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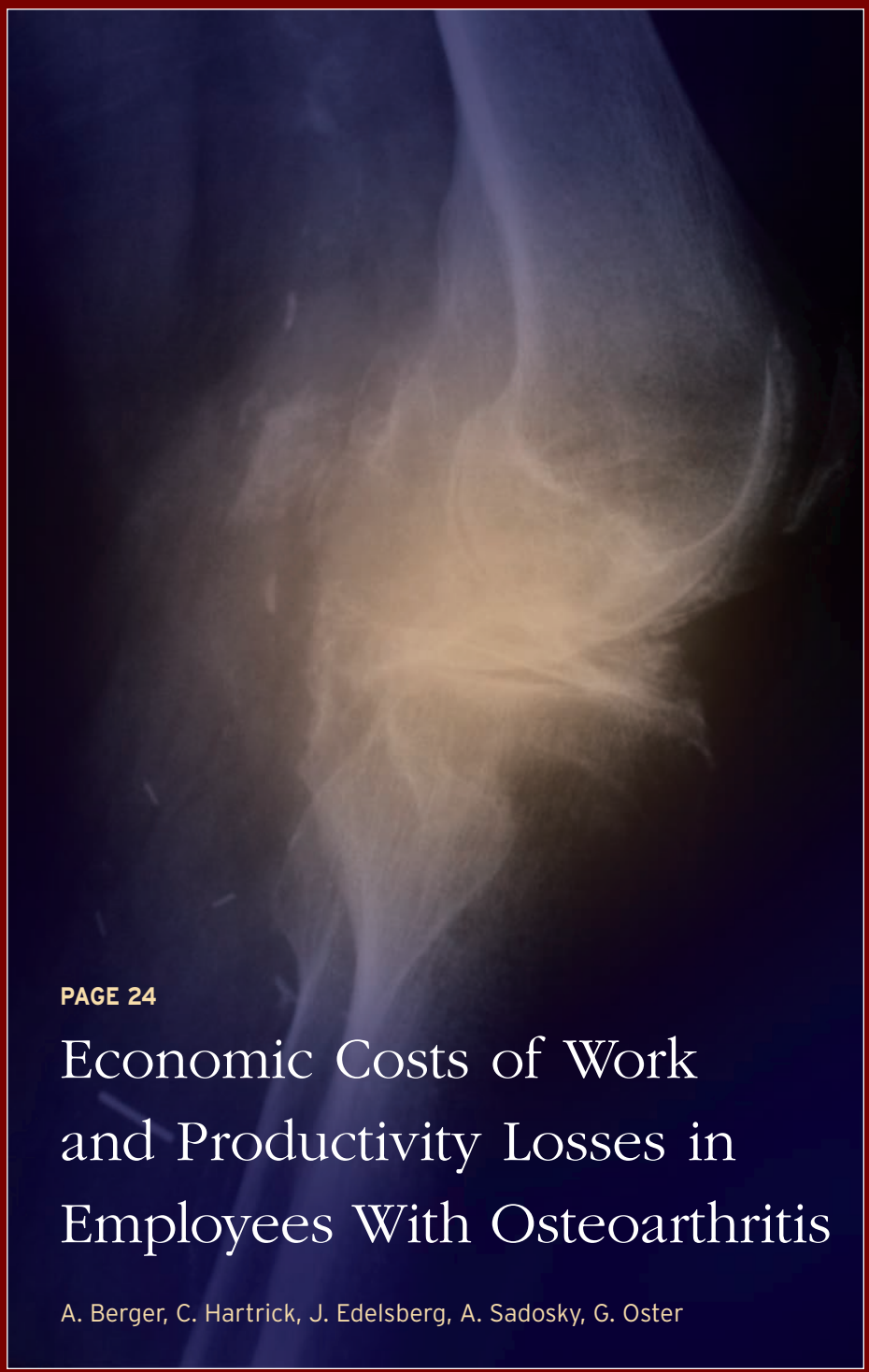

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FROM THE EDITOR

OA Study Shows Productivity Loss, but Questions Remain

Osteoarthritis (OA) is a major driver of health care and productivity costs. Approximately 10% of the US population has a diagnosis of OA, and the prevalence will increase as the population ages.

There are already health and safety concerns regarding current use of opioids in employed populations. In addition, the need for newer, more expensive pharmaceuticals will be a closely examined issue.

In this issue of *JHP,* the article "Economic Costs of Work and Productivity Losses in Employees With Osteoarthritis" (Berger et al) demonstrates a clear loss of productivity in the workplace. It also poses a number of questions that will require further study.

