

Antidepressant Adequacy and Work Status Among Medicaid Enrollees with Disabilities: A Restriction-based, Propensity Score-adjusted Analysis

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Abstract This cross-sectional study of adult survey respondents with disability and depression ($n = 199$) enrolled in Massachusetts' Medicaid program examined the association of adequately or inadequately prescribed antidepressant treatment and self-reported work status using conditional logistic regression, controlling for age, gender, race, marital status, education, receipt of SSI/SSDI, self-reported disabling condition, and health status. Confounding by severity was addressed by two methods: restriction of our sample and subsequent stratification by propensity score. Individuals receiving adequate antidepressant treatment had an increased odds of working compared to individuals receiving inadequate treatment, both in analyses in which restriction was used to limit confounding (OR = 3.45, 95% CI = 1.15–10.32, $P < .03$), and in analyses which combined restriction with adjustment by propensity

score stratification (OR = 3.04, 95% CI = 1.01–9.62, $P < .05$). Among this sample of Medicaid enrollees with disability and depression, those receiving adequate antidepressant treatment were significantly more likely to report working.

Keywords Depression · Disability · Employment · Antidepressant treatment · Restriction · Propensity score

Introduction

Whether a primary cause or a secondary consequence, depression is common among working-age people with disabilities (US Department of Health, Human Services 2005). Depression is a leading cause of productivity loss and work disability in the US (Greenberg et al. 2003; Kessler et al. 1999; Stewart et al. 2003). Among people with chronic physical illnesses or disabilities, depression is one of the most common secondary conditions (Kinne et al. 2004; McDermott et al. 2006; Mitra et al. 2005). The presence of comorbid depression along with chronic physical disorders (e.g., musculoskeletal disorders, chronic pain, asthma) has been found to increase the likelihood of work disability compared to physical disorders alone (Emptage et al. 2005; Stein et al. 2006; Waghorn et al. 2006).

A relationship between depression and functional work impairments has been reported in at least 10 studies of older antidepressants that were summarized in a review concluding that antidepressant treatment improved work outcomes when treatment was symptomatically effective (Mintz et al. 1992). Recent studies have examined associations between antidepressant treatment and receipt of private disability benefits. Dewa et al. (2003) found that workers adhering to guideline-recommended antidepressant

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treatment had an increased likelihood of returning to work rather than going onto disability benefits. Similar findings were reported by Burton et al. (2007), who found that adherence to antidepressant medication was associated with a decreased likelihood of filing short-term disability claims. No studies exist, to our knowledge, examining the effect of antidepressant treatment on the ability to work among individuals receiving public disability benefits such as Social Security Disability Insurance, Supplemental Security Income, Medicaid and/or Medicare. Qualifying for public disability benefits requires individuals to demonstrate severe disability, and, among people with disabilities, those receiving public disability benefits are the least likely to work (McNeil 2001).

In this cross-sectional study we sought to assess the effect of adequate antidepressant treatment on likelihood of working among people who qualified for the Massachusetts Medicaid program (“MassHealth”) on the basis of disability. We adopted two approaches, restriction of our sample and propensity score analysis, to address potential confounding by severity. Confounding by severity is a potential bias particularly relevant to observational studies of medication treatment that has been most thoroughly explored in the pulmonary and cardiology literature (e.g., Beasley et al. 1994; Clark et al. 2005; Garrett et al. 1996). In our study, confounding by severity refers to the phenomenon whereby individuals who are the most severely ill and least likely to work are more likely to come to the attention of prescribers and receive medication, thus potentially distorting the relationship between medication and work. Our primary hypothesis was that adequate antidepressant treatment among working-age Medicaid enrollees with disabilities diagnosed with major depression would be associated with a greater likelihood of participating in paid employment compared to those receiving inadequate treatment with antidepressants.

