Is There a Business Case for Reducing Employees' Antidepressant Prescription Drug Cost Sharing?

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ABSTRACT

OBJECTIVE To assess the impact of desvenlafaxine on work and activity impairment, health-related quality of life (HRQOL), and the use of medical services among employed patients with major depressive disorder (MDD), and then estimate the financial impact to an employer of reducing antidepressant drug cost sharing for employees.

METHODS Employed patients with MDD (n=427) were randomly assigned to 12 weeks of double-blind treatment with desvenlafaxine or placebo. The differences in mean changes in patient-reported outcomes between the desvenlafaxine and placebo groups were compared from baseline to week 12. A predictive model was then constructed to estimate the financial impact to an employer of promoting the use of antidepressant pharmacotherapy via reduced cost sharing.

RESULTS Relative to employees in the placebo group, employees receiving desvenlafaxine experienced a significant reduction in overall work impairment and improvement in HRQOL. For a company with 5000 full-time employees, the total costs associated with MDD are predicted to decrease by $24000 after eliminating antidepressant cost sharing.

CONCLUSION Reducing the amount employees and dependents pay out-of-pocket for antidepressant prescription drugs can generate productivity benefits and medical-cost offsets that are larger than the associated increase in prescription drug spending.

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INTRODUCTION

The societal costs associated with depression in the United States were an estimated $83 billion in 2000.[1] The majority of these costs (63%) were generated by depression-related absences and reduced on-the-job productivity (ie, presenteeism), whereas direct medical costs accounted for only 25% of total costs. Other studies have also concluded that the indirect costs of depression may be larger than the direct medical costs associated with treating the condition.[2,3] The development of newer pharmacotherapies has substantially increased the proportion of depressed individuals who are receiving medical treatment.[4] Nevertheless, a minority of individuals receive treatment that satisfies clinical guidelines.[5-7]

A practical question for employers, therefore, is, What is the return on investment for improving the health of employees with depression? Perhaps the biggest challenge when trying to answer this question is how to measure the causal effect of a medical intervention on employees' productivity. Comparing the productivity of employees who do and do not have depression is problematic because employees with depression may differ in many ways beyond their current health status, such as motivation, education, and ability. Randomized controlled trials are a persuasive way to estimate causal effects because if the sample size is large enough, the mean characteristics of participants in the treatment and control groups should be similar.

There are few randomized controlled trials examining the effect of medical interventions on work outcomes of employees with depression.* Rost, Smith, and Dickinson[9] randomly assigned 326 patients to usual care or enhanced depression management. In the latter group, physicians and care managers were trained to encourage patients to initiate guideline-concordant psychotherapy or pharmacotherapy. Patients exposed to enhanced therapy experienced 6.1% higher productivity over a 2-year period relative to patients receiving usual care. A separate trial ran-

*Williams et al[8] concluded that 20 out of 28 randomized controlled trials they reviewed were successful in improving patients' depression outcomes in primary care settings. These studies did not, however, examine the productivity effects associated with health improvement.

domly assigned 604 employees to usual care or a telephonic outreach and care management program that encouraged patients to seek psychotherapy or pharmacotherapy treatment and provided recommendations to providers.[10] Workers receiving the enhanced treatment experienced a reduction in absences of 2 weeks per year relative to the control group, although there was no significant difference in on-the-job productivity.

Randomized trials are widely used to measure the effect of prescription drugs on health; however, they are rarely designed to capture the effect of prescription drugs on productivity. The first objective of this paper is to report the results of a randomized controlled trial of treatment with desvenlafaxine, a serotonin and norepinephrine reuptake inhibitor antidepressant, on self-reported productivity, medical service use, and health-related quality of life (HRQOL) for employed individuals with a major depressive disorder (MDD). To the best of our knowledge, this is the first randomized controlled trial assessing the impact of an antidepressant drug on work and activity impairment, the use of medical services, and HRQOL among employed patients with MDD.

