Antidepressant Use in the Absence of Common Mental Disorders in the General Population

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Objective: To examine the prevalence of antidepressant use in the absence of lifetime mental disorders and to examine sociodemographic correlates, indicators of need (hospitalization, suicidal behavior, perceived need, subthreshold disorders, disability, traumatic events), and antidepressant characteristics of such use.

Method: Data came from the Collaborative Psychiatric Epidemiologic Surveys (N = 20,013), a nationally representative cross-sectional sample of community-dwelling adults in the United States. Sociodemographic correlates and indicators of need were examined as predictors of past-year use of antidepressants in the absence of a lifetime *DSM-IV* diagnosis as assessed by the World Mental Health Composite Diagnostic Interview. The surveys were conducted between 2001 and 2003.

Results: Among individuals who took an antidepressant in the past year (n = 1,441), 396 (26.3%) did not meet criteria for any lifetime diagnosis assessed. Respondents taking antidepressants in the absence of a lifetime diagnosis tended to be older, white, and female. All indicators of need except past-year suicidal behavior were significant predictors (adjusted odds ratios ranging from 2.12 to 14.22, $P < .001$), with 89% of individuals taking antidepressants in the absence of a lifetime diagnosis endorsing at least 1 indicator of need. Individuals taking antidepressants in the absence of a *DSM-IV* disorder were more likely to have been prescribed these medications by family physicians or other doctors compared to psychiatrists.

Conclusions: These results suggest that antidepressant use among individuals without psychiatric diagnoses is common in the United States and is typically motivated by other indicators of need. These findings have important implications for the delivery of medical and psychiatric care and psychiatric nosology.

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Studies from around the world have found that many, even a majority, of individuals utilizing mental health treatment resources do not have a diagnosable mental disorder.[1] Consequently, recent attempts have been made to understand the use of mental health treatment among individuals without mental disorder diagnoses.[2] Results suggest that most individuals utilizing mental health treatment resources in the absence of formal diagnoses have other indicators of need, such as a subthreshold disorder, serious stressor, or hospitalization.[2]

To date, research has focused on mental health treatment in general. However, with the current widespread use of antidepressant medications[3] as well as direct-to-consumer advertising and marketing campaigns of pharmaceutical companies[4] (spending on which totaled $3.2 billion in the United States in 2003[5]) and the emerging evidence of the adverse effects of antidepressant medications, the use of these medications among those without mental disorder diagnoses is of concern. The rate of antidepressant use in the US general population has increased from 2% in the early 1990s to over 10% in the early 2000s, and a more marked increase has been found specifically among individuals with less severe indications,[6] adding more fuel to concerns of overtreatment with antidepressants.[7] Specifically, while 30% of individuals taking antidepressants lacked a past-year mood or anxiety disorder in the early 1990s, this proportion had increased to 46% in the early 2000s.[6]

This use of antidepressants among individuals without diagnoses is especially important given recent controversy concerning the efficacy of antidepressant medications. Many separate clinical trials have found antidepressants to be efficacious in the treatment of all levels of major depressive disorder.[8] However, these positive findings are controversial due to recent evidence of publication bias in favor of such positive results.[9] Further, the efficacy of antidepressant use among individuals with subthreshold depression has not been conclusively established.[10,11] Although generating some controversy,[12,13] 3 meta-analyses[13–15] of randomized clinical trials data found that antidepressants performed no better than placebo in the treatment of mild to moderate depression. The authors found that a clinically significant effect of antidepressants versus placebo occurred only in the most severely depressed patients. In addition to these concerns are issues of difficulty in discontinuing antidepressant medication as well as negative side effects and associated consequences.[16–19] For example, recent studies have shown an increased risk for hypertension[20] and diabetes[21] among individuals taking antidepressants.

To our knowledge, no study has specifically examined the prevalence and correlates of antidepressant use among individuals without mental disorder diagnoses. In accordance, the current study sought to address this question