Method

Procedure

Study participants included adults aged 19–64 who qualified for MassHealth on the basis of disability (meeting federal Social Security Administration [SSA] criteria for disability or state SSA-based criteria) and who had responded to either the 2003 or the 2005 MassHealth Employment and Disability Survey (MHEDS I and II). The surveys were developed and administered under grants funded by the Centers for Medicare and Medicaid Services, and provided data on the disability, health and employment status of working-age adults with disabilities in the MassHealth program. Detailed discussions of survey

development efforts and major findings are reported elsewhere (Henry et al. 2005, 2007). Each survey was administered to just under 3,000 randomly selected MassHealth members with disabilities with a minimum of 6 months of continuous MassHealth enrollment immediately prior to survey administration. MHEDS I and II response rates were 58 and 54%, respectively, for a total of 3,201 respondents.

The method used to select study participants is shown in Fig. 1. Because we relied on MassHealth claims data to establish a diagnosis of major depression and to determine adequacy of antidepressant treatment, study participants were restricted to MHEDS I and II respondents who were only enrolled in MassHealth and had no other source of insurance (e.g., Medicare or private insurance). This reduced the set of possible participants from 3,201 to 821. Among these 821 members, we used the MassHealth claims data to identify members who had received a diagnosis of major depression (DSM-IV-TR diagnosis of 296.2x, 296.3x, or 311) and were continuously enrolled in MassHealth for a minimum of 12 months immediately prior to completing the survey, which further reduced the set of participants to 244. (80% of the 244 participants were continuously enrolled for 24 months or more prior to survey administration, while the remaining 20% were continuously enrolled for 12–24 months prior to the survey).

We then reviewed participants’ pharmacy claims for every month they were continuously enrolled in MassHealth

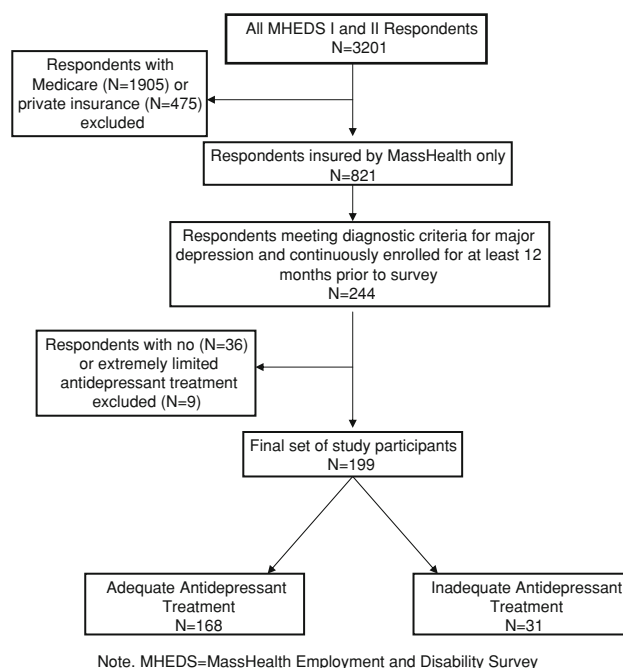


Fig. 1 Selection of study participants from MHEDS I and II respondents. Note: *MHEDS* MassHealth employment and disability survey

prior to the survey administration date (up to 24 months prior) to determine the adequacy of their antidepressant treatment. To compare members with similar depression severity, we restricted our sample by excluding members who either received no antidepressant treatment ($n = 36$) or only extremely limited treatment (duration and dose of antidepressants were both inadequate; $n = 9$), because they may have had less severe depression. For instance, individuals in the no or extremely limited treatment groups were significantly less likely to self-rate themselves as depressed compared to individuals in the included participants (71 vs. 91% reporting depression, $P < .0004$). The final set of study participants included 199 members.

