

Employment Effects of Healthcare Policy: Evidence from the 2007 FDA Black Box Warning on Antidepressants

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Web Appendix

A Figures and Tables

Figure A1: 2004 Black Box Warning on Antidepressants Text

Suicidality in Children and Adolescents

Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Drug Name] or any other antidepressant in a child or adolescent must balance this risk with the clinical need. Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. [Drug Name] is not approved for use in pediatric patients except for patients with [Any approved pediatric claims here]. (See Warnings and Precautions: Pediatric Use)

Pooled analyses of short-term (4 to 16 weeks) placebo-controlled trials of nine antidepressant drugs (SSRIs and others) in children and adolescents with MDD, obsessive compulsive disorder (OCD), or other psychiatric disorders (a total of 24 trials involving over 4400 patients) have revealed a greater risk of adverse events representing suicidal thinking or behavior (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.

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Figure A2: 2007 Black Box Warning on Antidepressants Text

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of [Insert established name] or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. [Insert Drug Name] is not approved for use in pediatric patients. [The previous sentence would be replaced with the sentence, below, for the following drugs: Prozac: Prozac is approved for use in pediatric patients with MDD and obsessive compulsive disorder (OCD). Zoloft: Zoloft is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD). Fluvoxamine: Fluvoxamine is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD).] (See Warnings: Clinical Worsening and Suicide Risk, Precautions: Information for Patients, and Precautions: Pediatric Use)

Figure A3: Timeline of FDA Actions and Announcements on Antidepressants and Suicidality