and has 5 main objectives. The first objective is to determine the prevalence of antidepressant use among individuals without past-year mental disorder diagnoses and among individuals without lifetime mental disorder diagnoses. Although anecdotal evidence suggests that many individuals may be taking antidepressants without meeting any formal criteria, the prevalence of this phenomenon has never been examined in a nationally representative sample. We address this issue by using data from the Collaborative Psychiatric Epidemiologic Surveys (CPES),[22] a large sample of over 20,000 respondents that is representative of the US population. The second objective is to determine sociodemographic correlates of antidepressant use among individuals without past-year or lifetime mental disorder diagnoses. The third objective is to examine other indicators of need explaining the use of antidepressants in the absence of mental disorder diagnoses, including subthreshold mental disorders, suicidal behaviors, traumatic events, hospitalization, past-month disability, and perceived need for mental health treatment. Indicators of need and correlates are examined among the group of individuals with past-year antidepressant use and no past-year or lifetime diagnoses in order to account for individuals who may have been appropriately treated with antidepressants and in remission despite continuing antidepressant medication. The fourth objective is to examine self-reported reasons for using antidepressants among individuals with and without a past-year or lifetime mental disorder. The fifth objective is to determine whether there are differences in the type, source, or dose of antidepressants for individuals who take them in the absence of mental disorder diagnoses versus those who do meet criteria for a past-year mental disorder.

METHOD

Sample

Data came from the CPES,[22] which consist of the National Comorbidity Survey Replication (NCS-R),[23] the National Survey of American Life (NSAL),[24] and the National Latino and Asian American Study (NLAAS),[25] all conducted between 2001 and 2003. The NCS-R focused on the noninstitutionalized English-speaking civilian household population of the United States, while the NSAL and NLAAS focused on specific ethnic groups. The NSAL examined black Americans of African and Caribbean descent, while the NLAAS specifically sampled Latino, Asian, and white respondents. All 3 surveys are nationally representative on their own, and the merged CPES results in a nationally representative sample of the US population age 18 and over consisting of 20,013 respondents. Trained lay-interviewers conducted interviews in all 3 surveys primarily in person, although telephone interviews were permitted if requested by the respondent. The average response rate of the CPES was 72.7%. Informed consent was obtained for participants and measures were taken to ensure confidentiality of participants. Specific response rates and details of each survey can be found elsewhere.[23–25]

Measures

Antidepressant use. Respondents were first asked if they had taken any prescription medications in the past 12 months for their emotions, nerves, or use of alcohol or drugs.

Respondents who endorsed taking prescription medications were given a list of medications and asked

> Which of the medicines on this list did you take in the past 12 months for any of the following problems: problems with your emotions, nerves, mental health, substance use, energy, concentration, sleep, or ability to cope with stress? Include medications even if you took them only once.

The CPES interviewers recorded up to 20 different medications for each respondent, and, if necessary, respondents were asked to consult their medication bottles for correct drug names. Twenty-seven antidepressant medications were included in this list. Respondents who endorsed taking any of these drugs in the past 12 months were coded as having antidepressant use in the past 12 months. Additionally, the antidepressants were coded into 4 drug groups as follows. Selective serotonin reuptake inhibitors included citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline. Tricyclic antidepressants included doxepin, amitriptyline, nortriptyline, desipramine, imipramine, protriptyline, amoxapine, clomipramine, and trimipramine. The serotonin-norepinephrine reuptake inhibitor venlafaxine and the norepinephrine-dopamine reuptake inhibitor bupropion were included in 1 group. The remaining antidepressants, including trazodone, phenelzine, isocarboxazid, moclobemide, amitriptyline/perphenazine, nefazodone, tranylcypromine, maprotiline, mirtazapine, amitriptyline/chlordiazepoxide, and unspecified antidepressant, were combined into "other antidepressants." Information on the dose for each medication endorsed was also collected. The dose in milligrams of antidepressant and frequency of use were multiplied to compute the daily dose of antidepressant. These doses were then categorized as above or equal to the lower bound of usual dose prescribed or below the lower bound of the usual dose prescribed based on the specific antidepressant endorsed and accepted guidelines for dose ranges of antidepressant medications.[8]

More specific information was obtained for up to 3 different medications reported. This information included source of the medications, reason for taking the medications, and dosage of the medications. Respondents were asked whether a psychiatrist, a general or family doctor, some other medical doctor, or some other health professional prescribed the medication. Respondents were given a list of 18 problems and were asked for which of these problems they took the medications. We combined these 18 problems into 13 reasons for taking antidepressants.

Sociodemographics. Sex, age, race/ethnicity, education, and marital status were examined in each survey. A specific emphasis on minority groups was a goal of the CPES, and race/ethnicity was thus assessed with options defined by those who developed the survey.

