.1138 | 0.1511 |
| | Any Cigarette Use, Past 30 days | | |
| | **All Coefficient (SE)** | **Females Coefficient (SE)** | **Males Coefficient (SE)** |
| Post-FDA*Depressed | 0.190*** | 0.187 | 0.164 |
| | (0.056) | (0.114) | (0.156) |
| Marginal Effect | 0.0459*** | 0.050 | 0.035 |
| (SE) | (0.016) | (0.034) | (0.038) |
| Depressed | 0.513*** | 0.557*** | 0.409*** |
| | (0.029) | (0.050) | (0.054) |
| Marginal Effect | 0.102*** | 0.110*** | 0.090*** |
| (SE) | (0.004) | (0.007) | (0.007) |
| Post-FDA | 0.044 | 0.090 | 0.002 |
| | (0.048) | (0.062) | (0.058) |
| Marginal Effect | -0.003 | 0.005 | -0.011 |
| (SE) | (0.007) | (0.006) | (0.007) |
| Pseudo-$R^2$ | 0.1354 | 0.1336 | 0.1394 |
| N | 121,785 | 59,589 | 62,196 |

Table 5: Effects of FDA Warnings on Substance Use, Ctd.

| | Illicit Drug Use, Past 30 days | | |
|---|---|---|---|
| | **All** **Coefficient** **(SE)** | **Females** **Coefficient** **(SE)** | **Males** **Coefficient** **(SE)** |
| Post-FDA*Depressed | 0.186** | 0.228** | 0.097 |
| | (0.079) | (0.105) | (0.099) |
| Marginal Effect | 0.04027* | 0.0542* | -0.031 |
| (SE) | (0.023) | (0.031) | (0.030) |
| Depressed | 0.491*** | 0.560*** | 0.397*** |
| | (0.045) | (0.044) | (0.096) |
| Marginal Effect | 0.101 | 0.103*** | 0.098*** |
| (SE) | (0.005) | (0.007) | (0.008) |
| Post-FDA | 0.023 | 0.071 | -0.022 |
| | (0.035) | (0.055) | (0.054) |
| Marginal Effect | -0.016 | -0.012 | -0.021** |
| (SE) | (0.007) | (0.009) | (0.009) |
| Pseudo-$R^2$ | 0.0711 | 0.0649 | 0.0788 |
| N | 121,785 | 59,589 | 62,196 |
| | Nonmedical Rx Drug Use, Past 30 days | | |
| | **All** **Coefficient** **(SE)** | **Females** **Coefficient** **(SE)** | **Males** **Coefficient** **(SE)** |
| Post-FDA*Depressed | 0.172 | 0.331** | -0.102 |
| | (0.129) | (0.143) | (0.185) |
| Marginal Effect | 0.018 | 0.0427* | -0.029 |
| (SE) | (0.020) | (0.024) | (0.044) |
| Depressed | 0.490*** | 0.519*** | 0.434*** |
| | (0.057) | (0.068) | (0.103) |
| Marginal Effect | 0.0437*** | 0.0434*** | 0.047*** |
| (SE) | (0.004) | (0.005) | (0.007) |
| Post-FDA | 0.087* | 0.026 | 0.152** |
| | (0.048) | (0.087) | (0.077) |
| Marginal Effect | -0.011* | -0.009 | -0.014 |
| (SE) | (0.006) | (0.012) | (0.009) |
| Pseudo-$R^2$ | 0.0409 | 0.0396 | 0.0433 |
| N | 121,785 | 59,589 | 62,196 |

Notes: All models exclude observations from first quarter of 2004. Standard errors of marginal effects are estimated from 500 bootstrap replications, clustered on the time period. All models include the same set of covariates as in Table 3.

Table 6: Effects of FDA Warnings on Delinquency Outcomes, Probit Models

| Fights past 12 months | All Coefficient (SE) | Females Coefficient (SE) | Males Coefficient (SE) |
|---|---|---|---|
| Post-FDA*Depressed | 0.187*** | 0.236*** | 0.155 |
|  | (0.054) | (0.071) | (0.124) |
| Marginal Effect | 0.065*** | 0.075*** | 0.045 |
| (SE) | (0.025) | (0.027) | (0.043) |
| Depressed | 0.589*** | 0.668*** | 0.488*** |
|  | (0.051) | (0.059) | (0.075) |
| Marginal Effect | 0.177*** | 0.175*** | 0.170*** |
| (SE) | (0.007) | (0.009) | (0.011) |
| Post-FDA | 0.205*** | 0.127*** | 0.266*** |
|  | (0.031) | (0.032) | (0.040) |
| Marginal Effect | -0.032** | -0.038** | -0.024 |
| (SE) | (0.015) | (0.017) | (0.020) |
| Pseudo-$R^2$ | 0.0348 | 0.0356 | 0.0219 |
| N | 116,371 | 57,030 | 59,341 |
| **Stealing past 12 months** | **All** | **Females** | **Males** |
| Post-FDA*Depressed | 0.263** | 0.445** | -0.006 |
|  | (0.126) | (0.199) | (0.181) |
| Marginal Effect | 0.046* | 0.069** | -0.023 |
| (SE) | (0.028) | (0.032) | (0.038) |
| Depressed | 0.673*** | 0.735*** | 0.587*** |
|  | (0.055) | (0.090) | (0.084) |
| Marginal Effect | 0.085*** | 0.071*** | 0.098*** |
| (SE) | (0.005) | (0.006) | (0.010) |
| Post-FDA | 0.009 | -0.015 | 0.020 |
|  | (0.068) | (0.093) | (0.105) |
| Marginal Effect | -0.003 | 0.002 | -0.008 |
| (SE) | (0.006) | (0.004) | (0.009) |
| Pseudo-$R^2$ | 0.0540 | 0.0544 | 0.0401 |
| N | 116,471 | 57,073 | 59,398 |

| Table 6: Effects of FDA Warnings on Delinquency Outcomes, Ctd. | | | |
|---|---|---|---|
| **Attacks past 12 months** | **All** | **Females** | **Males** |
| Post-FDA*Depressed | 0.034 | 0.143 | -0.070 |
| | (0.094) | (0.133) | (0.134) |
| Marginal Effect | 0.0004 | 0.019 | -0.021 |
| (SE) | (0.026) | (0.031) | (0.039) |
| Depressed | 0.646*** | 0.697*** | 0.605*** |
| | (0.050) | (0.056) | (0.074) |
| Marginal Effect | 0.117*** | 0.101*** | 0.133*** |
| (SE) | (0.006) | (0.007) | (0.009) |
| Post-FDA | 0.007 | -0.099 | 0.074 |
| | (0.054) | (0.085) | (0.055) |
| Marginal Effect | -0.010 | -0.010 | -0.009 |
| (SE) | (0.007) | (0.009) | (0.008) |
| Pseudo-$R^2$ | 0.0461 | 0.0544 | 0.0272 |
| N | 116,467 | 57,076 | 59,391 |

Notes: All models exclude observations from first and second quarters of 2004. Standard errors of marginal effects are estiamted from 500 bootstrap replications, clustered on the time period. All models include the same set of covariates as in Table 3.