The second objective is to translate the results of the randomized controlled trial into a practical policy that employers can implement for improving the management of MDD, and then evaluate the financial impact of that policy. About 29% of adults with MDD are currently treated with antidepressant prescription drugs, and 60% of patients who initiate pharmacotherapy adhere to recommended treatment.[7,11] Of course, employers cannot force employees to take antidepressant medication. However, an employer can regulate the cost and other access barriers to obtain prescription drugs that employees and dependents may face. Patients with depression are less likely to adhere to medical therapy when prescription drug co-payments rise,[12-14] and this same phenomenon has been documented for other health conditions.[15-19]

As a result, employers are experimenting with "value-based" insurance plans in which co-payments on certain types of drugs are reduced in order to increase adherence, improve health, and possibly reduce medical costs and improve productivity.[20,21] Although fewer than 20% of employers were using a value-based insurance design in 2007, 81% of employers with 10 000 or more beneficiaries were interested in such plans.[22] The early evidence indicates that medication adherence rates rise when employers reduce patient cost sharing. When one large employer reduced patients' drug co-payments in 2005 in 5 drug classes as part of a disease management program, adherence increased by 2.5 to 4.0 percentage points in 4 of the classes.[23] Likewise, adherence rates for statins and blood thinners increased by 2% to 4% after Pitney Bowes reduced patient co-payments in these drug classes in 2007.[24]

This paper estimates the financial impact to an employer of reducing antidepressant drug cost sharing for employees and covered adult dependents. The model, which is based on results of the desvenlafaxine randomized controlled trial and other published studies, examines the relationships between patient cost sharing and adherence; patient cost sharing and prescription drug spending; adherence and medical spending other than on prescription drugs; adherence and health-related absences; and adherence and health-related presenteeism.

METHODS

There are 2 analyses in this paper. First, we report the results of a randomized controlled trial in which the effect of desvenlafaxine on employees' work impairment, medical resource use, and HRQOL were evaluated. Second, we use the results of the randomized controlled trial along with other published literature to examine whether there is a compelling business case for an employer to reduce employee cost sharing and thereby promote the use of antidepressant pharmacotherapy.

STUDY DESIGN

The desvenlafaxine trial was a phase 3b, parallel-group, randomized, placebo-controlled, double-blind study that evaluated the safety and efficacy of desvenlafaxine 50 milligrams per day (mg/day) in employed adult outpatients with MDD experiencing functional impairment. The study was conducted at 55 research centers in the United States and Canada between February and November 2009. The design of the trial is described in Dunlop et al.[25]

SUBJECTS

Patients aged 18 to 75 years who met the criteria described in the *Diagnostic and Statistical Manual of Mental Disorders*[26] for a primary diagnosis of MDD without psychotic features were included in the study. All patients were required to be gainfully employed (or self-employed), which was defined as working 20 or more paid hours per week for at least 1 month prior to the baseline visit. To ensure baseline functional impairment, patients were required to have a Sheehan Disability Scale (SDS) total score of at least 10 at both the screening and baseline visits.[27]

The Mini-International Neuropsychiatric Interview

DISCLOSURES

The randomized controlled trial reported in this manuscript (NCT00824291) was sponsored by Wyeth, which was acquired by Pfizer Inc in October 2009. The economic modeling was conducted by Dr Nicholson and funded by Pfizer. Dr Nicholson was a paid consultant to Pfizer in connection with the development of the economic model and this manuscript. Drs Harnett and Whiteley are employees of and own stock in Pfizer.

was used to ascertain the presence of MDD.[28] Patients were required to have been experiencing depressive symptoms for 30 or more days prior to the baseline visit. In addition, participating patients were required to have a total Montgomery-Åsberg Depression Rating Scale (MADRS) score of at least 25 at both the screening and baseline visits, with no more than a 5-point improvement in total score between the screening and baseline visits.[29] The main inclusion and exclusion criteria are described in Dunlop et al.[25]

TREATMENTS

Individuals were randomly assigned in a 2:1 ratio (desvenlafaxine: placebo) to 12 weeks of double-blind treatment with 50 mg/day of desvenlafaxine, or placebo. This represented the intent to treat (ITT) population. The secondary sample consisted of a predefined modified intent to treat (mITT) population of relatively severe MDD patients. Specifically, individuals were included in the mITT sample if they had a Hamilton Rating Scale for Depression (HAM-D17) score of 20 or higher at baseline.

MEASURES

The Work Productivity and Activity Impairment (WPAI) questionnaire was self-administered to evaluate the percent of work time missed due to health (absenteeism), impairment while working due to health (presenteeism), overall work impairment due to health, and impairment in regular activities (including nonwork activities) due to health. The presenteeism question, for example, was worded as follows: "During the past seven days, how much did depression affect your productivity while you were working? Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If depression affected your work only a little, choose a low number. Choose a high number if depression affected your work a great deal." Respondents were asked to select a number between 0 (depression had no effect on my work) and 10 (depression completely prevented me from working). A response of 8 indicates that depression reduced a person's on-the-job productivity by 20%.