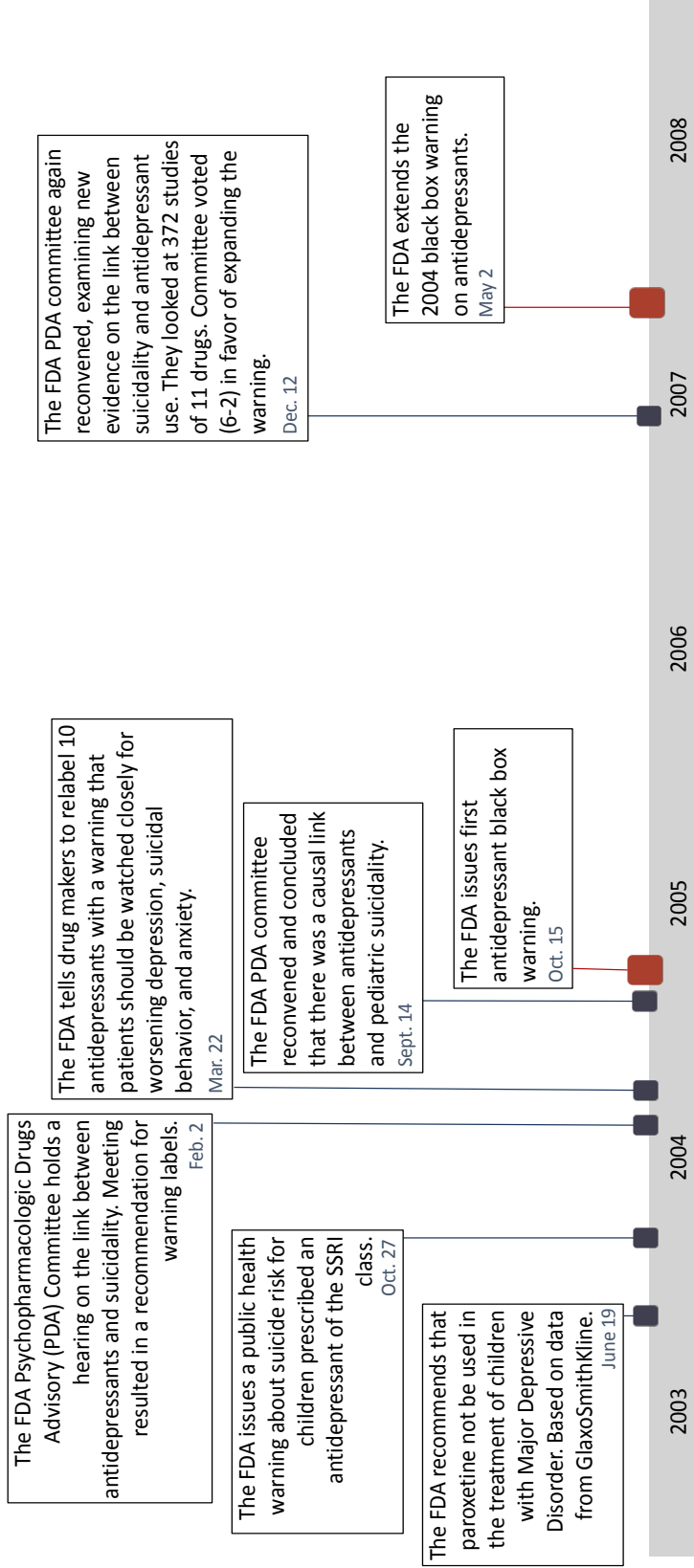
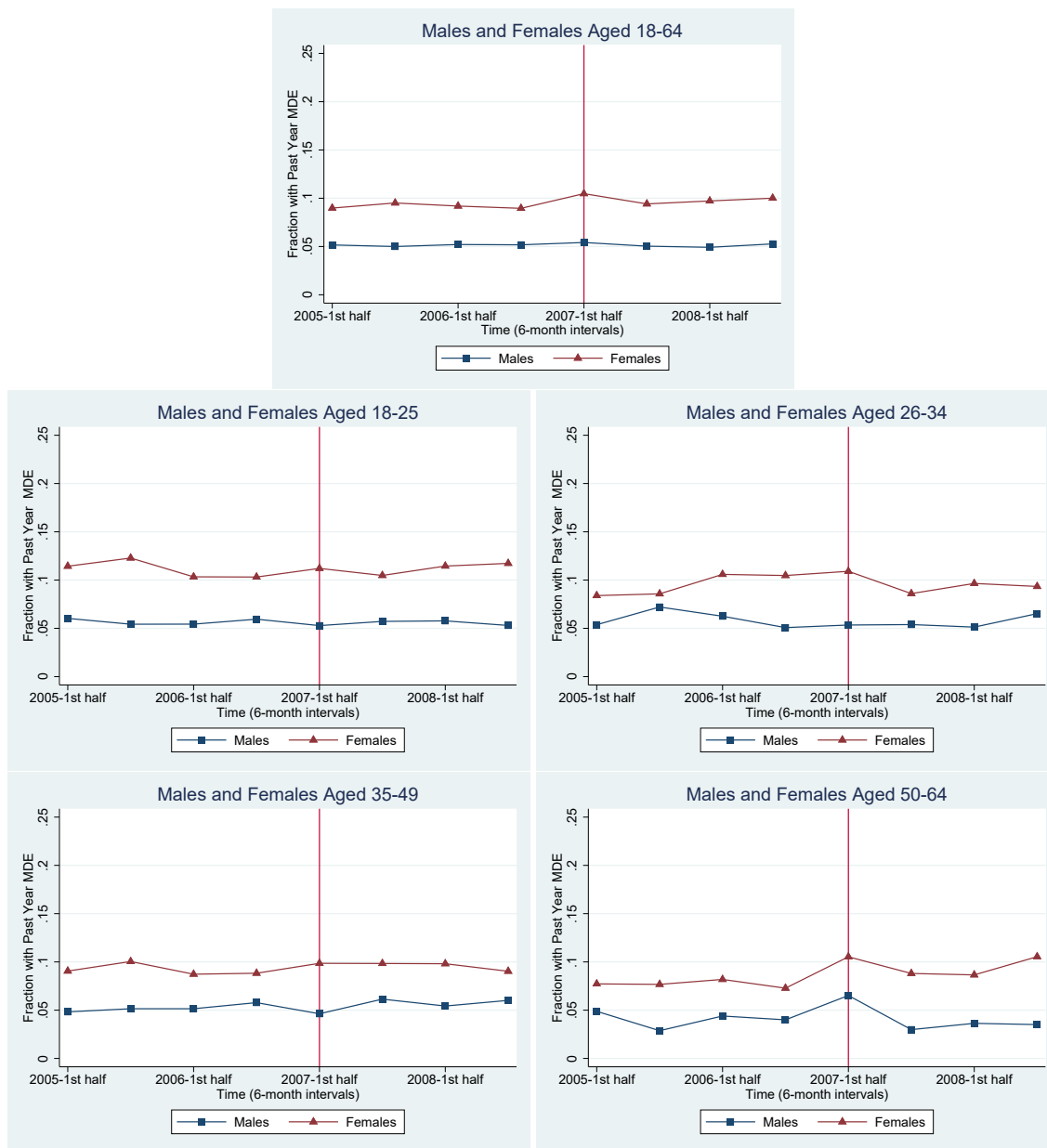