Table 7: Specification Check of Coefficients on "Depress*Post-FDA" in OLS regressions of covariates

| Variable | All | Females | Males |
|---|---|---|---|
| Age | 0.026 | 0.103 | -0.066 |
| | (0.091) | (0.112) | (0.153) |
| Race/ethnicity | | | |
| Black | 0.010 | 0.014 | 0.007 |
| | (0.020) | (0.025) | (0.033) |
| Native American | -0.007 | -0.008 | -0.004 |
| | (0.007) | (0.010) | (0.005) |
| Hawaiian/Pacific | | | |
| Islander | 0.001 | 0.003 | -0.001 |
| | (0.002) | (0.002) | (0.003) |
| Asian | 0.001 | -0.008 | 0.016 |
| | (0.009) | (0.012) | (0.015) |
| Multiple race | 0.004 | 0.007 | -0.001 |
| | (0.007) | (0.008) | (0.012) |
| Hispanic | 0.033 | 0.051 | 0.005 |
| | (0.23) | (0.030) | (0.033) |
| Family Income | | | |
| $10,000-$19,999 | 0.004 | 0.011 | -0.008 |
| | (0.020) | (0.027) | (0.031) |
| $20,000-$29,999 | -0.005 | -0.004 | -0.015 |
| | (0.017) | (0.021) | (0.029) |
| $30,000-$39,999 | 0.001 | 0.156 | -0.042 |
| | (0.017) | (0.025) | (0.027) |
| $40,000-$49,999 | 0.026 | 0.021 | 0.033 |
| | (0.018) | (0.024) | (0.028) |
| $50,000-$75,000 | -0.006 | -0.016 | 0.108 |
| | (0.028) | (0.02) | (0.035) |
| >$75,000 | -0.037 | -.0458 | -0.017 |
| | (0.024) | (0.032) | (0.039) |
| Female | -0.0178 | - | - |
| | (0.0266) | | |

Each cell shows the coefficient and, in ()s, standard error, from a separate model. The outcome variable in each model is indicated by the row. The other independent variables in the model include dummies for depression, post-FDA, a time trend, t, the interaction of post-FDA*t, and three indicators for the quarter (2nd, 3rd, 4th ) when a respondent completed the survey.

Figure 1: Timeline of FDA Actions & Counts of News Media Stories on Pediatric
Antidepressant Use and Suicidality (2003-2004)
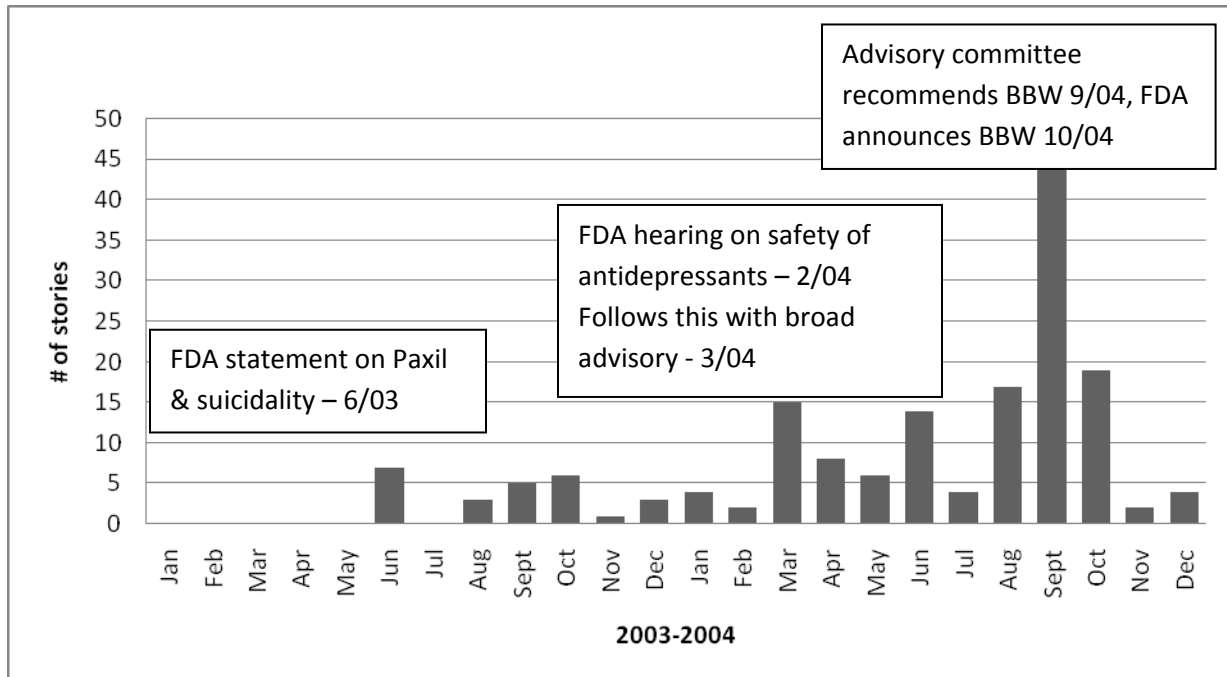


Notes: FDA=Food and Drug Administration; This data was originally displayed in Barry, CL et al. News Coverage of FDA warnings on Pediatric Antidepressant Use and Suicidality. Pediatrics 125; 88-95 (2009). Data reflects counts and timing of all news stories on pediatric antidepressant use and suicidality in 10 high circulation print newspapers and three major television networks and CNN from 1/2003-12/2004.

