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# Antidepressant Use and Lifetime History of Mental Disorders in a Community Sample: Results from the Baltimore Epidemiologic Catchment Area Study

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## Abstract

**Objectives—**Past studies have shown that many individuals who use antidepressants do not have a current or lifetime history of mental disorders. However, recent studies suggest that the one-time retrospective evaluation of mental disorders commonly used in such studies may substantially underestimate the true lifetime prevalence of mental disorders. We examined the prevalence of mental disorders, assessed prospectively over multiple interviews, among individuals currently using antidepressants in a community sample.

**Methods—**Using data from the Baltimore Epidemiologic Catchment Area (ECA) Survey Wave 1 (1981) through Wave 4 (2004) (N = 1071), we assessed lifetime prevalence of common mood and anxiety disorders according to the DSM-III and DSM-III-R criteria, based on 4 interviews, among participants who reported current antidepressant use. Furthermore, we examined factors associated with current antidepressant use.

**Results—**Thirteen percent of participants at Wave 4 reported currently using antidepressant medications. Among antidepressant users, 69% never met criteria for major depressive disorder (MDD), and 38% never met criteria for MDD, obsessive-compulsive disorder, panic disorder, social phobia, or generalized anxiety disorder in their lifetime. Female gender, Caucasian ethnicity, recent or current physical problems (e.g., loss of bladder control, hypertension and back pain) and recent mental health facility visits were associated with antidepressant use in addition to mental disorders.

**Conclusions—**Many individuals who are prescribed and use antidepressant medications may not have met criteria for mental disorders. Our data indicate that antidepressants are commonly used in the absence of clear evidence-based indications.

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Additional information

Baltimore ECA database is owned by the Department of Mental Health, Johns Hopkins Bloomberg School of Public Health and is not publicly available

## Introduction

Antidepressant (AD) prescribing and use have increased rapidly in the past two decades.[1-3] The introduction of new agents such as selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs), which are better tolerated than the older tricyclic antidepressants (TCA), has contributed to the rapid rise in AD prescription.[2]

The rise in prescription and use of ADs has coincided with increased numbers of individuals using these medications who do not meet criteria for mental disorders [4-6] and who may suffer from mild mood or anxiety symptoms.[7] Recent studies suggest that up to 73% of AD users may not carry any psychiatric diagnosis.[6] There is some evidence that this potential AD use without an indicated mental disorder diagnosis may be more pronounced in some population subgroups, including females, [8-11] older adults,[8, 10] whites [2] and individuals with physical health problems. [8, 9, 11] Furthermore, some of the individuals who continue to use antidepressants on a long-term basis might have met the criteria for a mental disorder in remote past. While long-term maintenance AD treatment may be indicated in some of these individuals,[12] long-term use of these medications is not always indicated. Unnecessary long-term AD use may expose individuals to increased risks of adverse effects ranging from severe health risks such as suicidality [13] to problems affecting quality of life,[14] such as sexual dysfunction as well as unnecessary financial burden.

Past studies that examined AD use without an indicated mental disorder diagnosis often have used one-time retrospective evaluation of current or lifetime mental disorders.[4-6] Retrospective evaluations may substantially underestimate the true lifetime prevalence of mental disorders, as noted in a recent study that compared one-time retrospective evaluations with cumulative evaluations based on repeated interviews over time.[15] In that study by Moffit et al.,[15] the lifetime prevalence estimates based on prospective evaluation using multiple interviews were typically 2-3 times higher than those based on one-time retrospective evaluations. Underestimation of prevalence of mental disorders may have influenced the results of previous studies that examined whether those receiving AD treatment actually met diagnostic criteria for mental disorders.[4-6]

In the current study, we used data from the Baltimore Epidemiologic Catchment Area (ECA) Follow-up Study Waves 1 (1981) through 4 (2004-2005) to assess the proportion of AD use in the community that is not associated with a lifetime history of common mental disorders, ascertained by cumulative evaluation over four Waves. We also explored socio-demographic and other clinical factors associated with AD use in this community sample.

## Methods

### Sample

The Baltimore ECA Follow-Up Study is a longitudinal, population-based cohort study of adult participants. The participants were originally interviewed in 1981 (Wave 1, N = 3,481) and followed up in 1982 (Wave 2, N = 2,768), 1993-1996 (Wave 3, N = 1,920), and 2004-2005 (Wave 4, N = 1,071). The ECA study was primarily designed to collect data to

estimate the prevalence and incidence of mental disorders in a representative community sample according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (DSM-III, for Waves 1 and 2) or its revised edition (DSM-III-R, for Waves 3 and 4). Methods for the Baltimore ECA Follow-Up Study have been described in detail elsewhere.[16] The study was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board. All participants provided written informed consent.