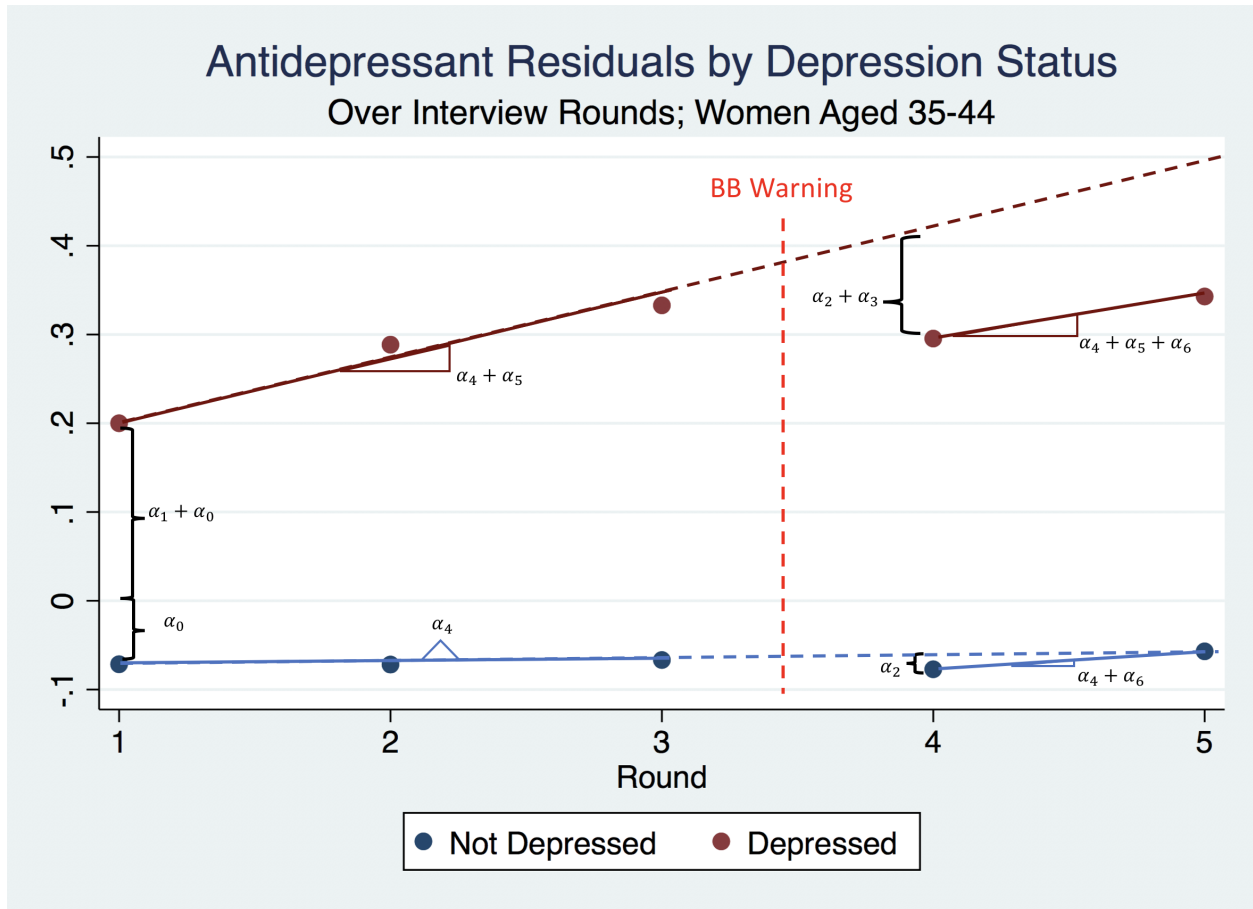