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Mental disorders. The World Mental Health Composite Diagnostic Interview (WMH-CIDI)[26] was used to assess past-year and lifetime disorders according to the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision (*DSM-IV-TR*).[27] Blind clinical reinterviews with the Structured Clinical Interview for *DSM-IV* (SCID) suggested good concordance with the WMH-CIDI diagnoses for Axis I disorders.[23] Diagnoses included in all 3 surveys were major depressive disorder, dysthymia, generalized anxiety disorder, panic disorder, agoraphobia, social anxiety disorder, posttraumatic stress disorder (PTSD), alcohol abuse and dependence, drug abuse and dependence, anorexia nervosa, bulimia nervosa, and binge eating disorder. These diagnoses were combined to reflect any disorder for both lifetime and past-year time frames. Past-year subthreshold versions of all disorders except dysthymia were also combined to reflect any past-year subthreshold disorder. The coding for subthreshold disorders was consistent with previous studies using this dataset.[2] This involved positive responses to stem questions for each disorder and, possibly, additional symptoms in the past 12-months, while not meeting full criteria for the disorder. For instance, stem questions for major depression included depressed mood or anhedonia.

Suicidal behaviors. Respondents who could read were given a list of experiences and asked whether or not each experience happened to them. Respondents who could not read were asked directly by the interviewer. The question corresponding to suicidal ideation was "Have you ever seriously thought about committing suicide?" The question corresponding to a suicide plan was, "Have you ever made a plan for committing suicide?" Finally, the question corresponding to a suicide attempt was, "Have you ever attempted suicide?" Respondents who endorsed each question were then asked if that behavior had occurred at any time in the past 12 months. Past-year suicidal ideation, suicide plan, and suicide attempt were combined to reflect any past-year suicidal behavior.

Traumatic events. Traumatic events were assessed among CPES respondents in the PTSD module of the WMH-CIDI. Respondents were asked if they experienced any of these events in their lifetime. The occurrence of any of the following events in the individual's lifetime were combined to reflect any lifetime traumatic event: (1) having a life-threatening illness, (2) being beaten by one's parents, (3) being beaten by one's spouse or romantic partner, (4) being beaten by anyone else, (5) being raped, (6) being sexually assaulted, (7) being stalked, and (8) being in a life-threatening automobile accident.

Past-month disability. The CPES respondents were asked how many days out of the past 30 they experienced several forms of disability as a result of problems with physical health, mental health, or use of alcohol or drugs. Since the large majority of respondents (57%–66%) reported zero days of disability for each variable, responses were dichotomized to reflect no disability versus at least 1 day of disability in the past 30 days. The occurrence of any of the following forms of disability were combined to reflect any past-month disability: (1) inability to work or carry out normal activities, (2) staying in bed more than half of the day, (3) cutting down on what the respondent did or if the respondent did not get as much done as usual, (4) cutting back on the quality of work or how carefully the respondent worked, and (5) taking extreme effort to perform up to the usual level at work or at other daily activities.

Perceived unmet need for mental health treatment. Perceived unmet need for mental health care[28–32] in the past year was examined among individuals who did not report contact with a health professional for mental health concerns in the past year. This was assessed with the following question: "Was there ever a time during the past 12 months when you felt that you might need to see a professional because of problems with your emotions or nerves or your use of alcohol or drugs?"

Past-year hospitalization. Respondents were asked if they had ever been admitted for an overnight stay in a hospital or other facility to receive help with their emotions, nerves, mental health, or use of alcohol or drugs. If an overnight hospitalization was endorsed, respondents were asked if this occurred in the past year.

Analytic Strategy

First, cross-tabulations were used to determine the prevalence of past-year antidepressant use among individuals without a past-year mental disorder diagnosis and among individuals without a lifetime mental disorder diagnosis. Sensitivity analyses were conducted to test assumptions made in calculating these prevalence figures. We used data from past research to estimate the prevalence of antidepressant-treated disorder-free individuals if the diagnoses were based on clinician-administered structured interviews and to assess the effect of recall bias on reporting of lifetime disorders. Cross-tabulations and logistic regression models were then used to examine the sociodemographic correlates of past-year antidepressant use among individuals without lifetime *DSM-IV* diagnoses. Next, cross-tabulations and logistic regression models adjusted for significant ($P < .05$) sociodemographic correlates were used to examine independent variables of past-year hospitalization, past-year suicidal behavior, past-year perceived need, past-year subthreshold *DSM-IV* disorders, past-month disability, and lifetime traumatic events as potential correlates of the use of antidepressants among respondents without lifetime *DSM-IV* disorders. The sample for these analyses was limited to participants without a CIDI *DSM-IV* diagnosis whether or not they received antidepressants. Next, cross-tabulations and χ^2 tests of association were used to examine differences in reasons endorsed for taking antidepressants among respondents with and without lifetime *DSM-IV* disorders. Finally, cross-tabulations and logistic regression models adjusted for sociodemographic factors were used to examine differences in the type, source, and dose of antidepressants among respondents with and without lifetime *DSM-IV* disorders. The sample for these 2 last sets of analyses was limited to participants with and without a CIDI *DSM-IV* diagnosis who received antidepressants.