Figure 2: Declines in Antidepressant Use among Privately and Publicly Insured Pediatric Patients
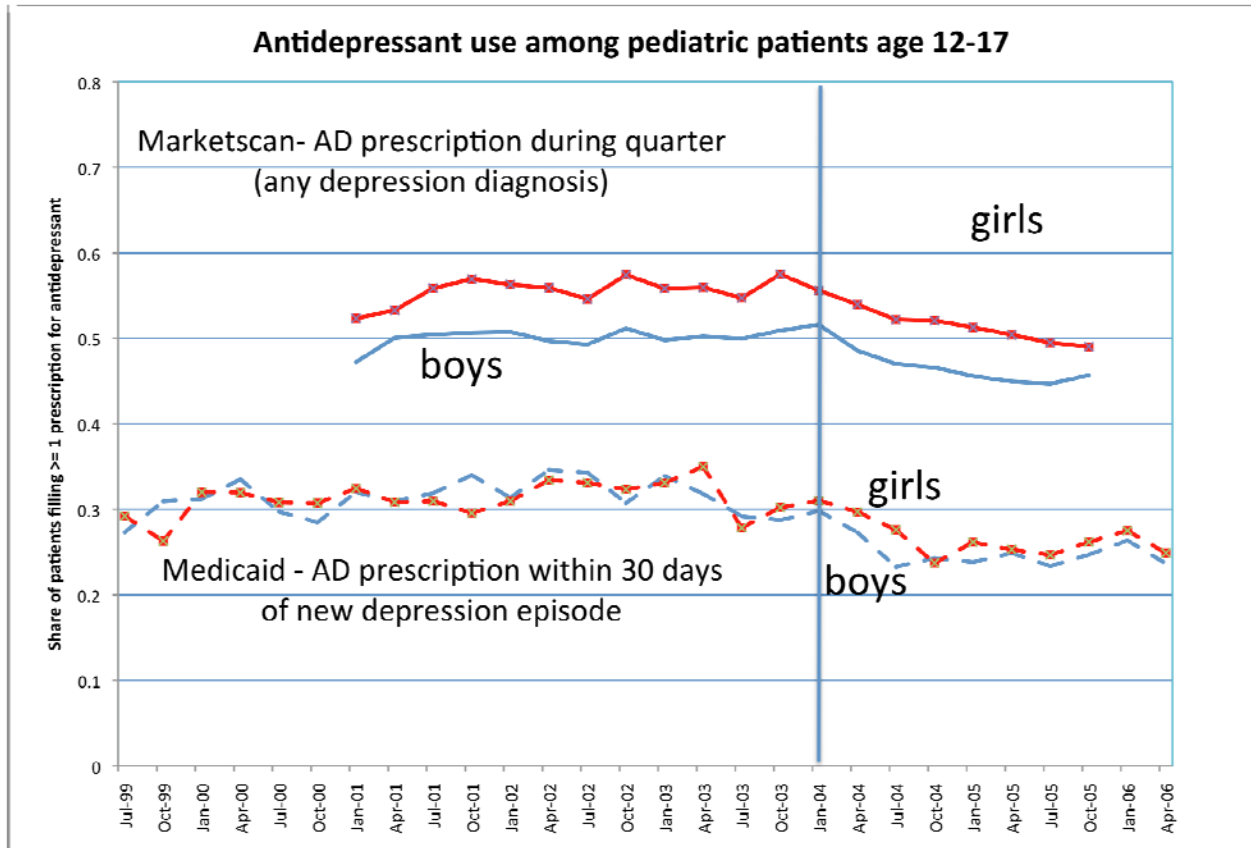


Note: Medicaid data reflect pediatric patients with a diagnosis of depression in the Florida Medicaid program. Marketscan data reflect privately insured pediatric patients with a diagnosis of depression. Antidepressant use is defined as a claim for any one of 36 antidepressants. See text for full details.

Figure 3: Annual Antidepressant Use among Kids 12-17 Seeing a Medical Provider for Depression Symptoms (Medical Expenditure Panel Survey)
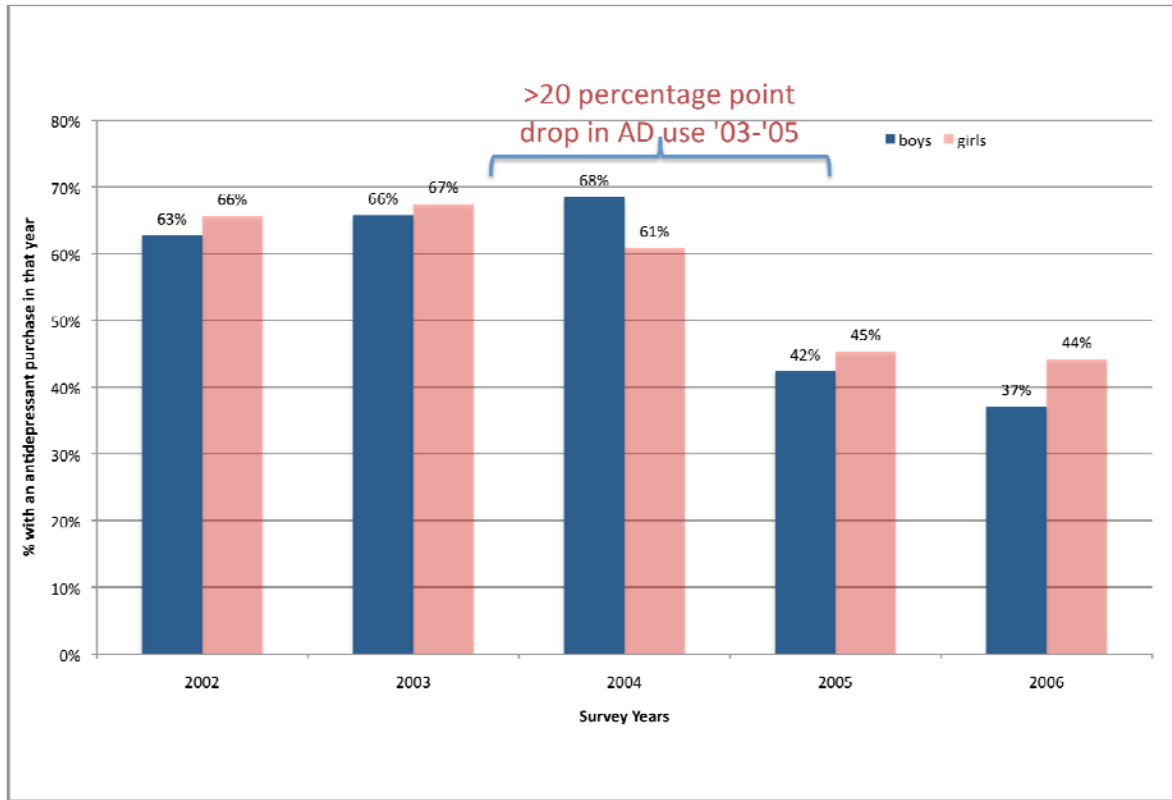


Note: Reflects 12 month prevalence of any antidepressant claim during that calendar year for respondents with a medical encounter including a 3-digit International Classification of Disease Code of 296, 300, or 311. Data for 2004 reflect a mix of pre- and post- period data.