## Assessments

*Antidepressant use* at Wave 4 was assessed by asking participants to list all of the medications they had taken in the past week. They were instructed to include both prescribed and over-the-counter medications. The interviewer recorded the names of all medications. For this study, two experienced psychiatrists (YT and OJB) independently coded all antidepressant drugs recorded by lay-interviewers including amitriptyline, bupropion, citalopram, clomipramine, doxepin, duloxetine, escitalopram, fluoxetine, fluvoxamine, imipramine, mirtazapine, nortriptyline, paroxetine, sertraline, trazodone, and venlafaxine. A high inter-rater reliability was obtained between the two raters (Cohen's kappa = 0.99).

*Cumulative lifetime history of mental disorders* was assessed based on interviews in Waves 1 through 4 using the Diagnostic Interview Schedule (DIS).[17] At each Wave, trained interviewers administered the DIS. In Waves 1 and 2, the DIS version III [18] (based on DSM-III criteria) was used; in Waves 3 and 4, the DIS version III-R [19] (based on DSM-III-R criteria) was used. At each Wave, lifetime history of the following seven mental disorders was evaluated: major depressive disorder (MDD), obsessive-compulsive disorder (OCD), panic disorder, social phobia, generalized anxiety disorder (GAD), alcohol abuse or dependence, and drug (including cocaine, marijuana, stimulants, sedatives, and tranquilizers) abuse or dependence. Lifetime prevalence of mental disorders was estimated using the assessments of lifetime disorders at each Wave over Waves 1 through 4. However, GAD was evaluated only at Waves 3 and 4. We therefore estimated the lifetime prevalence of GAD solely based upon data from Waves 3 and 4. Participants were rated as having a lifetime history of a mental disorder if they met the criteria for that disorder at least once over the course of the four interviews.

*Cumulative lifetime history of medical disorders* was estimated using the assessments of lifetime history of these disorders at each Wave over Waves 1 through 4. Participants were asked if they ever had the following physical illnesses: diabetes, hypertension, arthritis, stroke and cancer (any type).

*Somatic symptoms* were assessed at Wave 4 interview by asking each participant if they ever had the following somatic symptoms: back pain, loss of bladder control, fainting spells, and dizziness.

*Socio-demographic characteristics* included in the analyses were based on Wave 4 data and included age (categorized here into four groups: ≤49, 50–59, 60–69, and ≥70 years), sex, race (non-Hispanic Caucasian vs. other racial/ethnic group, including African American,

Hispanic, Asian American, Native American, and Pacific Islander), educational attainment (less than 12 years [less than high school] vs. ≥12 years of school [high school or more]) and marital status (currently married vs. not married). Mental health service use (at least one visit within the 6-month period prior to the Wave 4 interview vs. no visits within the past 6 months) and coverage by Medicare or other health insurance at Wave 4 interview were also recorded.

### Statistical Analysis

We calculated the cumulative lifetime prevalence of MDD or any of the covered anxiety disorders among the Wave 4 AD users. Multivariable logistic regression analysis was used to identify factors associated with the binary outcome of current AD use, recorded at Wave 4. Mental disorders, medical disorders, somatic symptoms at Wave 4 interview, socio-demographic variables and mental health service use were entered as independent variables in the models. We first calculated unadjusted odds ratios. Next, for mental disorders, medical disorders, somatic symptoms, and mental-health service use, we calculated odds ratios adjusted for sex and race (Caucasian vs. other racial/ethnic group). We limited the covariates to sex and race based on the results of the unadjusted analysis. Statistical analyses were carried out using SPSS software version 20 (IBM, Chicago, IL).

## Results

### Characteristics and AD use in Baltimore ECA Wave 4 participants

Participants had a mean (± standard deviation) age of 58.9 ± 12.9 years at Wave 4, and the majority of participants were 50 years old or older. Approximately 63% were female, 62% were Caucasian (35% were African American, and 3% were of another race/ethnicity), 56% were married at the time of Wave 4 interview, and 73% had educational attainments of ≥12 years (Table 1). Of 1,071 participants, 137 (13%) were taking ADs at the time of the Wave 4 interview. Among the 137 AD users, 94 (69%) never met criteria for MDD, and 52 (38%) never met criteria for MDD or the anxiety disorders evaluated in this study (i.e., OCD, panic disorder, social phobia and GAD) in any of the four interviews. Of the 1,071 participants, 129 (12%) had used mental health services within 6 months prior to the Wave 4 interview.