Figure A4: Proportion of Males and Females with a Past Year MDE Over Time (NSDUH)



Notes: Proportions are calculated using the NSDUH sampling weights and include all observations in our sample from 2005-2008.

Figure A5: Identification Visualization (2006 MEPS Cohort)



Notes: The figure plots mean residuals, by depression status and round, from a regression of antidepressant use on controls, X_{it} , for 35-44 year old women with a round 4 transition period (i.e., roughly 85 percent of the 35-44 year old subgroup). The figure visually depicts the variation in the data that identifies constant (α_0, α_1), trend ($\alpha_4, \alpha_5, \alpha_6$), and trend break (α_2, α_3) parameters.

Table A1: Robustness Checks of the Effect of the Warning on Employment of Females Aged 35-49 (NSDUH)

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Drop 2007-1st Half	Post=0 in 2007-1st Half	Drop 2005-1st Half	Drop 2005	Dep. Trend	Alt. Dep. Defn. 1	Alt. Dep. Defn. 2	No Samp. Weights
MDE	-0.054*** (0.015)	-0.059*** (0.013)	-0.038** (0.018)	-0.029 (0.022)	-0.080*** (0.027)			-0.075*** (0.012)
MDE × t					0.011 (0.010)			
MDE × Post	-0.051** (0.023)	-0.046** (0.010)	-0.059** (0.023)	-0.069** (0.027)	-0.089** (0.044)			-0.034** (0.017)
Diagnosed anx./dep.						-0.049*** (0.014)		
Diagnosed anx./dep. × Post						-0.039** (0.019)		
MDE or diagnosed anx./dep.							-0.053*** (0.013)	
MDE or diagnosed anx./dep. × Post							-0.036** (0.018)	
R ²	0.048	0.046	0.045	0.046	0.046	0.044	0.046	0.053
N	15081	17343	15176	12866	17343	17310	17260	17343

Notes: All models are estimated by OLS with heteroskedasticity-robust standard errors (in parentheses). Columns 1-7 use NSDUH sampling weights. Each column represents a separate regression. The dependent variable is an indicator for whether the individual was employed in the past week. Unreported covariates include indicator variables for age (when possible), education, marital status, race and ethnicity, metro type, and time (measured in 6-month periods). In column (1), observations from the first half of 2007 are excluded. In column (2), the post-warning period is redefined as starting in the second half of 2007. In columns (3) and (4), observations from the first half of 2005 and all of 2005 are excluded, respectively. In column (5), an ever-depressed-specific linear time trend is included. In column (6), the treated group is redefined as those who have ever been told by a doctor or medical professional they have depression or anxiety, and in column (7), the treated group is redefined as anyone with a lifetime MDE or who has ever been told by a doctor they have depression or anxiety. In column (8), we estimate our main model without NSDUH sampling weights.

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A2: Difference-in-Differences Estimates
of the Effect of the Warning on Employment of Males with Chronic Health Conditions (NSDUH)