The overall work impairment variable is the sum of a person's absence rate (hours missed due to health problems, divided by hours missed plus hours actually worked) and his or her reduced productivity on days when he or she was present for work, multiplied by 100. The validity of the WPAI has been established for a number of different diseases, including mental health.[30,31] A complete description of the WPAI survey questions is available at http://www.reillyassociates.net/WPAI_SHP.html (accessed October 12, 2010).

Other secondary outcomes included 12-week medical service use as reported by patients via the Utilization and Cost (UAC) questionnaire.[32] Patients reported the number of the following types of medical services they received over the prior 3 months: emergency room visits for MDD, other psychiatric problems, and general medical problems; mental health advice received over the phone; and hospital days for MDD, other mental health problems, and general medical problems. In addition, patient HRQOL was assessed using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q).[33] The outcomes assessed are described in greater detail in Dunlop et al.[25]

STATISTICAL METHODS

Analysis of covariance was used to compare differences between the desvenlafaxine and placebo groups in mean changes from baseline to week 12 for all the outcomes of interest: absences, presenteeism, overall work impairment, impairment in regular activity, HRQOL, and medical service use. Last observation carried forward (LOCF) was used for missing values.

PREDICTIVE MODEL

There is no single study that performs a complete analysis of the financial impact of changing antidepressant drug cost sharing on adherence, health care expenditures, absences, and on-the-job productivity from the perspective of an employer. The objective of the second part of this paper is to perform such an analysis for MDD by constructing a financial model that links together results from several different published studies with the results of the clinical trial described above. This is a disease-specific application of a general model proposed by Nicholson et al.[34]

Adherence and costs (MDD prescription drug spending, other medical spending, and costs associated with work impairment) were estimated for a baseline scenario where employees and adult covered dependents who have MDD face average cost sharing for prescription drugs. We then estimated annual costs per affected person in a scenario where employers reduce patients' cost sharing for prescription antidepressant medications.

Sources for each part of the model are indicated in the final column of Table 3. We estimated the number of workers who have MDD and are treated with antidepressant medication using prevalence data from the National Comorbidity Survey, demographic

data on the workforce from the Bureau of Labor Statistics, and 2 studies[7,11] that examine the use of pharmacotherapy among adult MDD patients.

Medical spending data were derived from 6 different studies covering almost 400000 subjects.[35-40†] Because these studies measure costs in different years, we inflated spending to 2008 dollars by applying actual national growth rates in prescription drug and total spending.

Nine separate studies examined how often 8800 workers with depression were absent due to their health condition. Although the questions differed somewhat across the studies, the data were generally self-reported by surveyed employees who have depression, and employees were usually asked to distinguish health-related absences from overall absences. The number of annual self-reported absence days ranged from 2.3 to 28.4 across these 9 studies, with a weighted (by number of observed employees) mean of 5.9 and an unweighted median of 6.2.[3,41,2,42-46]

Seven separate studies examined how depression affects on-the-job productivity of 8300 workers. As with absences, the survey questions differed somewhat across the studies based on the specific instrument used. The reduction in on-the-job productivity associated with depression ranged from 3.0% to 24.5% across these 7 studies, with a weighted (by number of observed employees) mean of 6.5% and an unweighted median of 16.0%.[43,2,47,44-46]

In order to estimate the annual costs associated with depression-related absences, we multiplied the estimated absence days per year (5.9) by the mean daily wage of an employee in the United States, including fringe benefits.[‡] This is based on the assumption that workers are paid according to the average value they provide a firm, and an absence results in 1 day's worth of output not being produced. If labor markets are competitive, the cost of an absence should be at least as large as the employee's wage.[48] We assume that the average on-the-job productivity decrement (6.5%) occurs persistently throughout the year. The estimated presenteeism loss is therefore 6.5% of an employee's compensation for the days he or she is present for work.

Pauly et al[48] argued that if it is difficult for a firm to substitute for an absent worker, the worker operates as part of a team, and/or the worker's output cannot be postponed without some penalty (eg, lost sales or overtime payments), the true cost of an absence will exceed the worker's daily wage. Nicholson et al[49] examined more than 30 different jobs and concluded that the median "multiplier" is 1.28; the actual cost of an absence is 28% greater than the wage of the absent worker.