Figure 4: Suicides by Age and Sex
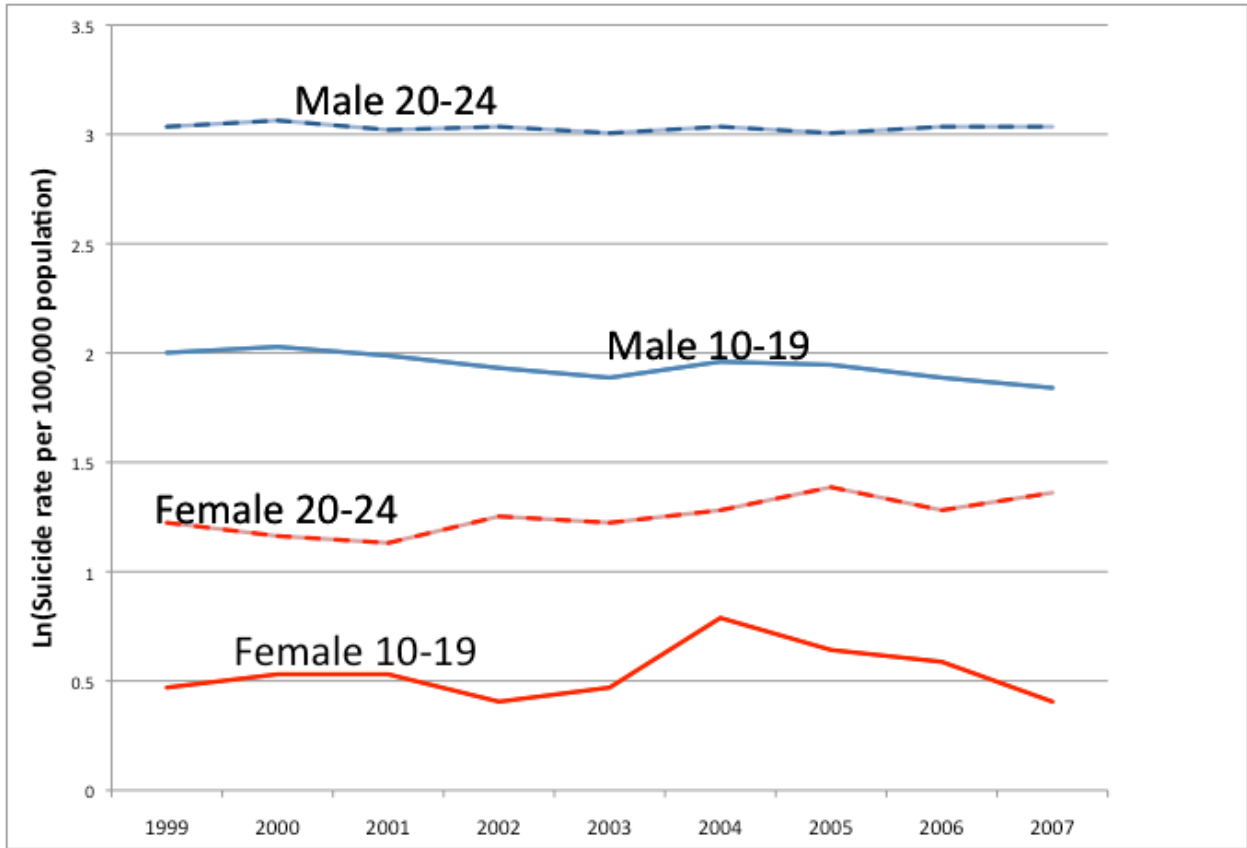


Source: Centers for Disease Control and Prevention, National Center for Health Statistics, Compressed Mortality File 1999-2007. CDC WONDER On-line Database, compiled from Compressed Mortality File 1999-2007 Series 20 No. 2M, 2010. Accessed at http://wonder.cdc.gov/cmf-icd10.html on Mar 21, 2011.

Figure 5: Raw Data on Grade Point Average by Depression Status in Last Year
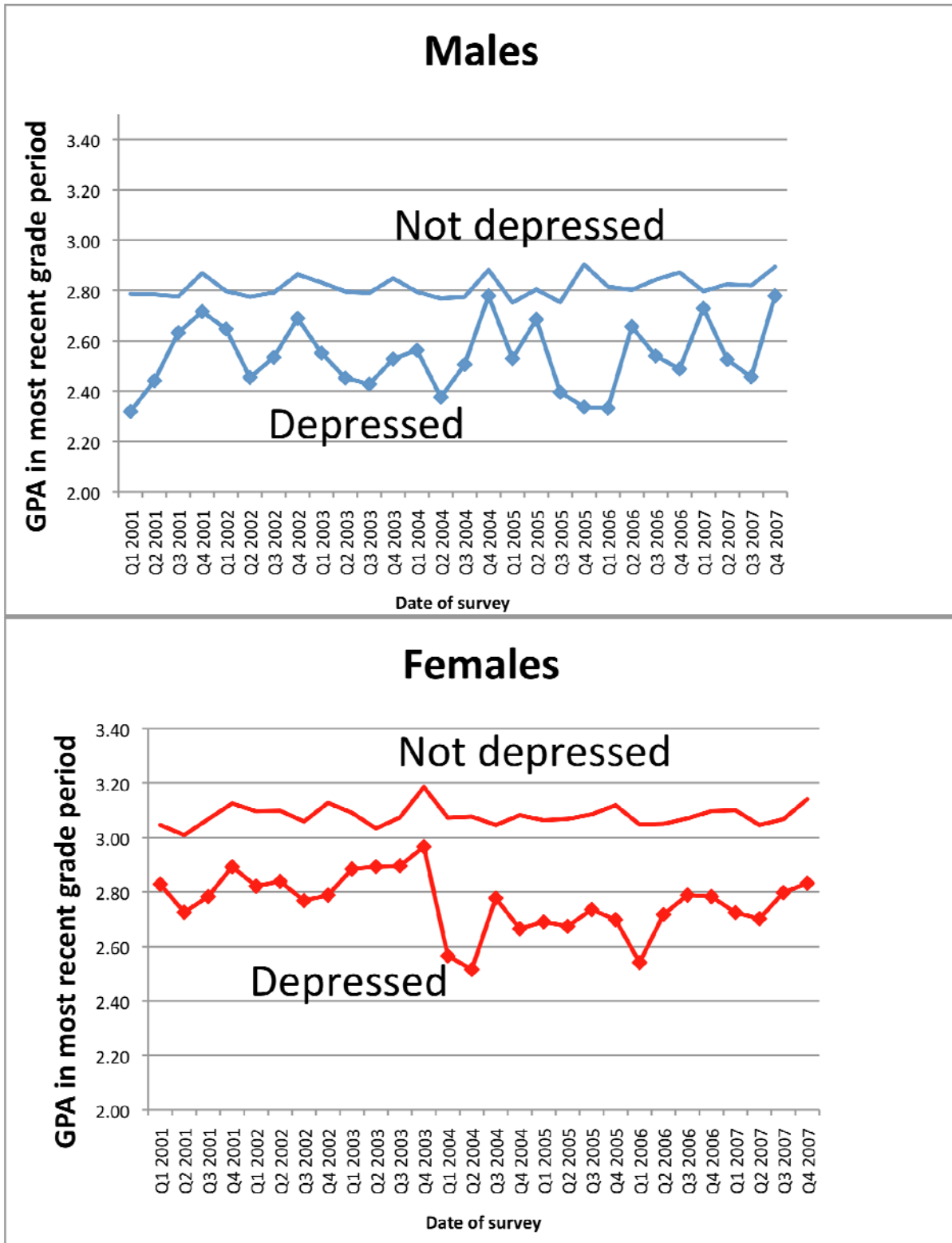


Note: N=56340 (males), N=54278 (females), means estimated with NSDUH sampling weights