	All	18-25	26-34	35-49	50-64
Panel A: Asthma					
Asthma	-0.027** (0.011)	-0.025** (0.013)	-0.019 (0.020)	-0.042** (0.017)	-0.018 (0.035)
Asthma \times Post	-0.014 (0.016)	-0.001 (0.018)	0.029 (0.026)	-0.009 (0.026)	-0.074 (0.052)
R ²	0.087	0.078	0.034	0.069	0.059
N	64208	33901	10157	14107	6043
Panel B: Diabetes					
Diabetes	-0.103*** (0.021)	-0.076 (0.048)	-0.086* (0.052)	-0.125*** (0.029)	-0.083*** (0.032)
Diabetes \times Post	-0.003 (0.029)	0.000 (0.069)	-0.043 (0.075)	0.043 (0.038)	-0.042 (0.045)
R ²	0.091	0.077	0.036	0.073	0.065
N	64208	33901	10157	14107	6043
Panel C: High Blood Pressure					
High BP	-0.040*** (0.011)	0.012 (0.021)	-0.020 (0.019)	-0.036*** (0.012)	-0.037* (0.021)
High BP \times Post	-0.010 (0.015)	-0.011 (0.030)	-0.007 (0.028)	0.007 (0.017)	-0.054* (0.030)
R ²	0.089	0.077	0.034	0.069	0.064
N	64208	33901	10157	14107	6043

Notes: All models are estimated by OLS with heteroskedasticity-robust standard errors (in parentheses) and NSDUH sampling weights. Each column within a panel represents a separate regression. The dependent variable is an indicator for whether the individual was employed in the past week. Unreported covariates include indicator variables for age (when possible), education, marital status, race and ethnicity, metro type, and time (measured in 6-month periods). In Panels A, B, and C, the treated group is defined as those who have ever been diagnosed with asthma, diabetes, and high blood pressure, respectively.

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A3: Difference-in-Differences Estimates
of the Effect of the Warning on Employment of Females with Chronic Health Conditions (NSDUH)

	All	18-25	26-34	35-49	50-64
Panel A: Asthma					
Asthma	-0.046*** (0.012)	-0.004 (0.012)	0.009 (0.023)	-0.068*** (0.019)	-0.084*** (0.031)
Asthma \times Post	0.021 (0.016)	-0.008 (0.017)	0.014 (0.031)	0.015 (0.026)	0.044 (0.042)
R ²	0.065	0.080	0.088	0.042	0.062
N	74278	38037	11805	17310	7126
Panel B: Diabetes					
Diabetes	-0.102*** (0.020)	-0.001 (0.036)	-0.010 (0.043)	-0.062** (0.026)	-0.149*** (0.032)
Diabetes \times Post	-0.004 (0.028)	-0.041 (0.051)	-0.041 (0.064)	-0.007 (0.036)	0.007 (0.045)
R ²	0.067	0.080	0.088	0.041	0.070
N	74278	38037	11805	17310	7126
Panel C: High Blood Pressure					
High BP	-0.050*** (0.012)	-0.074*** (0.023)	-0.008 (0.030)	-0.013 (0.016)	-0.075*** (0.021)
High BP \times Post	-0.013 (0.017)	0.047 (0.033)	-0.016 (0.042)	0.008 (0.022)	-0.037 (0.030)
R ²	0.066	0.080	0.087	0.040	0.070
N	74278	38037	11805	17310	7126

Notes: All models are estimated by OLS with heteroskedasticity-robust standard errors (in parentheses). Each column within a panel represents a separate regression. The dependent variable is an indicator for whether the individual was employed in the past week. Unreported covariates include indicator variables for age (when possible), education, marital status, race and ethnicity, metro type, and time (measured in 6-month periods). In Panels A, B, and C, the treated group is defined as those who have ever been diagnosed with asthma, diabetes, and high blood pressure, respectively.

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A4: Difference-in-Differences Estimates
and Time-Varying Effects of the Warning on Weekly Work Hours of Females Aged 35-49 (NSDUH)

	(1)	(2)	(3)	(4)
	Unconditional on Working		Conditional on Working	
MDE	-2.159*** (0.728)	-2.157*** (0.728)	0.083 (0.564)	0.085 (0.564)
MDE × Post	-2.851*** (1.019)		-1.631** (0.824)	
MDE × 2007Q1/2		-2.683* (1.541)		-2.484** (1.247)
MDE × 2007Q3/4		-3.969** (1.604)		-1.151 (1.319)
MDE × 2008Q1/2		-1.393 (1.656)		-0.319 (1.320)
MDE × 2008Q3/4		-3.417** (1.619)		-2.518* (1.426)
R ²	0.047	0.047	0.023	0.023
N	16387	16387	12216	12216

Notes: All models are estimated by OLS with heteroskedasticity-robust standard errors (in parentheses). Each column represents a separate regression. The dependent variable is hours worked in the past week. In columns (1) and (2), those not employed in the past week are included and assigned zero hours. In columns (3) and (4), the sample consists only of those who worked in the past week. Unreported covariates include indicator variables for age (when possible), education, marital status, race and ethnicity, metro type, and time (measured in 6-month periods).