In order to estimate the effect of reducing prescription drug co-payments, we need to determine baseline adherence rates, the effect of cost sharing on adherence, and the effect of cost sharing or adherence on medical costs and productivity. As indicated in the final column of Table 4, eight studies examined the medication adherence rates for 178000 patients with MDD. The definitions of adherence varied somewhat across the studies, with the most common being the HEDIS (Healthcare Effectiveness Data and Information Set) measure of 84 days supplied during the first 114 days of treatment. Adherence rates ranged across the 8 studies from 28% to 69%, with a patient-weighted mean of 60.0% and an unweighted median of 60.0%.[4,35,36,38,40,50-52]

The estimated impact of cost sharing on adherence is based on 3 studies that examined the relationship between the amount a patient with MDD is required to pay out-of-pocket for a prescription and the quantity of prescriptions he or she uses.[§] Goldman et al[12] reported that doubling the co-payment, which represents an increase of $9.39 in the average co-payment in their sample, is associated with a 26% reduction in spending on antidepressant drugs. That is, they estimated a price elasticity of -0.26; a 1% increase in the price is associated with a 0.26% reduction in the quantity of drugs used. Klepser et al[14] compared the behavior of employees who were shifted from a 3-tier co-pay structure to a co-insurance structure with employees who remained in the 3-tier system. They estimated a price elasticity of -0.37 for the SSRI/SSNRI (selective serotonin reuptake inhibitor/selective serotonin-norepinephrine reuptake inhibitor) drug class. Finally, Landsman et al[13] compared patients who were switched from a 2- to a 3-tier benefit design and estimated a price elasticity for SSRI drugs of -0.27. The average price elasticity across these 3 studies, weighted by the number of patients using antidepressant drugs, is -0.26.[**] The average amount patients paid for a prescription in 2010 was estimated to be $16.2.[53††] Thus, a $16.2 reduction in a patient's price of an antidepressant prescription drug (or 100% of the price) is estimated to increase MDD prescription use by 26%. We assume that the increase in adherence (26%) will be proportional to the increase in the quantity of prescriptions used. In other words, we assume that patients are uniformly distributed from low adherence to perfect adherence rather than, for example, having patients clustered right below the adherence threshold.

We were unable to find any published studies for MDD that examine how a change in a patient's prescription drug cost sharing affects his or her other (ie,

†Four of the studies, which collectively account for 81.2% of the employees and dependents examined, measured the payer's cost only; the other 2 studies measured the sum of the payer's and the patient's cost.

‡The data on average salary are from the Bureau of Labor Statistics, and data on fringe benefits as a percentage of salary are from the Department of Labor.

§We were unable to find studies examining the relationship between cost sharing and whether patients are adherent.

**The average price elasticity of -0.26 is consistent with a recent literature review by Goldman, Joyce, and Zheng,[19] who concluded that most price elasticities range from -0.2 to -0.6 across all health conditions.

††The Kaiser survey reports average patient cost sharing for generic drugs (tier 1), preferred branded drugs (tier 2), and non-preferred branded drugs (tier 3) for managed care patients. We take a weighted average, with weights of 75%, 15%, and 10% on the 3 tiers, respectively.

TABLE 1 Demographic and Baseline Characteristics of ITT and Modified-ITT (Patients With a Baseline HAM-D17 >20 [Moderately/Severely Depressed Patients])