Figure 6: Depression Status Over Time in the NSDUH
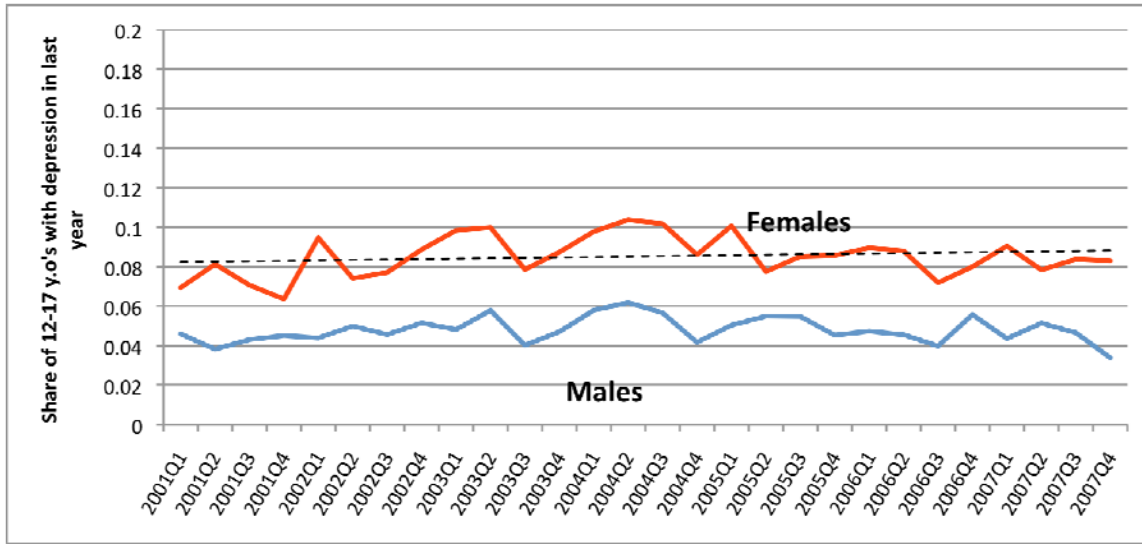


Note: A linear probability model of the quarterly rate of depression on a quarterly time trend, an indicator for post-FDA advisories (after Q1 of 2004), and their interaction yields coefficients (robust standard errors clustered on the time period) on post-FDA of 0.0436 (.009) for females and .0255 (.006) for males. For females, the coefficient on time is 0.0024 (0.0006) and the coefficient on the interaction between the time trend and post-FDA is -0.0034 (0.0007). For males, the coefficient on time is 0.0007 (0.0004) and the coefficient on the interaction between the time trend and post-FDA is -0.016 (0.0005). All models are adjusted for seasonality and sociodemographic characteristics (as described by the specification in Table 3).

**APPENDIX FOR "THE FDA AND ABCS: UNINTENDED CONSEQUENCES OF ANTIDEPRESSANT WARNINGS ON HUMAN CAPITAL"**

**Appendix table A1: Peer-reviewed studies of declines in pediatric antidepressant use in the United States**

| Citation | Population/Data | Results |
|---|---|---|
| Nemeroff et al., 2007 | Verispan data; represents ~ ½ of retail prescriptions in US (ages 0-17) | 5% decline in pediatric antidepressant volume in Q1 2004;  Additional 11% decline in Q2 2004; No further change through March 2005 |
| Gibbons et al.,  2007 | IMS pharmacy data;  aggregated to national level (ages 0-14) | 22% decline in youth antidepressant volume from 2003 to 2005; 30% decline in new youth antidepressant prescription volume from 2003 to 2005 |
| Kurian et al., 2007 | Tennessee Medicaid pharmacy data; (ages 2-17) | 33% decline in new antidepressant use (i.e. individual fills any antidepressant prescription in month) |
| Busch et al., 2010 | Medical Expenditure Panel Survey; nationally representative survey data (ages 5-21) | 26% decline in twelve-month prevalence rates of antidepressant use from 2002/3 to 2005/6 (i.e., individual fills any antidepressant prescription in year) |
| Libby et al., 2009 | PharMetrics Patient-Centric Database; eighty-five managed care plans (ages 5-18) | After accounting for prescribing trends, 58 % decline in antidepressant use among individuals newly diagnosed with depression (within 30 days post diagnosis.) |
| Busch et al., 2010b | Marketscan data; privately insured (ages 5-17) | 19% decline in antidepressant use among individuals newly diagnosed with depression (within 30 days post diagnosis.) |
| Valluri et al, 2010 | i3 Innovus database; commercial insurance enrollees (ages 2-17) | 17% decline in antidepressant use among individuals newly diagnosed with depression (within 180 days post diagnosis.) |

# Appendix Table A2: Regression Results for Binge Drinking

| | Any Binge Drinking, Past 30 days | | |
| --- | --- | --- | --- |
| | All | Females | Males |
| | Coefficient (SE) | Coefficient (SE) | Coefficient (SE) |
| Post-FDA*Depressed | -0.062 | 0.038 | -0.262 |
| | (0.112) | (0.105) | (0.205) |
| Marginal Effect (SE) | -0.014 | 0.009 | -0.055 |
| | (0.025) | (0.023) | (0.043) |
| Depressed | 0.272*** | 0.331*** | 0.184** |
| | (0.045) | (0.039) | (0.087) |
| Marginal Effect (SE) | 0.058 | 0.066 | 0.046 |
| | | | |
| Post-FDA | 0.079** | 0.110** | 0.051 |
| | (0.038) | (0.049) | (0.047) |
| Marginal Effect (SE) | 0.000 | 0.003 | -0.003 |
| | | | |
| Time | 0.000 | 0.001 | -0.001 |
| | (0.003) | (0.003) | (0.004) |
| Time*Post-FDA | -0.005 | -0.007 | -0.004 |
| | (0.003) | (0.004) | (0.004) |
| Time*Depressed | 0.005 | 0.000 | 0.014 |
| | (0.006) | (0.005) | (0.011) |
| Female | -0.070 | | |
| | (0.011) | | |
| Quarter=2 | -0.048 | -0.024 | -0.071 |
| | (0.014) | (0.021) | (0.016) |
| Quarter=3 | 0.018 | 0.052 | -0.016 |
| | (0.013) | (0.023) | (0.017) |
| Quarter=4 | -0.065 | -0.030 | -0.100 |
| | (0.017) | (0.022) | (0.022) |
| Age | 0.311 | 0.274 | 0.347 |
| | (0.005) | (0.007) | (0.007) |
| Black | -0.517 | -0.508 | -0.526 |
| | (0.027) | (0.041) | (0.035) |
| Native Am | 0.135 | 0.103 | 0.157 |
| | (0.092) | (0.146) | (0.096) |
| Native HI/PI | -0.342 | -0.510 | -0.170 |
| | (0.132) | (0.192) | (0.168) |
| Asian | -0.568 | -0.485 | -0.647 |
| | (0.053) | (0.070) | (0.094) |
| Multiple | -0.135 | -0.131 | -0.136 |
| | (0.048) | (0.063) | (0.081) |
| Hispanic | -0.110 | -0.111 | -0.111 |
| | (0.026) | (0.033) | (0.040) |
| $10k-$20k | -0.031 | -0.062 | -0.002 |
| | (0.038) | (0.052) | (0.040) |
| $20k-$30k | -0.079 | -0.044 | -0.119 |
| | (0.046) | (0.064) | (0.059) |
| $30k-$40k | -0.059 | -0.083 | -0.041 |
| | (0.038) | (0.048) | (0.053) |
| $40k-$50k | -0.093 | -0.053 | -0.133 |
| | (0.039) | (0.059) | (0.047) |
| $50k-$75k | -0.087 | -0.087 | -0.091 |
| | (0.033) | (0.049) | (0.043) |
| >$75k | -0.096 | -0.096 | -0.098 |
| | (0.036) | (0.053) | (0.041) |
| Constant | -2.293 | -2.244 | -2.409 |
| | (0.052) | (0.064) | (0.069) |