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A5: Difference-in-Differences Estimates of the Effect of the Warning on Antidepressant Use Excluding Differential Linear Trends (2006 MEPS Cohort)

	All	18-25	26-34	35-49	35-44	50-64
Panel A: Males						
Dep	0.339*** (0.022)	0.257*** (0.074)	0.232*** (0.060)	0.315*** (0.035)	0.233*** (0.039)	0.435*** (0.035)
Post	0.008** (0.004)	0.009 (0.007)	0.020* (0.011)	0.005 (0.007)	0.005 (0.009)	0.005 (0.010)
Dep × Post	0.016 (0.018)	-0.034 (0.077)	0.014 (0.047)	0.028 (0.030)	0.010 (0.038)	0.025 (0.030)
R ²	0.2736	0.234	0.220	0.268	0.175	0.320
N	3760	491	601	1315	831	1125
Panel B: Females						
Dep	0.380*** (0.016)	0.166*** (0.049)	0.241*** (0.037)	0.377*** (0.026)	0.351*** (0.034)	0.485*** (0.026)
Post	-0.011* (0.007)	0.017 (0.014)	0.000 (0.018)	-0.033*** (0.010)	-0.045*** (0.013)	-0.000 (0.013)
Dep × Post	0.030** (0.014)	0.048 (0.050)	0.065* (0.038)	0.040* (0.022)	0.034 (0.031)	0.016 (0.022)
R ²	0.292	0.142	0.198	0.291	0.263	0.358
N	4484	476	793	1638	1012	1308

Notes: All models are estimated by OLS using the MEPS longitudinal sampling weights. Standard errors (in parentheses) are clustered at the individual level. Each column within a panel represents a separate regression. The dependent variable is an indicator for whether the individual filled an antidepressant prescription in the interview round. Unreported covariates include age, age squared, family size, interview period length, and indicators for male, nonwhite (race), highest educational degree, Census region, living in an MSA, marital status, and interview round.

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A6: Robustness Checks
of the Effect of the Warning on Antidepressant Use of Females Aged 35-49 (2006 MEPS Cohort)

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Drop Transition Round		Individual FE		Alt. Dep. Defn.		No Samp. Weight	
	35-49	35-44	35-49	35-44	35-49	35-44	35-49	35-44
Dep	0.286*** (0.039)	0.214*** (0.049)			0.097*** (0.023)	0.056** (0.027)	0.286*** (0.032)	0.232*** (0.040)
Post	0.024 (0.019)	0.036 (0.026)	-0.001 (0.007)	-0.010 (0.010)	-0.006 (0.025)	-0.008 (0.017)	0.001 (0.007)	-0.004 (0.008)
Dep × Post	-0.083 (0.055)	-0.157** (0.076)	-0.044 (0.033)	-0.088* (0.048)	-0.071*** (0.025)	-0.081** (0.033)	-0.074** (0.036)	-0.118** (0.047)
t	-0.001 (0.005)	0.001 (0.007)	-0.004 (0.005)	-0.000 (0.006)	0.006 (0.007)	0.006 (0.009)	-0.001 (0.004)	0.002 (0.004)
Dep × t	0.047*** (0.016)	0.070*** (0.021)	0.038*** (0.012)	0.055*** (0.016)	0.032*** (0.009)	0.037*** (0.011)	0.042*** (0.012)	0.057*** (0.016)
Post × (t-t _{i, BB})	-0.014 (0.020)	-0.018 (0.027)	0.014* (0.008)	0.012 (0.011)	-0.010 (0.013)	0.002 (0.017)	0.002 (0.009)	0.003 (0.012)
R ²	0.291	0.264	0.014	0.022	0.094	0.081	0.282	0.251
N	1638	1012	1638	1012	1638	1012	1638	1012