	ITT Population		mITT Population	
Characteristic	Desvenlafaxine (n=285)	Placebo (n=142)	Desvenlafaxine (n=208)	Placebo (n=102)
Age, years Mean (SD)	43.2 (11.7)	41.6 (12.6)	43.3 (12.2)	40.1 (12.1)
Sex Female, n (%)	188 (66)	93 (66)	142 (68)	69 (68)
Race n (%)				
Asian	0 (0)	3 (2)	0 (0)	1 (1)
Black or African American	46 (16)	17 (12)	38 (18)	16 (16)
White	229 (80)	117 (82)	162 (78)	80 (78)
Other	10 (4)	5 (4)	8 (4)	5 (5)
Duration of current episode, months Mean (SD)	13.5 (24.2)	13.9 (24.4)	13.6 (26.0)	13.2 (22.9)
HAM-D17, total score Mean (SD)	22.0 (4.2)	21.8 (4.5)	23.8 (3.2)	23.9 (3.0)
Q-LES-Q, total score Mean (SD)	39.87 (12.76)	41.59 (38.29)	39.82 (10.53)	38.29 (11.83)
WPAI at baseline Mean (SD)				
Percent work time missed due to health	9.44 (15.05)	8.20 (14.59)	9.79 (15.15)	8.54 (14.19)
Percent impairment while working due to health	55.55 (21.44)	55.71 (24.35)	56.02 (20.62)	58.4 (21.64)
Percent overall work impairment due to health	58.61 (22.20)	57.97 (24.62)	59.14 (21.45)	61.00 (21.49)
Percent regular activity impairment due to health	65.23 (18.76)	66.52 (21.15)	66.36 (17.72)	67.72 (19.23)

Abbreviations: HAM-D17, Hamilton Rating Scale for Depression; ITT, intent to treat; Q-LES-Q, Quality of Life Enjoyment and Satisfaction Questionnaire; WPAI, Work Productivity and Activity Impairment.

nonprescription drug) medical spending. There are, however, 3 studies that compared medical spending among MDD patients who are adhering to recommended pharmacotherapy with patients who are nonadherent.[35,36,38] Across these 3 studies, adherent patients received $960 fewer medical services per year, on average (weighted by the number of patients in each study), than nonadherent patients (Table 4).

We assume that employees with MDD who become adherent once cost sharing is eliminated experience the same reduction in work impairment that was observed in the desvenlafaxine treatment arm at week 12. We also assume that this reduction persists throughout the entire year.[‡‡]

RESULTS

SAMPLE CHARACTERISTICS OF THE RANDOMIZED CONTROLLED TRIAL

As reported in Table 1, there were no statistically significant differences at baseline in the primary outcome measures between the placebo and desvenlafaxine groups in either the ITT or mITT populations. Two-thirds of the participants were women. Depression had a strong negative effect on workers' productivity at baseline. Workers were absent about 9% of the time; when they were present, MDD reduced their productivity by about 50%. The final row of Table 1 indicates that depression also affected employees outside of the work environment.

[‡‡]Adult covered dependents who become adherent are not included in this calculation because they are not employed by the employer who reduced cost sharing.

IMPACT OF DESVENLAFAXINE ON PRODUCTIVITY, MEDICAL COSTS, AND HRQOL

Analyzing the same randomized controlled trial, Dunlop et al[25] reported that employees treated with desvenlafaxine experienced an improvement in health between baseline and week 12, as measured by the change in the HAM-D17, relative to the control group. Employees in both arms experienced improved health, with the improvement in the desvenlafaxine group being significantly larger.

Table 2 reports results for worker productivity, medical resource use, and HRQOL. In the ITT population, the adjusted mean absence rate decreased in the placebo and desvenlafaxine groups over the 12-week period by 3.5% and 4.1%, respectively. The 0.55% difference in adjusted mean changes was not statistically significant (P=.69). The difference in adjusted mean changes in impairment while at work between the placebo and desvenlafaxine groups at week 12 was 5.11% (P=.045). The difference in adjusted mean changes in overall work impairment and regular activity impairment was 5.09% (P=.054) and 3.89% (P=.124), respectively. For the mITT population, the difference in adjusted mean changes between placebo (n=102) and desvenlafaxine (n=208) at week 12 was 2.00% (P=.240) for work time missed, 7.40% (P=.015) for impairment while at work, 7.30% (P=.021) for overall work impairment, and 6.47% (P=.030) for regular activity impairment.