Adequacy of antidepressant treatment was assessed using the Antidepressant Treatment History Form (ATHF) rating system, which is a widely accepted method for assessing adequacy of antidepressant treatment trials (Oquendo et al. 2003). We applied the ATHF dosage criteria, with treatments scoring 3 or 4 on the 0–4 scale, equivalent to 20 mg fluoxetine daily being judged “adequate.” However, we modified the minimum duration from 28 to 60 continuous days because we felt this period (8+ weeks) represented the minimum duration of treatment that could be confidently assumed to produce mood responses in individuals responsive to adequate doses of the antidepressant. In addition, this duration also provided evidence that members had likely completed their initial prescription and refilled their prescription at least once, since 96% of the antidepressant prescriptions were for 30 days or less. Table 1 shows all antidepressant medications and dosage equivalents included in the analysis.

Pharmacy claims data were linked with data from the MHEDS I and II. The surveys provided information on members’ demographic characteristics [age, gender, race, marital status, level of education and receipt of Supplemental Security Income (SSI) or Social Security Disability Insurance (SSDI)], self-reported disabling conditions (psychiatric disability; physical disability; both psychiatric and physical disabilities; other disabling conditions), and self-reported current health status (excellent, very good, good, fair or poor). Members’ employment status (currently working versus not) was derived from their answer to the MHEDS question “Are you currently working at a job for pay?”

Data Analysis

Data were analyzed using SAS for Windows, Version 9.1 statistical software (SAS Institute Inc. 2002–2003). Results of preliminary (uncontrolled) analyses showed that both MHEDS I and II members with adequate antidepressant trials had an increased likelihood of working (OR’s = 4.23

Table 1 Antidepressant medications and dosages representing adequate treatment

Antidepressant	Dosage (mg/day)
Fluoxetine	≥20
Paroxetine	≥20
Citalopram	≥20
Sertraline	≥50
Fluvoxamine	≥200
Bupropion	≥300
Nefazadone	≥300
Venlafaxine	≥150
Mirtazepine	≥15
Amitriptyline	≥200
Amoxapine	≥300
Clomipramine	≥200
Desipramine	≥200
Doxepin	≥200
Imipramine	≥200
Nortriptyline	≥75
Phenelzine	≥60
Protriptyline	≥30
Tranlycypromine	≥40
Trazadone	≥300
Duloxetine	≥30

and 3.10, respectively). The ORs did not differ significantly across the two survey samples ($P < .81$), verifying our decision to combine the two surveys. To control for possible residual confounding from demographic and health factors and to incorporate a number of covariates in our model without consuming excessive degrees of freedom, we used member characteristics to generate propensity scores (Braitman and Rosenbaum 2002; Wang and Donnan 2001). Using logistic regression, we generated a propensity score for each member, modeling antidepressant treatment (adequate versus inadequate) from the following covariates: age, gender, race, marital status, education level, receipt of SSI/SSDI, self-reported disabling condition and health status (C-statistic = 0.64). Members were then grouped into three strata based on propensity scores, which reflected their likelihood (high, intermediate, or low) of being prescribed adequate treatment (Wang and Donnan 2001). With the two survey samples pooled, we used logistic regression to test the uncontrolled association of adequate antidepressant treatment with employment status, and subsequently used conditional logistic regression to test the association, controlling for strata. In addition, we used conditional logistic regression in sensitivity analyses testing whether findings were consistent when we altered the definition of the study sample.

Disclosure

The first author has received research grants from Forest Pharmaceuticals, a company that produces an antidepressant, to fund research separate from this study. None of the other authors report any known or possible conflicts of interest. All authors certify responsibility for this manuscript. This study was approved by the Committee for the Protection of Human Subjects in Research at the University of Massachusetts Medical School.

Results

Over 84% of participants ($n = 168$) were found to have received adequate antidepressant treatment in the 12–24 months prior to responding to the MHEDS. Demographic information, health characteristics, and employment status of MassHealth members receiving adequate versus inadequate antidepressant treatment are shown in Table 2. No significant differences in demographics or health characteristics between adequately and inadequately treated members were observed, either in bivariate comparisons or multivariate comparisons in which the significance of a covariate was tested in a generalized linear model adjusting for the other covariates in a propensity score (the “propensity adjusted P -value”). The only variable to approach significance (race) became less significant once adjustment was made for this and other variables by using

propensity scores. Members receiving adequate antidepressant treatment were significantly more likely to report currently working at a job for pay than those receiving inadequate treatment (34 vs. 13%, $P < .02$).