**Appendix Table A3: Regression Results for Cigarette Use**

| | Any Cigarette Use, Past 30 days | | |
| --- | --- | --- | --- |
| | **All** | **Females** | **Males** |
| | Coefficient (SE) | Coefficient (SE) | Coefficient (SE) |
| Post-FDA*Depressed | 0.190*** | 0.187*** | 0.164 |
| | (0.056) | (0.114) | (0.156) |
| Marginal Effect (SE) | 0.0459*** | 0.050 | 0.035 |
| | (0.016) | (0.034) | (0.038) |
| Depressed | 0.513 | 0.557*** | 0.409*** |
| | (0.029) | (0.050) | (0.054) |
| Marginal Effect (SE) | 0.102 | 0.110 | 0.090 |
| | | | |
| Post-FDA | 0.044 | 0.090 | 0.002 |
| | (0.048) | (0.062) | (0.058) |
| Marginal Effect (SE) | -0.003 | 0.005 | -0.011 |
| | | | |
| Time | -0.002 | -0.005 | 0.001 |
| | (0.003) | (0.004) | (0.003) |
| Time*Post-FDA | -0.006 | -0.006 | -0.005 |
| | (0.003) | (0.004) | (0.003) |
| Time*Depressed | -0.010 | -0.011 | -0.004 |
| | (0.003) | (0.006) | (0.008) |
| Female | 0.020 | | |
| | (0.012) | | |
| Quarter=2 | -0.010 | -0.017 | -0.004 |
| | (0.019) | (0.028) | (0.023) |
| Quarter=3 | 0.005 | 0.011 | -0.003 |
| | (0.019) | (0.027) | (0.021) |
| Quarter=4 | -0.013 | 0.005 | -0.032 |
| | (0.023) | (0.029) | (0.027) |
| Age | 0.293 | 0.270 | 0.316 |
| | (0.003) | (0.006) | (0.007) |
| Black | -0.567 | -0.641 | -0.495 |
| | (0.026) | (0.037) | (0.035) |
| Native Am | 0.221 | 0.163 | 0.281 |
| | (0.061) | (0.089) | (0.094) |
| Native HI/PI | -0.475 | -0.451 | -0.511 |
| | (0.136) | (0.171) | (0.202) |
| Asian | -0.686 | -0.789 | -0.597 |
| | (0.056) | (0.089) | (0.081) |
| Multiple | -0.074 | -0.081 | -0.068 |
| | (0.042) | (0.051) | (0.059) |
| Hispanic | -0.377 | -0.429 | -0.326 |
| | (0.025) | (0.037) | (0.034) |
| $10k-$20k | -0.103 | -0.110 | -0.097 |
| | (0.032) | (0.048) | (0.052) |
| $20k-$30k | -0.115 | -0.065 | -0.168 |
| | (0.034) | (0.048) | (0.048) |
| $30k-$40k | -0.198 | -0.172 | -0.226 |
| | (0.037) | (0.042) | (0.058) |
| $40k-$50k | -0.217 | -0.205 | -0.229 |
| | (0.027) | (0.040) | (0.044) |
| $50k-$75k | -0.368 | -0.349 | -0.389 |
| | (0.026) | (0.049) | (0.038) |
| >$75k | -0.447 | -0.436 | -0.458 |
| | (0.030) | (0.045) | (0.052) |
| Constant | -1.918 | -1.784 | -2.033 |
| | (0.048) | (0.080) | (0.066) |

# Appendix Table A4: Regression Results for Illicit Drug Use

| | Any Illicit Drug Use, Past 30 days | | |
| --- | --- | --- | --- |
| | All | Females | Males |
| | Coefficient (SE) | Coefficient (SE) | Coefficient (SE) |
| Post-FDA*Depressed | 0.186** | 0.228** | 0.097 |
| | (0.079) | (0.105) | (0.099) |
| Marginal Effect (SE) | 0.04027* | .0542* | -0.031 |
| | (0.023) | (0.031) | (0.030) |
| Depressed | 0.491*** | 0.560*** | 0.397*** |
| | (0.045) | (0.044) | (0.096) |
| Marginal Effect (SE) | 0.101 | 0.103 | 0.098 |
| | | | |
| Post-FDA | 0.023 | 0.071 | -0.022 |
| | (0.035) | (0.055) | (0.054) |
| Marginal Effect (SE) | -0.016 | -0.012 | -0.021 |
| | | | |
| Time | 0.005 | 0.008 | 0.003 |
| | (0.002) | (0.002) | (0.003) |
| Time*Post-FDA | -0.009 | -0.012 | -0.007 |
| | (0.002) | (0.003) | (0.003) |
| Time*Depressed | -0.008 | -0.014 | 0.000 |
| | (0.005) | (0.005) | (0.008) |
| Female | -0.047 | | |
| | (0.012) | | |
| Quarter=2 | 0.016 | 0.024 | 0.007 |
| | (0.011) | (0.024) | (0.020) |
| Quarter=3 | -0.022 | -0.018 | -0.027 |
| | (0.013) | (0.027) | (0.024) |
| Quarter=4 | -0.029 | -0.011 | -0.046 |
| | (0.016) | (0.026) | (0.025) |
| Age | 0.203 | 0.180 | 0.226 |
| | (0.005) | (0.006) | (0.006) |
| Black | -0.088 | -0.122 | -0.057 |
| | (0.022) | (0.026) | (0.030) |
| Native Am | 0.402 | 0.395 | 0.409 |
| | (0.064) | (0.099) | (0.102) |
| Native HI/PI | -0.044 | -0.218 | 0.130 |
| | (0.126) | (0.148) | (0.192) |
| Asian | -0.333 | -0.341 | -0.326 |
| | (0.040) | (0.059) | (0.069) |
| Multiple | 0.087 | 0.125 | 0.043 |
| | (0.047) | (0.061) | (0.067) |
| Hispanic | -0.095 | -0.120 | -0.072 |
| | (0.017) | (0.026) | (0.027) |
| $10k-$20k | -0.050 | -0.020 | -0.078 |
| | (0.038) | (0.058) | (0.055) |
| $20k-$30k | -0.067 | 0.010 | -0.144 |
| | (0.036) | (0.048) | (0.046) |
| $30k-$40k | -0.142 | -0.096 | -0.187 |
| | (0.034) | (0.047) | (0.047) |
| $40k-$50k | -0.148 | -0.099 | -0.193 |
| | (0.035) | (0.042) | (0.046) |
| $50k-$75k | -0.199 | -0.140 | -0.258 |
| | (0.025) | (0.044) | (0.039) |
| >$75k | -0.221 | -0.180 | -0.263 |
| | (0.031) | (0.046) | (0.042) |
| Constant | -1.856 | -1.891 | -1.871 |
| | (0.037) | (0.052) | (0.060) |