TABLE 2 Work Productivity, Medical Service Use, and Quality of Life Endpoints

	ITT				mITT			
	Adjusted Mean Change, Week 12 (SEM)				Adjusted Mean Change, Week 12 (SEM)			
	Desvenlafaxine 50 mg (n=285)	Placebo (n=142)	Difference (95% CI)	*P*	Desvenlafaxine 50 mg (n=208)	Placebo (n=102)	Difference (95% CI)	*P*
Work Productivity and Activity Impairment								
Percent work time missed	-4.08 (0.89)	-3.54 (1.19)	0.55 (-2.11, 3.20)	0.686	-4.73 (1.24)	-2.72 (1.61)	2.00 (-1.35, 5.36)	0.240
Percent impairment	-23.71 (1.68)	-18.60 (2.22)	5.11 (0.13, 10.10)	**0.045**	-25.33 (2.18)	-17.94 (2.81)	7.40 (1.45, 13.34)	**0.015**
Percent overall work impairment	-24.08 (1.74)	-18.99 (2.31)	5.09 (-0.09, 10.26)	0.054	-26.08 (2.28)	-18.78 (2.98)	7.30 (1.12, 13.48)	**0.021**
Percent regular activity impairment	-29.85 (1.68)	-25.96 (2.20)	3.89 (-1.07, 8.86)	0.124	-31.65 (2.15)	-25.18 (2.76)	6.47 (0.63, 12.32)	**0.030**
Utilization and Cost Questionnaire, Over Past 3 Months								
Hospital days	-0.06 (0.01)	-0.04 (0.01)	0.02 (-0.01, 0.05)	0.232	-0.07 (0.01)	-0.04 (0.02)	0.03 (-0.02, 0.08)	0.194
ER visits, general problems	-0.06 (0.02)	-0.07 (0.02)	-0.01 (-0.07, 0.04)	0.659	-0.09 (0.02)	-0.10 (0.03)	-0.01 (-0.08, 0.05)	0.693
Times received mental health advice over phone	0.12 (0.15)	-0.07 (0.23)	-0.19 (-0.72, 0.35)	0.495	0.23 (0.20)	-0.07 (0.31)	-0.30 (-1.04, 0.44)	0.429
Health-Related Quality of Life (Q-LES-Q)								
Percentage of max score	21.73 (1.51)	16.28 (2.06)	-5.45 (-9.80, -1.10)	**0.014**	20.40 (1.41)	14.97 (1.83)	-5.43 (-9.32, -1.54)	**0.006**

Abbreviations: CI, confidence interval; ITT, intent to treat; mITT, modified intent to treat; Q-LES-Q, Quality of Life Enjoyment and Satisfaction Questionnaire; SEM, standard error of the mean. *P* = p-value of the difference between the desvenlafaxine and placebo adjusted mean change. Bold values are significantly different from zero at the 5% level. Standard error or confidence intervals are displayed in parentheses.

The changes in medical service use were not significantly different between the 2 treatment groups in either the ITT or mITT populations. Finally, HRQOL significantly improved for those who received desvenlafaxine relative to placebo in both populations (*P*=.014 and *P*=.006 for the ITT and mITT populations, respectively).

PREDICTIVE MODEL

Baseline Scenario for an Employer

In Table 3, we report baseline data for a hypothetical company with 5000 full-time employees. A company of this size is estimated to have 103 employees and 58 covered adult dependents with MDD who are receiving antidepressant drug therapy for the condition. These adults are estimated to incur average annual MDD prescription drug costs and other medical costs of $1217 and $7688, respectively. With a mean annual compensation of $61700 (including fringe benefits) per employee based on national data, the estimated annual cost of total work loss (absence plus presenteeism) associated with depression is $5353 per affected worker. The productivity related costs are about 40% of the estimated total health-related costs associated with depression ($14257).

If the absence multiplier described above also applies to presenteeism, then the total annual health-related costs associated with depression (prescription drug costs, other medical costs, and productivity-related costs) would be $15800. For an employer with 5000 full-time workers, the total health-related costs for all workers with MDD are estimated to be $2.0 million per year without applying the multiplier, and $2.1 million with the multiplier, as reported at the bottom of Table 3.

Simulating the Effect of Eliminating Antidepressant Drug Co-payments

If the employer reduced antidepressant cost sharing from the current average of $16.2 per prescription to $0, the model predicts that the percent of patients adhering to drug therapy would increase by 15.7 percentage points (from 60.0% to 75.7%), or 26%. As a result, 122 of the 161 employees and adult covered dependents with MDD would be predicted to adhere to their recommended drug treatment under the lower co-payment design, an increase of 25 patients.

As a result of the increased use of antidepressant medication, annual spending on MDD prescription drugs per patient is predicted to increase by 26%, or $320 (Table 4). Medical spending would decrease by $149 per patient (25 newly adherent patients x -$960 per adherent patient/161 MDD patients) for a net increase of $171 per MDD patient ($320-$149) in health care-related costs.