### Comparison of AD users and non-users

In unadjusted analyses, female gender, Caucasian race, having a lifetime history of MDD, OCD, panic disorder, social phobia, GAD, hypertension, arthritis, or stroke, and reporting a lifetime history of back pain, loss of bladder control, fainting spells, or dizziness, and having a mental health visit in the past 6 months were associated with AD use. When adjusted for sex and race, lifetime histories of all mental disorders but OCD were associated with AD use. Recent or lifetime histories of hypertension, stroke, back pain, loss of bladder control, fainting spells, and dizziness also remained significantly associated with AD use. The association of AD use with a mental health visit in the past 6 month persisted in the adjusted analysis (Table 1).

## Discussion

To our knowledge, this is the first study that has examined AD use and lifetime prevalence of mental disorders ascertained by cumulative evaluation using multiple interviews in a community sample. We found that a sizable proportion of AD use was not associated with lifetime mental disorder history, with 38% of current AD users never having met criteria for MDD, OCD, panic disorder, social phobia, or GAD, and 69% of current AD users never having met the criteria for MDD, in their lifetimes. Because we used cumulative evaluation based on four interviews, the lifetime prevalence estimates of mental disorders are likely closer to the true lifetime prevalence of these mental disorders than the estimates based on one-time retrospective evaluation. Nonetheless, like past studies,[4-6] we found that a substantial proportion of AD users do not have a history of meeting criteria for MDD or the anxiety disorders assessed, even when these disorders are evaluated by a cumulative approach. Our data thus support the view that ADs are commonly prescribed for patients who may have mild psychiatric symptoms but do not meet the full criteria for depression or other common mental disorders for which these medications are indicated.

Past studies have found that 20-30 % of AD prescriptions are prescribed for off-label indications.[20, 21] Furthermore, prescriptions written by non-psychiatrist physicians have been growing;[1] based on one estimate, 60% of AD prescriptions in this country are written by such providers.[22] Although the majority of these medications are prescribed for depression or anxiety complaints, [4, 23, 24] many of these complaints may not meet the diagnostic criteria for conditions for which there is strong empirical evidence of AD treatment efficacy and safety. Moreover, as the results of the current study indicate, many patients who are prescribed antidepressants may never have met these criteria throughout their lifetimes.

Consistent with past research, [8, 9, 11] medical illnesses and somatic complaints were associated with AD use. It might be the case that associations between a physical complaints or illnesses and AD use are explained by access to primary care physicians by individuals with chronic medical conditions. Individuals who are in frequent contact with their primary care providers due to physical health conditions may simply have a greater chance of receiving AD treatment.

FDA-approved uses of ADs for non-psychiatric condition such as premenstrual dysphoric disorder (PMDD), fibromyalgia and chronic pain, or use for smoking cessation and off-label AD use might partly explain the substantial proportion of AD users without lifetime histories of MDD or anxiety disorders. However, we note that other studies have found that only a small proportion of antidepressants are prescribed for these conditions. In a 2010 study based on a survey of a nationally representative sample of practices, no more than 7 percent of antidepressant prescriptions were for physical health conditions. [23] Less than two percent of all antidepressant prescriptions were for the diagnostic groups that include fibromyalgia and PMDD. Thus, the majority of the prescriptions in the absence of psychiatric diagnoses of MDD and anxiety disorders in this study were likely for mental health complaints that did not meet the criteria for these disorders. While there is some evidence supporting the efficacy of ADs for sub-syndromal depressive symptoms and

dysthymic disorder, [25, 26] and for off-label use of ADs in the treatment of sleep disorders, [27] these uses are controversial. [28, 29]