**Appendix Table A5: Regression Results for Misuse of Rx Drugs**

| | Any Inappropriate Prescription Drug Use, Past 30 days | | |
| | All | Females | Males |
| Post-FDA*Depressed | Coefficient (SE) | Coefficient (SE) | Coefficient (SE) |
|---|---|---|---|
| | 0.172 | 0.331** | -0.102 |
| Marginal Effect (SE) | (0.129) | (0.143) | (0.185) |
| | 0.018 | .0427* | -0.029 |
| Depressed | (0.020) | (0.024) | (0.044) |
| | 0.490*** | 0.519*** | 0.434*** |
| Marginal Effect (SE) | (0.057) | (0.068) | (0.103) |
| | 0.044 | 0.043 | 0.047 |
| Post-FDA | | | |
| | 0.087* | 0.026 | 0.152** |
| Marginal Effect (SE) | (0.048) | (0.087) | (0.077) |
| | -0.011 | -0.009 | -0.014 |
| Time | | | |
| | 0.014 | 0.012 | 0.016 |
| Time*Post-FDA | (0.003) | (0.005) | (0.005) |
| | -0.016 | -0.012 | -0.021 |
| Time*Depressed | (0.004) | (0.006) | (0.006) |
| | -0.011 | -0.021 | 0.007 |
| Female | (0.008) | (0.008) | (0.011) |
| | 0.067 | | |
| Quarter=2 | (0.018) | | |
| | -0.023 | 0.013 | -0.066 |
| Quarter=3 | (0.026) | (0.039) | (0.031) |
| | -0.061 | -0.055 | -0.071 |
| Quarter=4 | (0.021) | (0.034) | (0.030) |
| | -0.052 | -0.039 | -0.070 |
| Age | (0.023) | (0.041) | (0.026) |
| | 0.116 | 0.104 | 0.129 |
| Black | (0.006) | (0.008) | (0.010) |
| | -0.128 | -0.131 | -0.127 |
| Native Am | (0.028) | (0.033) | (0.043) |
| | 0.184 | 0.082 | 0.289 |
| Native HI/PI | (0.094) | (0.138) | (0.146) |
| | 0.099 | 0.011 | 0.211 |
| Asian | (0.161) | (0.194) | (0.262) |
| | -0.268 | -0.295 | -0.239 |
| Multiple | (0.049) | (0.089) | (0.093) |
| | -0.033 | 0.075 | -0.212 |
| Hispanic | (0.050) | (0.070) | (0.089) |
| | -0.145 | -0.191 | -0.097 |
| $10k-$20k | (0.022) | (0.028) | (0.045) |
| | -0.093 | -0.054 | -0.140 |
| $20k-$30k | (0.046) | (0.073) | (0.069) |
| | -0.158 | -0.116 | -0.209 |
| $30k-$40k | (0.045) | (0.070) | (0.055) |
| | -0.182 | -0.122 | -0.252 |
| $40k-$50k | (0.050) | (0.072) | (0.064) |
| | -0.178 | -0.205 | -0.153 |
| $50k-$75k | (0.039) | (0.052) | (0.052) |
| | -0.277 | -0.248 | -0.311 |
| >$75k | (0.044) | (0.068) | (0.052) |
| | -0.329 | -0.349 | -0.312 |
| Constant | (0.036) | (0.059) | (0.052) |
| | -2.094 | -1.984 | -2.143 |
| | (0.046) | (0.071) | (0.070) |

## Appendix Table A6: Regression Results on Fighting

| | Any Fights Past 12 Months | | |
|---|---|---|---|
| | All | Females | Males |
| | Coefficient (SE) | Coefficient (SE) | Coefficient (SE) |
| Post-FDA*Depressed | 0.187*** | 0.236*** | 0.155 |
| | (0.054) | (0.071) | (0.124) |
| Marginal Effect (SE) | 0.0653*** | .0754*** | 0.0445 |
| | (0.025) | (0.027) | (0.043) |
| Depressed | 0.589*** | 0.668*** | 0.488*** |
| | (0.051) | (0.059) | (0.075) |
| Marginal Effect (SE) | 0.177 | 0.175 | 0.170 |
| | | | |
| Post-FDA | 0.205*** | 0.127*** | 0.266*** |
| | (0.031) | (0.032) | (0.040) |
| Marginal Effect (SE) | -0.032 | -0.038 | -0.024 |
| | | | |
| Time | 0.022 | 0.024 | 0.020 |
| | (0.002) | (0.003) | (0.003) |
| Time*Post-FDA | -0.021 | -0.019 | -0.023 |
| | (0.003) | (0.003) | (0.003) |
| Time*Depressed | -0.011 | -0.016 | -0.006 |
| | (0.004) | (0.005) | (0.008) |
| Female | -0.293 | | |
| | (0.011) | | |
| Quarter=2 | 0.000 | -0.008 | 0.009 |
| | (0.017) | (0.017) | (0.022) |
| Quarter=3 | 0.032 | -0.016 | 0.072 |
| | (0.015) | (0.016) | (0.021) |
| Quarter=4 | -0.084 | -0.089 | -0.078 |
| | (0.019) | (0.019) | (0.025) |
| Age | -0.024 | -0.010 | -0.036 |
| | (0.004) | (0.007) | (0.004) |
| Black | 0.231 | 0.290 | 0.180 |
| | (0.015) | (0.029) | (0.021) |
| Native Am | 0.143 | 0.103 | 0.178 |
| | (0.062) | (0.098) | (0.086) |
| Native HI/PI | 0.126 | 0.255 | -0.022 |
| | (0.087) | (0.134) | (0.097) |
| Asian | -0.219 | -0.207 | -0.228 |
| | (0.035) | (0.062) | (0.051) |
| Multiple | 0.183 | 0.220 | 0.150 |
| | (0.028) | (0.050) | (0.044) |
| Hispanic | 0.100 | 0.126 | 0.080 |
| | (0.017) | (0.027) | (0.019) |
| $10k-$20k | -0.053 | -0.049 | -0.060 |
| | (0.028) | (0.043) | (0.036) |
| $20k-$30k | -0.116 | -0.086 | -0.142 |
| | (0.027) | (0.043) | (0.038) |
| $30k-$40k | -0.138 | -0.130 | -0.147 |
| | (0.025) | (0.041) | (0.034) |
| $40k-$50k | -0.190 | -0.176 | -0.204 |
| | (0.030) | (0.050) | (0.038) |
| $50k-$75k | -0.274 | -0.286 | -0.268 |
| | (0.028) | (0.047) | (0.037) |
| >$75k | -0.350 | -0.366 | -0.340 |
| | (0.029) | (0.045) | (0.039) |
| Constant | -0.599 | -0.959 | -0.544 |
| | (0.037) | (0.055) | (0.038) |