Similarly, results of logistic and conditional logistic regression analyses showed members receiving adequate antidepressant treatment to be significantly more likely to be working in both the unadjusted (OR = 3.45, 95% CI = 1.15–10.32, $P < .03$) and propensity-adjusted (OR = 3.04, 95% CI = 1.01–9.20, $P < .05$) analyses (Table 3). To test the appropriateness of deriving a pooled odds ratio across propensity score-based strata, we also calculated ORs within each stratum. These ORs ranged from 2.4 to 4.4, and a Breslow–Day test showed no significant difference in the ORs across the three strata ($P = .91$).

While our total sample was moderately sized (199 individuals), the number of individuals with inadequate treatment was comparatively small ($n = 31$), implying our results might be sensitive to changes in the definition of our study sample. Thus, we conducted two sensitivity analyses. First, the study sample included a fraction of individuals diagnosed with either schizophrenia or bipolar disorder in addition to depression ($n = 45$). When members with co-occurring schizophrenia/bipolar disorder were excluded from the sample, the central estimate of the odds of working with adequate antidepressant treatment remained virtually unchanged, although the result were not statistically significant (OR = 3.03, 95% CI = 0.85–10.89, $P < .09$). In the second sensitivity analysis, we expanded

Table 2 Demographic and health characteristics and employment status of MassHealth members with disabilities receiving adequate versus inadequate antidepressant treatment ($n = 199$)

Characteristics	Adequate ($n = 168$)	Inadequate ($n = 31$)	P	Propensity adjusted P
<i>Demographics</i>				
Age, mean (sd)	43.5 (11.8)	43.0 (10.7)	.80	.62
Female	111 (66%)	19 (61%)	.61	.73
White	150 (89%)	24 (77%)	.07	.27
Married	31 (18%)	7 (23%)	.59	.99
Some college education	62 (37%)	8 (26%)	.23	.34
Receiving SSI and/or SSDI	81 (48%)	16 (51%)	.73	.79
<i>Self-reported disabling condition</i>				
Psychiatric disability only	82 (49%)	11 (36%)	.17	.93
Physical disability only	7 (4%)	1 (3%)	.81	.73
Both psychiatric and physical disabilities	73 (44%)	17 (55%)	.24	.95
Other disabling conditions	6 (4%)	2 (7%)	.45	.69
<i>Self-reported health status</i>				
Health is excellent, very good or good	45 (27%)	8 (26%)	.91	.59
<i>Employment status</i>				
Currently working at a job for pay	57 (34%)	4 (13%)	.02	

Note: SSI/SSDI, Supplemental security income/social security disability insurance; Propensity-adjusted P refers to the P value (significance) of the covariate in a general linear model adjusted for all the remaining covariates in a propensity score

Table 3 Results of unadjusted logistic regression and propensity-adjusted conditional logistic regression analyses predicting members' employment status from adequacy of antidepressant treatment ($n = 199$)

	OR	95% CI	<i>P</i>
<i>Unadjusted model</i>			
Adequate antidepressant treatment only	3.45	1.15–10.32	<.03
<i>Propensity-adjusted model</i>			
Adequate antidepressant treatment adjusting for demographic and health characteristics	3.04	1.01–9.20	<.05

Note: Demographic characteristics included age, gender, race, marital status, education and receipt of SSI/SSDI; Health characteristics included self-reported disabling condition and health status; Employment status: 1 = currently working for pay, 0 = not currently working; Adequacy of antidepressant treatment: 1 = adequate treatment, 0 = inadequate treatment

our study sample by including individuals with dysthymia ($n = 19$), although treatment guidelines are less developed for this population. We observed a somewhat lower but still positive odds of working (OR = 2.0, 95% CI = .77–5.20, $P < .16$) with adequate antidepressant treatment in this expanded sample ($n = 218$), although these results also were not statistically significant.