Appropriate statistical weights were applied in all analyses to ensure the data were representative of the general

population. Weights are provided specifically for analysis of the CPES as a whole. Taylor series linearization, a variance estimation procedure, was also used in all analyses to account for the complex sampling design of the surveys. This procedure was conducted with SUDAAN software[33] by using the statistical weight and stratification information provided by the CPES. All percentages reported are weighted.

RESULTS

Of all CPES respondents, 1,441 (9.5%; 95% CI, 8.6%–10.3%) reported taking antidepressant medications in the past 12 months. Among these individuals taking antidepressants, 723 (52.1%) did not have any of the past-year psychiatric disorders that were assessed, and 396 (26.3%) did not have any lifetime psychiatric disorder. This results in a past-year prevalence of 4.9% (95% CI, 4.3%–5.5%) for taking antidepressants in the absence of a past-year psychiatric condition and a past-year prevalence of 2.5% (95% CI, 2.1%–2.9%) for taking antidepressants in the absence of a lifetime psychiatric condition.

In order to examine whether our findings could be the result of false-negative CIDI cases (ie, participants with clinician-assessed disorder but without disorder according to the CIDI), we conducted a sensitivity analysis using data from a study comparing CIDI diagnoses against diagnoses based on clinician-administered SCID.[34] The positive predictive values (PPVs [proportion of CIDI-positive cases that would also be SCID positive cases]) of CIDI in that study ranged from 0.21 to 1.00 for different disorders, with a median of 0.74. The negative predictive values (NPVs [proportion of CIDI-negative cases that would also be SCID negative]) ranged from 0.50 to 1.00, with a median value of 0.83. On the basis of these numbers, approximately 773 antidepressant-taking participants with positive CIDI diagnoses would be expected to meet the clinician-administered SCID criteria for mental disorders ($1,045 \times 0.74 = 773$) and 329 participants without a CIDI diagnosis would be rated as not having a SCID diagnosis ($396 \times 0.83 = 329$). Another 67 participants would be rated as having a positive SCID diagnosis ($396 \times [1 - 0.83] = 67$]). Adding the number of participants with positive CIDI diagnoses who would meet SCID criteria (773) and the number of participants with negative CIDI diagnoses who meet SCID criteria (67) shows that 840 participants (58.3%) of the 1,441 will be expected to have a clinician-administered *DSM-IV* SCID diagnosis. This calculation leaves 601 participants (42.7%) who would not have a SCID diagnosis. Thus, our substantive finding that a large proportion of the general population without a psychiatric diagnosis receives antidepressants appears to hold despite imperfect measurement of mental disorders.

In our sensitivity analysis examining the potential effect of recall bias, we focused on lifetime disorders, since disorders in the past 12 months are less likely to have been influenced by recall bias.[35] The estimates of PPV and NPV for this analysis were based on a twin study of major depression assessed at 2 time points 1 year apart.[36] Assuming that the baseline diagnosis of lifetime depression is the gold standard (as it predates the follow-up interview), we estimated PPV and NPV from the numbers reported in that study. When assessed a year later, the PPV for predicting a

Table 1. Sociodemographic Correlates of Antidepressant Use in the Past Year Among Individuals Without Lifetime *DSM-IV* Disorders[a]