Several limitations to this study should be noted. First, the ECA study used different versions of DSM criteria for Waves 1-2 and Waves 3-4. Second, we were unable to include a number of other indicated uses of antidepressants, including bipolar disorder and post traumatic stress disorder (PTSD), because these disorders were not evaluated in Waves 3 and 4 (bipolar disorder) or were not accessed at any Waves (PTSD). In addition, GAD was not evaluated in Waves 1 and 2. Therefore we might have overestimated the AD use without an indicated mental disorder diagnosis in this community sample. However, the lifetime prevalence of bipolar spectrum disorders in Waves 1 and 2 was very low (less than 1%, even when Waves 1 and 2 were combined) and all subjects (n = 9) who met the criteria of bipolar disorder at Waves 1 or 2 also had a lifetime history of MDD or anxiety disorders evaluated in this study. Third, as evidenced by this study and others, AD use without an indicated mental disorder diagnosis, occurs in conjunction with under-diagnosis and under-treatment of major depression and other common mood and anxiety disorders in community settings.[30] While we were able to estimate how many people without lifetime mental disorders used AD, we were unable to estimate how many people with lifetime disorders had ever used any AD. Fourth, because the information regarding current AD use was based on participant self-report, reporting bias may have influenced the results. Fifth, because no measures for the severity of mental disorders were available, we did not examine the relationship between of severity of symptoms of MDD or anxiety disorders and AD use. Past studies have shown that the benefit from ADs varies depending on the severity of symptoms (i.e., patients with more severe symptoms receive greater benefits). [31, 32] Sixth, we were unable to identify whether the ADs were prescribed by primary care provider or psychiatrists. The high prevalence of false positive diagnoses of depression in primary care has been previously documented. [33] The prevalence of prescriptions without a diagnosis may be higher among patients of primary care providers. Finally, lifetime history of a mental disorder is not by itself an indication for use of antidepressants. Many of the patients with a positive lifetime history of MDD or other episodic mental disorders recover from these disorders on their own. Practice guidelines for treatment of mental disorders only recommend long-term treatment for patients who experience repeated episodes or severe and disabling illness. [12] Furthermore, while the assessment of mental disorders in this study was based on lifetime history and consecutive interviews, assessment of antidepressant use was based on interviews in Wave 4 only and solely covered current use. Assessment of lifetime AD use would likely reveal a larger number of AD users without a lifetime major depression or anxiety disorder diagnosis.

In conclusion, our data add to the accumulating literature on the use of ADs in the absence of clear evidence-based psychiatric indications. The findings call for broad reforms, including improved communication and referral between primary care providers and psychiatrists, education of primary care providers on appropriate use of ADs, and possibly selective use of screening measures to enhance the match between the diagnosis of common mental disorders and AD treatment.[34] With the expected expansion in the role of primary care providers in diagnosis and management of common mental disorders following the

implementation of the Affordable Care Act, there is an urgent need for initiatives aimed at improving the diagnosis and treatment of these disorders in primary care settings.[6]

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### Clinical points

- One-time retrospective evaluation of mental disorders commonly used in surveys could substantially underestimate the true lifetime prevalence of mental disorders.
- Many individuals who are prescribed and use antidepressant medications may not have met criteria for mental disorders, even when these disorders are evaluated prospectively.
- Antidepressants are commonly used in the absence of clear evidence-based indications.

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**Table 1**

Characteristics of 1,071 participants of wave 4 Baltimore Epidemiologic Catchment Area study and comparison of antidepressant (AD) users and non-users.