Discussion

In our sample of continuously enrolled Massachusetts Medicaid members with disability and depression who had recently received treatment for depression, self-reported employment status varied significantly based on whether members had received adequate or inadequate antidepressant treatment. Our findings were statistically significant, but not robustly so (lower bound of the 95% CI = 1.01), likely due to the small number of inadequately treated members in our sample. Counterbalancing (in part) the borderline statistical significance we observed was the substantial strength of the association we observed. Members receiving adequate treatment were approximately three times as likely as those receiving inadequate treatment to report working in both unadjusted and adjusted analyses. Our results are generally consistent with those reported in previous studies of individuals either receiving private short-term disability benefits (OR of 1.9 for returning to work with adequate antidepressant treatment; Dewa et al. 2003), or filing for short-term disability benefit (OR of 1.39 for individuals non-adherent to antidepressant treatment; Burton et al. 2007).

Multiple limitations to our investigation must be acknowledged, some of which we attempted to address in our analyses. Our sample included a fraction of members diagnosed with either schizophrenia or bipolar disorder in addition to depression ($n = 45$); results were similar for those with and without co-occurring schizophrenia/bipolar disorder. The role of antidepressants in bipolar depression is controversial, with many practitioners using these agents

and some observational data indirectly supporting their use (Altshuler et al. 2003) although recent randomized data does not (Sachs et al. 2007). The use of antidepressants for depression in schizophrenia is a Level II recommendation of the most recent American Psychiatric Association (APA) clinical practice guideline (APA 2004), and may be quite common. One survey estimates that antidepressants are used as adjunctive treatment in one-third of patients with schizophrenia (Addington et al. 2002). A recent meta-analysis found that antidepressants do not improve schizophrenia outcomes overall, but may exhibit a moderate-sized beneficial effect among “chronic” patients (Sepehry et al. 2007). Excluding individuals with bipolar disorder or schizophrenia made little difference to our effect estimate (3.03 vs. 3.10). However, as might be expected given the reduction in sample size, the estimate was not statistically significant ($P < .09$). Our sample did not include individuals with dysthymia because treatment recommendations are less developed for these individuals. (For instance, they may require higher doses of antidepressants to achieve “adequate” treatment). Including individuals with dysthymia in our sample reduced our effect estimate substantially (2.00 vs. 3.10) as well as eliminated its statistical significance ($P < .16$). The reduction in significance is not unexpected given the increase in diagnostic heterogeneity in the sample including individuals with dysthymia.

Our definition of adequate treatment differed from some used previously in the literature (e.g., Burton et al. 2007) and in some practice guidelines. Those practice recommendations are clinically based, however, often presuming that the response of the individual to the treatment can be observed (most specifically, the point at which remission of symptoms is reached). For example, the APA guidelines (APA 2000) recommend that “treatment should continue for 16–20 weeks after remission.” As this study relied on Medicaid claims data to determine treatment adequacy, we were unable to judge whether individuals receiving antidepressants were achieving a response or remission. Furthermore and more importantly, a primary basis behind this recommendation that treatment continue considerably after remission is to ensure sufficient length of treatment

to prevent relapse shortly after discontinuation of the medication. We hypothesized that for our study period (in which all individuals had received treatment within 2 years of the assessment of working status), an individuals' likelihood of working was more likely to be dependent on whether they had received sufficient dose and duration of antidepressant medication (i.e., 2 months or more) to facilitate an initial symptomatic response or remission, rather than whether their treatment persisted long enough to buffer them against eventual relapse. Our approach is consistent with some previous observations regarding antidepressant treatment and functioning (Mintz et al. 1992).