Based on the desvenlafaxine trial discussed above, the financial benefit to the employer of reduced work impairment due to improved adherence is estimated to be 5.1% of an average employee's annual compensation, or $3145 per year (Table 4).[§§] If one incorpo-

[§§]Employees may ultimately be the beneficiaries of reductions in work impairment rather than the employers if other potential employers bid up workers' wages once they become more productive.[48]

TABLE 3 Baseline Model Values for an Employer's Adult Covered Lives With MDD

		Cumulative			
Eligible MDD Population	**Parameter**	**Employees**	**Adult Dependents**	**Total**	**Sources**
Dependent: employee ratio	0.56	5000	2800	7800	Kaiser Family Foundation survey
Prevalence of MDD in employed population	7.3%	363	203	566	National Comorbidity Survey
Percentage of adults with MDD treated with pharmacotherapy	28.5%	103	58	161	2 studies; 2190 patients
Baseline Costs	**Per Person With MDD**	**Employees**	**Adult Dependents**	**Total**	**Sources**
Annual MDD prescription drug costs	$1217	$125 706	$70 395	$196 101	6 studies; 388 000 patients
Annual medical costs (non-Rx)	$7688	$79 4212	$444 759	$1 238 970	6 studies; 388 000 patients
a. Average hourly wage with benefits	$30.9	$6 384 348	N/A	$6 384 348	Department of Labor
b. Annual health-related absence hours (5.9 days x 8 hours per day)	47	4839	0	4839	9 studies; 8800 employees
c. Annual reduced on-the-job productivity hours (6.5% x 244.1 days x 8 hours)	126	13 056	0	13 056	7 studies; 8300 employees
Annual productivity costs without a multiplier: a x (b + c)	$5353	$553 014	$0	$553 014	Calculation
Annual MDD prescription drug, medical, and productivity costs	$14 257	$1 472 932	$515 154	$1 988 086	Calculation
Annual MDD prescription drug, medical, and productivity costs with a multiplier of 1.28	$15 756	$1 627 776	$515 154	$2 142 930	Pauly et al, 2006

Abbreviation: MDD, major depressive disorder

rates a multiplier of 1.28, the work impairment reduction is $4 026 per newly adherent employee.

In the middle column of Table 4, we report the predicted financial impact of eliminating antidepressant cost sharing for an employer with 5 000 workers, by applying the per-person effects across the entire workforce. MDD prescription drug spending is predicted to rise by $51 500, other medical spending is predicted to fall by $24 400, and work impairment costs are predicted to fall by $51 200. The net effect of this policy is a decrease of $24 000 in health-related costs without the multiplier, and a decrease of $38 400 if one incorporates the multiplier. Therefore, there is a business case for reducing cost sharing for MDD drugs when one incorporates the effect of prescription drugs on productivity. Although we did not quantify the value of improved quality of life associated with treatment with desvenlafaxine, this value would be captured by the newly adherent patients.

The model is flexible enough to predict the impact of reduced cost sharing to particular types of employers. For example, a similarly sized employer with an average salary of $100 000 (rather than the national average of $62 000) would experience an estimated financial benefit of $55 700 (vs the $24 000 reported above) due to the greater value of reducing work impairment. Another possibility is that some employees with MDD may not work full-time. If one-half of a company's employees with MDD work part-time (ie, 20 hours per week), the estimated financial benefit from eliminating cost sharing would be $11 200 (vs the $24 000 reported above) due to the diminished importance of reducing work impairment.

DISCUSSION

Data from the randomized trial of gainfully employed adults demonstrates the potential impact of desvenlafaxine on reducing overall work impairment and improving HRQOL. Work impairment fell by 5.1% over a 12-week period among employees in the desvenlafaxine group relative to employees in the placebo group, and the effect was almost significant at conventional levels. The productivity improvements were more pronounced and statistically significant for more severely ill employees. The change in the use of medical services was not significantly different between the 2 treatment groups, whereas HRQOL significantly improved for the desvenlafaxine group. To the best of our knowledge, this is the first randomized controlled trial assessing the impact of an antidepressant drug on work and activity impairment, the use of medical services, and HRQOL among employed patients with MDD.