Variable	No Antidepressant Use, (n = 13,198), n (%)	Antidepressant Use, (n = 396), n (%)	OR (95% CI)
Gender			
Male	5,923 (49.7)	104 (26.8)	1.00
Female	7,275 (50.3)	292 (73.2)	2.70 (1.83–4.00)***
Age, y			
18–24	1,809 (14.6)	20 (7.3)	1.00
25–44	5,661 (36.3)	139 (25.8)	1.41 (0.69–2.87)
45–64	3,718 (29.1)	144 (43.5)	2.97 (1.48–5.98)***
65+	2,010 (20.1)	93 (23.4)	2.31 (1.05–5.09)***
Race/ethnicity			
Non-Hispanic white	4,562 (67.5)	215 (82.6)	1.00
Asian	1,828 (5.7)	27 (2.3)	0.33 (0.19–0.55)***
Hispanic	2,362 (13.0)	67 (7.2)	0.45 (0.30–0.69)***
Black	4,305 (12.6)	80 (6.7)	0.43 (0.30–0.62)***
Other	141 (1.2)	7 (1.3)	0.88 (0.28–2.73)
Education			
Less than high school	2,626 (18.8)	77 (15.7)	1.00
High school or more	10,572 (81.2)	319 (84.3)	1.24 (0.80–1.92)
Marital status			
Married/cohabiting	7,429 (61.4)	211 (57.2)	1.00
Separated/widowed/divorced	2,713 (17.9)	122 (24.3)	1.46 (1.07–1.99)*
Never married	3,046 (20.7)	63 (18.5)	0.96 (0.55–1.70)

[a]Percentages are weighted.
*$P < .05$. ***$P < .001$.

Table 2. Correlates of Antidepressant Use Among Individuals Without Lifetime *DSM-IV* Disorders[a]

Variable	No Antidepressant Use, (n = 13,198), n (%)	Antidepressant Use, (n = 396), n (%)	AOR (95% CI)[b]
Past-year suicidal behavior	70 (0.6)	11 (1.3)	2.16 (0.53–8.80)
Cumulative percent	0.6	1.3	
Past-year hospitalization	17 (0.1)	8 (2.1)	14.22 (3.61–56.08)***
Cumulative percent	0.7	3.1	
Past-year perceived need[c]	272 (2.6)	18 (12.4)	5.41 (2.32–12.64)***
Cumulative percent	3.4	17.5	
Past-year subthreshold disorder	1,079 (9.4)	81 (23.6)	3.11 (2.02–4.78)***
Cumulative percent	14.5	41.6	
Past-month disability	2,293 (25.8)	158 (54.9)	3.11 (2.05–4.72)***
Cumulative percent	39.5	78.0	
Lifetime traumatic event	3,678 (37.8)	170 (57.8)	2.12 (1.47–3.05)***
Cumulative percent	63.3	89.2	

[a]Percentages are weighted.
[b]All AORs are adjusted for gender, age, race/ethnicity, education, and marital status.
[c]Perceived need is only assessed among individuals who did not see a health professional in the past year for problems with mental health.
***$P < .001$.
Abbreviation: AOR = adjusted odds ratio.

Table 3. Reasons for Taking Antidepressants in the Past Year Among Individuals With and Without Lifetime *DSM-IV* Disorders[a]

Reason	Any Lifetime *DSM-IV* Disorder, (n = 979), n (%)	No Lifetime *DSM-IV* Disorder, (n = 396), n (%)	χ^2	*df*	*P*
Depressive symptoms[b]	699 (69.2)	202 (47.8)	13.48	1	<.001
Anxiety symptoms[c]	388 (38.1)	100 (35.9)	0.13	1	.13
Poor sleep	253 (24.7)	89 (20.1)	0.85	1	.36
Other problem	100 (9.3)	57 (15.8)	3.14	1	.08
Anger or irritability	108 (12.1)	19 (4.3)	11.97	1	<.001
Poor memory or concentration	94 (9.6)	19 (4.1)	6.97	1	.009
Manic mood	53 (5.3)	5 (0.9)	13.89	1	<.001
Little or no sexual functioning	28 (2.9)	3 (0.5)	10.36	1	.002
Marital problems	23 (2.7)	3 (0.3)	9.00	1	.003
Alcohol/drug problem	9 (1.4)	1 (0.4)	1.62	1	.21
Poor work performance	21 (2.1)	1 (0.3)	9.90	1	.002
Not getting along with others	20 (2.2)	0 (0.0)	8.77	1	.004
Physical pain	0 (0.0)	0 (0.0)	…	…	…

[a]Percentages are weighted.
[b]Depressive symptoms include sadness/depression/crying, suicidal thoughts, low energy, and poor appetite.
[c]Anxious symptoms include nerves/anxiety and panic.