Other limitations include the fact many of our variables were self-reported, including our outcome variable of current work status. It would be helpful in the future to conduct a similar investigation using a database linked to verifiable employment data, such as state unemployment insurance data. Although we lacked a specific measure of disability severity, our use of self-reported disabling condition allowed us to distinguish members reporting psychiatric disability only from those reporting both psychiatric and physical disabilities (and to control for this in the propensity score). In a previous study (Henry et al. 2006), we found Medicaid enrollees with co-occurring psychiatric and physical disabilities to be less likely to work (and were presumably more severely disabled) than those with psychiatric disability alone. Although we did determine that members refilled their antidepressant medication at appropriate times, it is possible that members did not actually use the antidepressant medication as prescribed. And, because the study is cross-sectional, it is possible some members began work before they started antidepressants.

We also had incomplete information about potentially important confounding variables. The quality of a propensity score analysis is directly related to the quality of information available: in our case, further information about depression severity and history (e.g., past suicide attempts) and information about provider factors (how likely a given provider is to attain adequate doses and duration of antidepressant treatment with their patients) would have been helpful. This lack of information may have accounted for the limited C-statistic (0.64) we obtained for the propensity score model using the covariates we had available. However, our decision to employ propensity score adjustment as the second stage of our approach to limiting confounding by severity may have also contributed to our small C-statistic: we applied propensity scores only after restricting our sample fairly stringently to produce groups fairly similar in all covariates except the receipt of adequate or inadequate antidepressant treatment. Restricting a sample has been reported as an alternative approach to substantially limiting confounding (Joffe and Colditz 1998; Schneeweiss et al. 2007).

An additional potential limitation to consider is the possibility that our results are confounded by the phenomenon frequently observed that individuals adherent to one treatment (antidepressant medication) were more likely to be adherent to other medications and health practices [the so-called "healthy adherer" effect (Simpson et al. 2006)]. However, we did not observe any correlation between adequate or inadequate treatment in our sample and adherence to non-psychiatric medications ($P < .6$, data not shown).

Finally, a concern that always exists with the use of voluntary survey data is that respondents may be very different from non-respondents; in this study the concern is that MHEDS I and II respondents may have been healthier or more functional than non-respondents. However, examining MassHealth claims in the 12 months prior to the month the surveys were administered, we found that respondents and non-respondents did not differ significantly on MassHealth healthcare expenditures or on an index of chronic disease burden (generated using the Chronic Illness and Disability Payment System; Kronick et al. 2000). Moreover, respondents were significantly more likely to use MassHealth-paid personal care attendant services than non-respondents ($P < .004$), suggesting that respondents had more functional impairments than non-respondents. It remains possible that residual bias may exist in terms of disability severity between respondents and non-respondents that we have been unable to detect.

Strengths of our study include verifiable pharmaceutical claims information, information about potential confounders in multiple domains (health status, age, education, etc.), and our use of the dual techniques of sample restriction and propensity score analysis at least partially address confounding by severity, since confounding by severity can severely bias observational studies of the effects of medication. In addition, our use of multiple sensitivity analyses helped evaluate the robustness of our results. Although our study had limitations, it is to our knowledge the first report indicating individuals with disabilities enrolled in Medicaid may be more likely to work if they receive adequate antidepressant treatment. It is also only the second report of which we are aware to analyze the impact of antidepressants on work status while formally adjusting for confounding by severity (along with Schoenbaum et al. 2002).

Conclusion

This study might be best interpreted as showing that, at a minimum, repeated receipt of an adequate dose of antidepressant (i.e., for 60 days or longer) among Medicaid members with disabilities appears to be positively associated with work status compared to those who do not

achieve even this minimal criteria. While this moderately sized study has some limitations of statistical power given the relatively small number of individuals receiving inadequate antidepressant, we observed a substantial effect showing adequate antidepressant treatment to be associated with working status among a broad sample of Medicaid enrollees with disabilities. This study contributes to a small but growing body of literature showing that adequate antidepressant treatment may have tangible economic benefits, but also suggests the need for further studies in larger samples, with more covariate information, further investigation of varying definitions of treatment adequacy, and better documentation of work status.

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