Notes: All models are estimated by OLS. Columns 1-6 use MEPS longitudinal sampling weights. Standard errors (in parentheses) are clustered at the individual level. Each column represents a separate regression. The dependent variable is an indicator for whether the individual filled an antidepressant prescription in the interview round. In columns (1) and (2), the transition round for each individual is dropped. In columns (3) and (4), individual-specific fixed effects are included. In columns (5) and (6), an alternative definition of depression is used where $Dep_i = 1$ if $K6 > 4$ in any interview round. In columns (7) and (8), we estimate the main model without MEPS sampling weights. Unreported covariates include age, age squared, family size, interview period length, and indicators for male, nonwhite (race), highest educational degree, Census region, living in an MSA, and marital status.

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A7: Difference-in-Differences Estimates of the Effect of May 1 Placebo Warning on Antidepressant Use of Females Aged 35-49 in Other Years (MEPS)

	35-49	35-44
Dep \times Post _{1/5/2003}	0.026 (0.046) [329]	0.057 (0.057) [204]
Dep \times Post _{1/5/2004}	0.036 (0.045) [364]	0.055 (0.054) [237]
Dep \times Post _{1/5/2005}	0.060 (0.041) [347]	0.041 (0.048) [211]
Dep \times Post _{1/5/2006}	-0.032 (0.043) [359]	-0.040 (0.056) [210]
Dep \times Post _{1/5/2007}	-0.076** (0.039) [364]	-0.126** (0.055) [203]
Dep \times Post _{1/5/2008}	0.022 (0.044) [230]	0.049 (0.055) [141]
Dep \times Post _{1/5/2009}	0.002 (0.039) [361]	0.059 (0.043) [236]

Notes: All models are estimated by OLS using the MEPS longitudinal sampling weights. Standard errors (in parentheses) are clustered at the individual level. Each cell represents a separate regression with the number of depressed individuals in brackets. The dependent variable is an indicator for whether the individual filled an antidepressant prescription in the interview round. Unreported covariates include an indicator for being depressed, an indicator for the post-“warning” period, a linear time trend, an interaction between the time trend and being depressed, an interaction between the time trend and the post-“warning” period, age, age squared, family size, interview period length, and indicators for male, nonwhite (race), highest educational degree, Census region, living in an MSA, and marital status.

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A8: Robustness Checks of the Effect of the Warning on Antidepressant Use of Females Aged 35-49 Using Alternative Control Groups (2006 MEPS Cohort)

	(1)	(2)	(3)	(4)	(5)	(6)
	None		Migraine/Insomnia		Other Chronic	
	35-49	35-44	35-49	35-44	35-49	35-44
Dep			0.223***	0.194***	-0.241***	-0.316***
			(0.044)	(0.056)	(0.060)	(0.086)
Post	-0.085**	-0.142***	-0.040	-0.042	0.054	0.120
	(0.039)	(0.053)	(0.029)	(0.037)	(0.054)	(0.088)
Dep × Post			-0.051	-0.104	-0.113*	-0.254**
			(0.046)	(0.064)	(0.065)	(0.101)
t	-0.054***	0.072***	-0.013	0.024*	0.013	0.009
	(0.020)	(0.024)	(0.011)	(0.014)	(0.022)	(0.032)
Dep × t			0.044***	0.060***	0.024	0.068**
			(0.015)	(0.020)	(0.023)	(0.034)
Post × (t-t _{i, BB})	-0.026	-0.055	-0.027	-0.035	0.008	-0.022
	(0.038)	(0.047)	(0.026)	(0.032)	(0.030)	(0.042)
R ²	0.079	0.107	0.196	0.201	0.094	0.108
N	363	202	566	339	620	329

Notes: All models are estimated by OLS using the MEPS longitudinal sampling weights. Standard errors (in parentheses) are clustered at the individual level. Each column represents a separate regression. In columns (1) and (2), the sample is restricted to ever-depressed individuals. In columns (3) and (4), the sample includes ever-depressed individuals as well as individuals who ever report migraines or sleep disorders. In columns (5) and (6), the sample includes ever-depressed individuals as well as individuals who ever report diabetes, hypertension, or high cholesterol, and the dependent variable is an indicator for filling an illness-specific prescription in the interview round. Unreported covariates include age, age squared, family size, interview period length, and indicators for male, nonwhite (race), highest educational degree, Census region, living in an MSA, and marital status.