baseline diagnosis of lifetime major depression was a modest 0.59 and the NPV was 0.78. Thus, only 616 of the 1,045 with a positive lifetime CIDI diagnosis would be expected to have had a positive lifetime history had they been assessed 1 year earlier ($1{,}045 \times 0.59 = 616$). Whereas, about 309 of the 396 with negative lifetime CIDI diagnosis would be expected to have a similarly negative lifetime history had they been assessed 1 year earlier ($396 \times 0.78 = 309$) and another 87 would be expected to have a positive lifetime history if evaluated earlier ($396 \times [1 - 0.78] = 87$). Adding the number of participants with positive CIDI diagnoses with accurate recall (616) and the number of participants with negative CIDI diagnoses who failed to recall a true episode (87) shows that 703 participants, or less than half of the 1,441 antidepressant treated participants, would be expected to have had a lifetime history of a CIDI diagnosis had they been assessed at baseline. Using estimates from another study of the stability of lifetime diagnoses of major depression over an 18-month period,[37] we found that only 52% of those with a lifetime CIDI-positive diagnosis of major depression would be expected to have had a lifetime disorder if assessed earlier. We are not aware of any longer follow-up studies that have examined the stability of lifetime diagnoses of mental disorders assessed using structured interviews.

Overall, the results of the sensitivity analyses suggest that our estimates of the prevalence of participants without diagnoses among those receiving antidepressant treatment is unlikely to be an overestimate. As the results of these sensitivity analyses show, adjustment for unreliability of CIDI diagnoses due to imperfect correspondence with clinical diagnoses or memory bias is likely to further increase the prevalence of disorder-free participants in the antidepressant-treated sample. This outcome is probable because the majority of the antidepressant-treated participants are CIDI positive, thus any corrections to adjust for unreliability would reduce a larger number of false-positive CIDI cases than false-negative cases.

Table 1 shows the results of cross-tabulations and logistic regression models examining sociodemographic correlates of antidepressant use among individuals without past-year *DSM-IV* disorders. Compared to individuals with neither antidepressant use nor *DSM-IV* diagnosis, individuals with antidepressant use in the absence of a diagnosis were more likely to be female, white, aged 45–64 years or 65 years and over, and separated, widowed, or divorced.

Table 2 shows the results for cross-tabulations and logistic regression models examining correlates of antidepressant use among individuals without lifetime *DSM-IV* diagnoses. All variables examined except past-year suicidal behavior were significantly associated with antidepressant use, with adjusted odds ratios between 2.16 and 14.22. The cumulative percentage shows that 89.2% of individuals taking antidepressants in the absence of a lifetime *DSM-IV* diagnosis had at least 1 of these indicators of need compared to 63.3% of respondents not taking antidepressants. It is notable that the high prevalence of a lifetime traumatic event inflates the similarity of these percentages; the cumulative percentage of all indicators other than a traumatic event accounts for 78.0% of those with antidepressant use and only 39.5% of those without antidepressant use.

The most common reason for reporting use of antidepressants among individuals without a lifetime *DSM-IV* diagnosis was depressive symptoms (47.8%), followed by anxiety symptoms (35.9%) and poor sleep (20.1%). The χ^2 tests of association comparing individuals with and without *DSM-IV* disorders who were prescribed antidepressants were significant for most problems, with the exceptions of anxiety symptoms, poor sleep, other problems, and alcohol/drug problems. No respondents endorsed taking antidepressants for pain. In comparison to respondents with a *DSM-IV* diagnosis, those without a diagnosis were less likely to endorse all reasons for taking antidepressants, except other problems (Table 3).

Examining the source of antidepressant medications among individuals without a lifetime diagnosis revealed that 61.0% of the individuals were prescribed antidepressants by a family physician, 16.3% by a psychiatrist, and 22.7% by another health professional. Compared to individuals using antidepressants who had a lifetime psychiatric diagnosis, individuals without a diagnosis were significantly more likely to have been prescribed antidepressants by a family physician or another source. There were no significant differences in the type or dose of antidepressant prescribed to individuals with or without a diagnosis (Table 4).

DISCUSSION

The current study found that approximately 5% of the US general population took antidepressants in the absence of an assessed psychiatric condition in the past year, and

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Table 4. Differences in the Source, Type, or Dose of Antidepressants Among Individuals With and Without Lifetime *DSM-IV* Disorders

Variable	Any Lifetime *DSM-IV* Disorder, (n = 979), n (%)[a]	No Lifetime *DSM-IV* Disorder, (n = 372), n (%)	AOR (95% CI)[b]
Who prescribed antidepressants			
Psychiatrist	354 (32.0)	67 (16.3)	1.00
Family physician	512 (56.5)	237 (61.0)	2.05 (1.34–3.14)***
Others	113 (11.6)	68 (22.7)	3.90 (2.12–7.17)***
Type of antidepressant			
Any other antidepressant	97 (11.1)	47 (10.4)	1.00
Any tricyclic antidepressant	99 (10.1)	59 (11.3)	1.08 (0.47–2.50)
Any selective serotonin reuptake inhibitor	611 (66.6)	227 (72.4)	1.26 (0.69–2.32)
Multiple types of antidepressant	117 (12.3)	25 (6.0)	0.62 (0.24–1.59)
Dose relative to usual range			
At or above lower bound	593 (67.5)	194 (59.3)	1.00
Below lower bound	307 (32.5)	155 (40.7)	1.37 (0.94–2.01)