## Appendix Table A7: Regression Results on Stealing

| | Any Stealing Past 12 Months | | |
| --- | --- | --- | --- |
| | All | Females | Males |
| | Coefficient (SE) | Coefficient (SE) | Coefficient (SE) |
| Post-FDA*Depressed | 0.263** | 0.445** | -0.006 |
| | (0.126) | (0.199) | (0.181) |
| Marginal Effect (SE) | 0.0464* | .0688** | -0.0234 |
| | (0.028) | (0.032) | (0.038) |
| Depressed | 0.673*** | 0.735*** | 0.587*** |
| | (0.055) | (0.090) | (0.084) |
| Marginal Effect (SE) | 0.085 | 0.071 | 0.098 |
| | | | |
| Post-FDA | 0.009 | -0.015 | 0.020 |
| | (0.068) | (0.093) | (0.105) |
| Marginal Effect (SE) | -0.003 | 0.002 | -0.008 |
| | | | |
| Time | 0.007 | 0.007 | 0.007 |
| | (0.004) | (0.004) | (0.005) |
| Time*Post-FDA | -0.005 | -0.004 | -0.006 |
| | (0.005) | (0.005) | (0.007) |
| Time*Depressed | -0.013 | -0.023 | 0.001 |
| | (0.007) | (0.011) | (0.011) |
| Female | -0.319 | | |
| | (0.018) | | |
| Quarter=2 | 0.004 | 0.017 | -0.005 |
| | (0.019) | (0.033) | (0.039) |
| Quarter=3 | -0.005 | 0.002 | -0.010 |
| | (0.028) | (0.038) | (0.040) |
| Quarter=4 | -0.035 | -0.040 | -0.033 |
| | (0.022) | (0.031) | (0.035) |
| Age | 0.113 | 0.101 | 0.121 |
| | (0.005) | (0.010) | (0.007) |
| Black | 0.070 | 0.046 | 0.085 |
| | (0.033) | (0.035) | (0.048) |
| Native Am | 0.281 | 0.156 | 0.359 |
| | (0.085) | (0.119) | (0.101) |
| Native HI/PI | 0.314 | 0.392 | 0.227 |
| | (0.110) | (0.145) | (0.180) |
| Asian | -0.036 | -0.017 | -0.045 |
| | (0.062) | (0.080) | (0.084) |
| Multiple | 0.173 | 0.200 | 0.151 |
| | (0.048) | (0.088) | (0.076) |
| Hispanic | 0.080 | 0.022 | 0.116 |
| | (0.025) | (0.045) | (0.036) |
| $10k-$20k | -0.023 | 0.051 | -0.071 |
| | (0.039) | (0.059) | (0.049) |
| $20k-$30k | -0.129 | -0.028 | -0.193 |
| | (0.040) | (0.062) | (0.063) |
| $30k-$40k | -0.055 | 0.046 | -0.120 |
| | (0.039) | (0.047) | (0.051) |
| $40k-$50k | -0.117 | -0.020 | -0.178 |
| | (0.050) | (0.059) | (0.065) |
| $50k-$75k | -0.150 | -0.067 | -0.202 |
| | (0.045) | (0.054) | (0.059) |
| >$75k | -0.203 | -0.163 | -0.230 |
| | (0.041) | (0.054) | (0.054) |
| Constant | -1.994 | -2.328 | -1.983 |
| | (0.043) | (0.073) | (0.073) |

## Appendix Table A8: Regression Results on Attacks

| | Any Attacking Past 12 Months | | |
| | All | Females | Males |
| | Coefficient (SE) | Coefficient (SE) | Coefficient (SE) |
|---|---|---|---|
| Post-FDA*Depressed | 0.034 | 0.143 | -0.070 |
| | (0.094) | (0.133) | (0.134) |
| Marginal Effect (SE) | 0.0004 | 0.0188 | -0.0213 |
| | (0.026) | (0.031) | (0.039) |
| Depressed | 0.646*** | 0.697*** | 0.605*** |
| | (0.050) | (0.056) | (0.074) |
| Marginal Effect (SE) | 0.117 | 0.101 | 0.133 |
| | | | |
| Post-FDA | 0.007 | -0.099 | 0.074 |
| | (0.054) | (0.085) | (0.055) |
| Marginal Effect (SE) | -0.010 | -0.010 | -0.009 |
| | | | |
| Time | 0.006 | 0.005 | 0.006 |
| | (0.003) | (0.005) | (0.003) |
| Time*Post-FDA | -0.005 | -0.001 | -0.008 |
| | (0.004) | (0.006) | (0.004) |
| Time*Depressed | -0.004 | -0.010 | 0.001 |
| | (0.006) | (0.006) | (0.009) |
| Female | -0.322 | | |
| | (0.016) | | |
| Quarter=2 | -0.006 | 0.036 | -0.035 |
| | (0.020) | (0.038) | (0.021) |
| Quarter=3 | -0.012 | -0.006 | -0.017 |
| | (0.016) | (0.028) | (0.020) |
| Quarter=4 | -0.031 | -0.005 | -0.049 |
| | (0.015) | (0.029) | (0.019) |
| Age | 0.029 | 0.014 | 0.039 |
| | (0.004) | (0.007) | (0.006) |
| Black | 0.317 | 0.401 | 0.253 |
| | (0.019) | (0.028) | (0.027) |
| Native Am | 0.145 | 0.135 | 0.153 |
| | (0.073) | (0.115) | (0.069) |
| Native HI/PI | 0.123 | 0.294 | -0.042 |
| | (0.113) | (0.137) | (0.144) |
| Asian | -0.081 | -0.045 | -0.102 |
| | (0.048) | (0.098) | (0.051) |
| Multiple | 0.211 | 0.250 | 0.185 |
| | (0.045) | (0.077) | (0.062) |
| Hispanic | 0.020 | 0.029 | 0.015 |
| | (0.026) | (0.040) | (0.033) |
| $10k-$20k | -0.009 | -0.011 | -0.011 |
| | (0.027) | (0.047) | (0.039) |
| $20k-$30k | -0.035 | -0.030 | -0.041 |
| | (0.026) | (0.044) | (0.042) |
| $30k-$40k | -0.065 | -0.089 | -0.051 |
| | (0.031) | (0.047) | (0.043) |
| $40k-$50k | -0.159 | -0.165 | -0.155 |
| | (0.035) | (0.038) | (0.049) |
| $50k-$75k | -0.213 | -0.213 | -0.215 |
| | (0.025) | (0.042) | (0.039) |
| >$75k | -0.315 | -0.393 | -0.272 |
| | (0.027) | (0.038) | (0.039) |
| Constant | -1.364 | -1.645 | -1.392 |
| | (0.041) | (0.067) | (0.047) |