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

Table A9: Difference-in-Differences

Estimates of the Effect of the Warning on Marijuana and Alcohol Use of Females Aged 35-49 (NSDUH)

	(1)	(2)	(3)	(4)	(5)
	Marijuana Use in Past Month		Alcohol Use in Past Month		
	Any	20+ Days	20+ Days	Binged	Heavy
MDE	0.014**	0.007	0.002	0.002	0.003
	(0.007)	(0.004)	(0.008)	(0.013)	(0.006)
MDE \times Post	0.003	0.002	-0.008	0.002	-0.007
	(0.010)	(0.006)	(0.011)	(0.019)	(0.008)
R ²	0.017	0.008	0.012	0.026	0.010
N	17343	17343	17343	17343	17343

Notes: All models are estimated by OLS with heteroskedasticity-robust standard errors (in parentheses) and NSDUH sampling weights. Each column represents a separate regression. In column (1), the dependent variable is an indicator for whether an individual used marijuana in the past month, and in column (2), the dependent variable is an indicator for whether an individual used marijuana 20 or more days in the past month. In column (3), the dependent variable is an indicator for consuming alcohol in any amount 20 or more days in the past month. In column (4), the dependent variable is an indicator for bingeing alcohol in the past month, defined as consuming 5 or more drinks on the same occasion. In column (5), the dependent variable is an indicator for using alcohol heavily in the past month, defined as consuming 5 or more drinks on the same occasion 5 or more days. Unreported covariates include indicator variables for age (when possible), education, marital status, race and ethnicity, metro type, and time (measured in 6-month periods).

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$

B NSDUH versus Other Data Sources

The data we use for our main employment analyses come from the National Survey on Drug Use and Health (NSDUH). The NSDUH is a nationally representative survey sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA) that provides information on demographics, substance use, mental health, other-health related issues, and labor market status. Every year the NSDUH surveys 67,500 individuals age 12 and older. We considered many other data sources for our analysis. Our identification strategy requires that individuals be categorized as depressed (or not) and employed (or not) consistently during our time period of interest. Administrative claims data from a single large employer or large private health insurance company are not ideal for our purposes, as depression status can only be inferred from the decision to seek treatment, which would leave a large fraction of the sample mis-categorized. Moreover, individuals exit these data upon leaving or switching employers, raising sample selection concerns.

Among survey data alternatives to the NSDUH, the NHIS (~90,000 annual participants) is the largest US dataset that meets the minimal criteria mentioned above. Unfortunately, the only consistently available measure of depression in the NHIS reflects current mental distress, which is a function of medications currently being taken. As such, the NHIS depression definition would lead us to misclassify individuals into the control group, particularly those with a history of depression who are effectively managing their symptoms, perhaps with antidepressants. Such misclassification would bias our estimates towards zero if those individuals responded to the warning. Alternatives, such as NHANES (~5,000 annual participants), NLSY97 (~7,500 annual participants), Add Health (~16,000 annual participants), PSID (~24,000 annual participants), and MEPS (~30,000 annual participants) contain employment and mental health information, but offer substantially smaller samples, especially when we consider heterogeneity by coarse age groups. Furthermore, survey waves during our period of interest in Add Health only occur in 2001-2002 and 2008 and provide us a narrow age range to study (24-32 year olds in 2008). Likewise, NLSY97 provides only a small age range to consider as individuals were aged 22-28 in the 2007 wave. Both the PSID and NLSY79 were conducted biennially during our period of interest, making them unattractive for our empirical design. BRFSS (~430,000 annual participants) contains a mental health/stigma module as well as an anxiety and depression module, but these modules are not asked consistently each year of the survey and different subsets of states ask them in different years.