[a]Percentages are weighted.
[b]Reference group for the dependent variable is individuals with any lifetime *DSM-IV* disorder. All AORs are adjusted for gender, age, race/ethnicity, education, and marital status.
***$P \leq .001$.
Abbreviation: AOR = adjusted odds ratio.

approximately 3% of the US general population took antidepressants in the absence of an assessed lifetime psychiatric condition. In other words, half of all individuals in the general population taking an antidepressant do not meet criteria for any of the assessed current mental disorders in the same time period. These individuals may be in remission from mental illness after successful treatment with antidepressants. In addition, however, over one-quarter of individuals taking antidepressants in the general population have never met criteria for 1 of the mental disorders assessed in this study. Proportions of individuals taking antidepressants in the absence of assessed mental disorders remain high, even after taking false-negative rates of assessment measures for psychiatric diagnoses and recall error into account. These results show that the use of antidepressants in the absence of the most prevalent Axis I psychiatric indications is a prevalent phenomenon. The sociodemographic profile of these individuals is consistent with the sociodemographic correlates of antidepressant use in general.[38]

These findings are especially important given that data collected more recently than the present data suggest continued high rates of treatment with antidepressants, with approximately 27 million Americans receiving this treatment in 2005.[39] Vital and health statistics data from the same year revealed antidepressants to be the most commonly prescribed class of drugs in primary care and hospital outpatient programs.[40,41] Attitudes in the United States toward antidepressant use have paralleled these increases in prescription rates, with more individuals reporting willingness to take these medications and more individuals endorsing medications to help with stress, interpersonal relationships, and their views of themselves in 2006 compared to 1998.[42] This context of increased prescribing and increased willingness to take medications suggests that the findings of the current study are relevant in the present day and emphasizes the importance of ensuring the efficacy and effectiveness of antidepressants.

Despite the proportion of individuals taking antidepressants who are lacking lifetime diagnoses, results suggest that these individuals are experiencing difficulties that lead them to seek treatment. Notably, only 11% of individuals with antidepressant use in the absence of a lifetime diagnosis did not endorse any of the indicators of need examined. Hospitalization, perceived unmet need, subthreshold disorders, disability, and traumatic events were all strongly associated with the use of antidepressants among respondents lacking psychiatric diagnoses. These individuals have other forms of mental health difficulties and needs for mental health treatment that may not be recognized by the psychiatric nosology described in the *DSM-IV*. These findings are consistent with research showing that subthreshold mood and anxiety disorders are associated with significant distress and impairment.[43] For example, the co-occurrence of subthreshold anxiety and depression (known as mixed anxiety-depression) has been shown to be problematic enough to cause dysfunction and may be common among individuals taking antidepressants in the absence of psychiatric diagnoses.[44] The findings provide further support for the assertion that dimensional models of psychiatric disorders may provide more information than categorical nosologic approaches.[45] This is not to suggest that the prescribing of antidepressants is appropriate among individuals lacking psychiatric diagnoses, only that the nosologic approach should take lower level psychiatric symptoms into consideration so that treatment options can be studied and administered. The large proportion of respondents taking antidepressants in the absence of a mental disorder who reported traumatic experiences is indicative of the potential importance of adjustment disorders and their treatment in this population.

Evidence from claims data also supports the findings of the current study. The proportion of individuals taking antidepressants in the absence of a mental disorder diagnosis in the current study is strikingly similar to a recent analysis[46] of claims data of nearly 400,000 antidepressant users, which found that 53% of antidepressant users did not have a diagnosis for which antidepressants are commonly prescribed listed in their claim. Similar to our results, this study also reported that the majority (72%) of antidepressant users without listed diagnoses also did not have a previous condition for which antidepressants are commonly prescribed.[46] Our findings are also consistent with previous literature suggesting that not-otherwise-specified diagnoses are commonly cited as reasons for the prescription of antidepressants in billing codes.[47] Although this could be interpreted as poor diagnostic precision, the current results suggest that the use of these codes may accurately represent the reason for prescribing

antidepressants, as many individuals taking antidepressants lack more specific diagnoses.