| Characteristics | Total | | AD users | | AD non-users | | Unadjusted comparison of AD users and non-users | | | Adjusted comparison of AD users and non-users[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | OR | 95% CI | | OR | 95% CI | |
| | | | | | | | | Lower | Upper | | Lower | Upper |
| Age at wave 4, mean (SD), years | | | | | | | | | | | | |
| < 50 | 271 | 25 | 32 | 23 | 239 | 26 | 1 (ref) | | | | | |
| 50 - 59 | 402 | 38 | 58 | 42 | 344 | 37 | 1.26 | 0.79 | 2 | | | |
| 60 - 69 | 182 | 17 | 21 | 15 | 161 | 17 | 0.97 | 0.54 | 1.75 | | | |
| ≥70 | 216 | 20 | 26 | 19 | 190 | 20 | 1.02 | 0.59 | 1.77 | | | |
| Gender (Female) | 674 | 63 | 107 | 78 | 567 | 61 | 2.31* | 1.51 | 3.53 | | | |
| Race (non-Caucasian) | 409 | 38 | 31 | 23 | 378 | 41 | 0.43* | 0.28 | 0.66 | | | |
| Marital status (married) | 581 | 56 | 74 | 54 | 507 | 56 | 0.91 | 0.64 | 1.31 | | | |
| Education attainment (≥ 12 years) | 779 | 73 | 99 | 72 | 680 | 73 | 0.97 | 0.65 | 1.45 | | | |
| Covered by Medicare | 368 | 34 | 50 | 37 | 318 | 34 | 1.11 | 0.77 | 1.62 | | | |
| Covered by health insurance | 834 | 78 | 99 | 72 | 735 | 79 | 0.71 | 0.47 | 1.06 | | | |
| Lifetime history of mental illness | | | | | | | | | | | | |
| MDD | 140 | 13 | 43 | 31 | 97 | 10 | 3.95* | 2.6 | 5.99 | 3.46* | 2.26 | 5.29 |
| OCD | 76 | 7 | 16 | 12 | 60 | 6 | 1.93* | 1.07 | 3.45 | 1.75 | 0.97 | 3.18 |
| Panic disorder | 72 | 7 | 28 | 20 | 44 | 5 | 5.20* | 3.11 | 8.69 | 4.26* | 2.52 | 7.21 |
| Social phobia | 271 | 25 | 51 | 37 | 220 | 24 | 1.93* | 1.32 | 2.81 | 1.97* | 1.34 | 2.89 |
| GAD[b] | 37 | 4 | 13 | 10 | 24 | 3 | 3.98* | 1.97 | 8.01 | 3.48* | 1.69 | 7.17 |
| Alcohol abuse or dependence | 277 | 26 | 42 | 31 | 235 | 25 | 1.32 | 0.89 | 1.95 | 1.94* | 1.26 | 2.99 |
| Drug abuse or dependence | 188 | 18 | 32 | 23 | 156 | 17 | 1.52 | 0.99 | 2.34 | 1.82* | 1.16 | 2.84 |
| MDD or any anxiety disorders | 412 | 39 | 85 | 62 | 327 | 35 | 3.03* | 2.10 | 4.39 | 2.86* | 1.96 | 4.17 |
| Lifetime history of medical illness | | | | | | | | | | | | |
| Diabetes | 216 | 20 | 31 | 23 | 185 | 20 | 1.18 | 0.77 | 1.82 | 1.22 | 0.79 | 1.90 |

| Characteristics | Total | | AD users | | AD non-users | | Unadjusted comparison of AD users and non-users | | | Adjusted comparison of AD users and non-users[a] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | OR | 95% CI | | OR | 95% CI | |
| | | | | | | | | Lower | Upper | | Lower | Upper |
| Hypertension | 593 | 55 | 87 | 64 | 506 | 54 | 1.47* | 1.02 | 2.13 | 1.57* | 1.07 | 2.29 |
| Arthritis | 578 | 54 | 85 | 62 | 493 | 53 | 1.46* | 1.01 | 2.11 | 1.36 | 0.94 | 1.99 |
| Stroke | 77 | 7 | 17 | 12 | 60 | 6 | 2.06* | 1.17 | 3.65 | 1.95* | 1.09 | 3.50 |
| Cancer | 112 | 11 | 16 | 12 | 96 | 10 | 1.15 | 0.66 | 2.03 | 0.92 | 0.52 | 1.63 |
| Somatic symptoms | | | | | | | | | | | | |
| Back pain | 383 | 36 | 74 | 54 | 309 | 33 | 2.38* | 1.65 | 3.41 | 2.33* | 1.61 | 3.37 |
| Loss of bladder control | 246 | 23 | 49 | 36 | 197 | 21 | 2.08* | 1.42 | 3.06 | 1.77* | 1.18 | 2.63 |
| Fainting spells | 75 | 7 | 16 | 12 | 59 | 6 | 1.96* | 1.09 | 3.52 | 2.09* | 1.15 | 3.80 |
| Dizziness | 209 | 20 | 52 | 38 | 157 | 17 | 3.03* | 2.06 | 4.45 | 2.90* | 1.95 | 4.30 |
| Mental health visit in past 6 months | 129 | 12 | 66 | 48 | 63 | 7 | 12.62* | 8.28 | 19.23 | 11.83* | 7.68 | 18.22 |

AD, antidepressant; CI, confidence interval; GAD, generalized anxiety disorder; MDD, major depressive disorder; OCD, obsessive-compulsive disorder;OR, odds ratio.

*$p < 0.05$

[a]Adjusted for gender and race.

[b]Evaluated only at waves 3 and 4