The predictive model describes a potential opportunity for employers to address productivity challenges associated with suboptimal treatment of MDD among their covered lives. The model demonstrates that by eliminating patient cost sharing for antidepressant medications, employers can generate productivity benefits and reduce nonprescription

TABLE 4 Model Predicting the Effect of Eliminating Patient Cost Sharing for MDD Prescription Drugs

	Baseline	Reduced Co-pay Scenario	Sources
Average patient co-payment per Rx	$16.2	$0.0	Kaiser Family Foundation
Number of patients adhering	97	122	8 adherence studies; 178 000 patients
Number of patients not adhering	64	39	3 price elasticity studies; 26 000 patients

		Cumulative			
	Effect per Person	Employees	Adult Dependents	Total	Sources
Change in MDD prescription drug spending per MDD patient	$320	$33 030	$18 497	$51 528	3 price elasticity studies; 26 000 patients
Change in medical (non-Rx) spending per newly adherent patient	-$960	-$15 628	-$8752	-$24 380	3 studies; 89 000 patients
Change in work impairment per newly adherent employee	-$3145	-$51 190	$0	-$51 190	Desvenlafaxine randomized controlled trial
Total change in direct and indirect costs without a multiplier		-$33 788	$9745	-$24 043	Calculation
Total change in direct and indirect costs with a multiplier of 1.28		-$4 8121	$9745	-$38 376	Calculation

Abbreviation: MDD, major depressive disorder

medical costs by more than the resulting increase in prescription drug spending. The mechanism for these gains is improved adherence; lower co-payments may address one barrier to patients taking their medication as recommended. Specifically, we estimate that a company with 5000 full-time workers would experience a $24 000 net decrease in health-related costs associated with depression if it eliminated employee/patient cost sharing for antidepressant medication. These estimated savings are larger if one accounts for potential spillovers that health problems might have on other team members and potential losses in revenue that might occur. Estimated savings are also larger at companies with wages above the national average due to the greater impact of productivity in these settings, and lower at companies where employees with depression work less than full-time.

There are several potential limitations of this study. First, it is difficult to measure the effect of a health condition on a worker's productivity. Researchers in a recent study administered the 4 most common questionnaires for measuring presenteeism to about 250 workers with rheumatoid arthritis or osteoarthritis.[54] The estimated average number of productive hours lost over the prior 2 weeks due to their health condition ranged across the questionnaires from a low of 1.6 hours to a high of 14.2 hours, and the largest value was generated by the WPAI questionnaire that was used in the desvenlafaxine trial. Although separate validation studies have been performed on these 4 instruments, the research community has yet to identify the most accurate instrument. Second, as with any randomized controlled trial, the productivity impact of desvenlafaxine may differ in practice from the experience in the well-controlled clinical trial setting.

One of the presumed strengths of this paper is also its weakness. The model uses a number of existing studies to predict how changes in drug co-payments affect adherence, medical costs, absences, and presenteeism. By linking different studies together, the model provides employers with a more complete understanding of the financial impact of their actions than currently exists in published literature. However, the model also requires a number of simplifying assumptions. The model assumes that the measured relationships in the literature are symmetric and linear. For example, if the average effect across several published studies is that a 10% increase in cost sharing is associated with a 20% reduction in adherence, the model would posit that a 20% *reduction* in cost sharing would be associated with a 40% *increase* in adherence. The true relationships between co-payments and adherence, medical spending, and productivity may, in fact, be nonlinear.

The model averages values (eg, the change in the quantity of antidepressant prescriptions associated with a $1 change in a patient's drug co-payment) across several different studies, and then links these values together to estimate the financial impact of drug co-payments on productivity and medical costs. Using multiple studies reduces the impact of outlier values and should derive a more accurate estimate of key parameters. However, an implicit assumption is that the patient populations and the examined interventions are similar across studies and are nationally representative.

CONCLUSION

Depression-related absences and reduced on-the-job productivity account for a substantial percentage of the costs associated with depression. One way to reduce productivity-related costs is to increase adherence rates among affected workers, which may be achieved through reducing a patient's cost share of prescription drugs. Based on what we believe is the

first randomized controlled trial demonstrating the impact of an antidepressant drug on overall work impairment among employed patients with MDD applied with estimates from other published references in a predictive model, we estimate that a company with 5 000 full-time workers would experience a $24 000 net decrease in health-related costs associated with depression if it eliminated employee/patient cost sharing for antidepressant medication. This study suggests there appears to be a business case for reducing patient cost sharing for MDD drugs based on the results of the randomized controlled trial and the peer-reviewed literature.•

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