The majority of individuals taking antidepressants in the absence of a diagnosis report that they are taking the antidepressant for depressive symptoms; however, the current literature does not provide clear evidence for the use of pharmacotherapy in subthreshold depression, and no treatment guidelines for minor depression exist.[10,11,48] There is a need for more well-designed randomized control trials of antidepressants among individuals suffering from depressive symptoms not reaching the diagnostic threshold to ensure the efficacy of these medications and the provision of optimal medical care.

The current study also found that individuals taking antidepressants in the absence of a diagnosis are more likely to receive these prescriptions from family physicians or other doctors relative to psychiatrists. This could be a result of many factors, including limited time in primary care settings to complete full diagnostic formulations, long waiting lists for specialized psychiatric care, and self-selection of primary care by patients with less severe symptoms. A recent qualitative study of general practitioners indeed found that most viewed subthreshold depression as a clinically significant issue, and some concerns were identified regarding diagnosis and patients' difficulties in accepting psychological causes for their symptoms.[49] Additionally, studies have suggested a tendency among general practitioners to misdiagnose major depressive disorder, a substantial portion of which are false-positive cases.[50] Many cases for which general practitioners utilize antidepressant therapy may also be related to mixed anxiety and depression syndromes.[44] In this context, the current results may suggest the need for increased education of general practitioners in appropriate diagnosis and treatment.

The risk-benefit balance regarding the prescription of antidepressants is affected by the potential for side effects and other negative consequences. Some complaints related to depressive symptoms may be transient and may be alleviated without mental health interventions.[51] On the other hand, psychotherapeutic interventions might offer the same benefit of pharmacotherapy without the negative consequences associated with antidepressant medications. Qualitative interviews with general practice patients with subclinical depressive symptoms have suggested some tendency toward preferring psychotherapy,[49] and some studies have found significant benefits of psychotherapeutic interventions among individuals with subthreshold depression.[10,48] Individuals taking antidepressants in the absence of diagnoses in the current study were more likely to have a perceived unmet need for care, and many studies have shown that perceived but unmet need is often for therapy or counseling.[29,32]

The results of the current study are influenced by the following limitations. First, the CPES is a cross-sectional dataset. This prevents any inference of causality. Psychiatric disorders and antidepressant use occurred at some point in the past year, but further specificity of the onset of disorders and the initiation of antidepressant use was not available. Second, antidepressant medication use was determined by self-report, although supplemented by information from medication bottles. The accuracy of such self-reports has been examined and shown to be sound, however.[52] Third, self-report bias may also limit the recall of psychiatric symptoms, outpatient visits, and inpatient admissions. Fourth, several diagnoses that may explain the prescription of antidepressants were not assessed in the CPES, including bipolar disorder, cyclothymic disorder, bereavement, adjustment disorder, sleep disorders, obsessive-compulsive disorder, specific phobia, nicotine dependence, and personality disorders, particularly borderline personality disorder. However, the efficacy of antidepressant treatment in many of these conditions has not been established. Fifth, the current study examines a representative sample of the United States, but generalization of results to other countries is impossible, as significant differences in health care systems and the delivery of medical care across countries may affect the results.

In conclusion, the results of the current study suggest that antidepressant use among individuals without psychiatric diagnoses is common in the United States and is nearly always motivated by other indicators of need, including subthreshold disorders and traumatic events. Future research needs to address the clinical significance of subthreshold psychological difficulties, perhaps by adopting a dimensional perspective on psychiatric problems, and examine optimal treatment modalities for individuals suffering from subthreshold disorders and other forms of psychological distress.

Drug names: amitriptyline/chlordiazepoxide (Limbitrol and others), bupropion (Aplenzin, Wellbutrin, and others), citalopram (Celexa and others), clomipramine (Anafranil and others), desipramine (Norpramin and others), doxepin (Zonalon, Silenor, and others), fluoxetine (Prozac and others), fluvoxamine (Luvox and others), imipramine (Tofranil and others), isocarboxazid (Marplan), mirtazapine (Remeron and others), nortriptyline (Pamelor, Aventyl, and others), paroxetine (Paxil, Pexeva, and others), phenelzine (Nardil), protriptyline (Vivactil and others), sertraline (Zoloft and others), tranylcypromine (Parnate and others), trazodone (Oleptro and others), trimipramine (Surmontil and others), venlafaxine (Effexor and others).

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