While the article focuses on absenteeism due to OA, presenteeism (the ability to work effectively) is likely an even larger concern. Understanding and quantifying presenteeism will be a more challenging endeavor.

In addition to presenteeism in the workforce, there is the issue of return to function among retirees and disabled individuals with OA. The justification of the cost of treatment must include the impact on productivity in the workforce as well as on the function of those not employed.

The issue of comorbidities and the relationship to OA is clearly shown in the study. However, the role of OA in the incidence of comorbidities or causal impact is an area for further study.

The use of opioids is a major workplace and societal concern. Safety, productivity, and other workplace issues surrounding prescribed opioids and nonprescribed drugs have been recognized but not clearly addressed.

Berger et al show a significant difference in absenteeism between persons using nonsteroidal anti-inflammatory drugs (NSAIDs) and those using opioids. However, there was only a small overall increase in lost productivity with opioids vs NSAIDs. This finding makes it difficult to determine if the severity of pain is the predominant issue in productivity loss or if the use of opioids has a significant impact. The quantification of the level of pain within the population would be helpful in clarifying this question.

The future (and current) use of biologix is another issue to be addressed. It is not clear what, if any, role biologix will have in the treatment of OA in the future. It is clear that their use will have a major impact on health care costs, which must be balanced with productivity or cost differences.

Another consideration is nonpharmaceutical treatments. The need for weight-loss and appropriate exercise programs as well as other wellness approaches must be evaluated. The concomitant use and impact of psychological support with pharmaceuticals also must be considered.

To conclude, the article clearly shows a significant impact of OA on absenteeism in the workplace. A similar or greater impact on presenteeism can be expected. With many questions left to be answered, however, continued study on the relationship of osteoarthritis and productivity is needed.

William B. Bunn, III, MD, JD, MPH
Editor-in-Chief
william.bunn@navistar.com

Safety, productivity, and other workplace issues surrounding prescribed opioids and nonprescribed drugs have been recognized but not clearly addressed.

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Measuring Workplace Depression to Manage It

Alberto Colombi, MD; Zorianna Hyworon, BS; Harris Allen, PhD

ABSTRACT

OBJECTIVES To examine depression symptom severity as (1) a predictor of employee health and productivity loss and (2) an outcome of contextual characteristics.

METHODS For objective No. 1: descriptive and predictive tests of the impact of depression symptom severity on health and productivity loss. For objective No. 2: tests differentiating the prediction of contextual characteristics on mild vs moderate to severe depressive symptoms. These tests were conducted on an international sample comprising 39097 administrations of a comprehensive health risk appraisal containing validated measures of depression and job performance. The analyses included controls for demographic, personal, job, and employer characteristics.

RESULTS Just under 23% of the study respondents recorded depressive symptoms, with just over two-thirds reporting mild (preclinical) depressive symptoms and the balance reporting moderate to severe symptoms indicative of a clinical diagnosis for depression. Depression severity exerted large effects on general health and productivity loss, with the mild group posting an aggregate productivity loss in dollars that was more than 33% greater than the loss associated with the moderate to severe groups combined. Adverse personal life impact more strongly predicted moderate to severe depression, while factors more directly amenable to employer health management efforts, most notably health risks, better predicted mild depression.

CONCLUSIONS By documenting the full range of the burden that depression fosters on employee health and productivity, these findings underscore the need for augmented programs for the detection, diagnosis, and treatment of the condition. By differentiating depression's predictive profile across levels of symptom severity, they further provide pointers for the allocation of available resources, including professional care by clinicians and employer health management programs, for reducing this burden. These results thus strengthen the business case for employer efforts to improve the management of employee depression and illustrate the usefulness of carefully conducted, standardized depression symptom screening for this purpose.

AUTHOR AFFILIATIONS
PPG Industries Inc, Pittsburgh, Pennsylvania (Dr Colombi); InfoTech Inc, Winnipeg, Manitoba, Canada (Ms Hyworon); and Harris Allen Group LLC, Brighton, Massachusetts (Dr Allen).

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KEYWORDS depression; employee health management; productivity loss; symptom screening; workplace

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INTRODUCTION

Findings from recent studies combine to make a strong business case for employer initiatives to manage depression in the workplace. The enormous toll it takes on employees—in terms of both direct costs from utilization of the health care system and indirect costs from lost productivity—has been well established.[1-6] The rates of underdetection of and undertreatment for depression, even for those with severe symptoms, are still substantial.[7] Moreover, the effectiveness of readily available options for treatment, including medications and counseling, has the capacity for savings resulting from such treatment to offset its cost.[8,9]

Yet most employers still remain passive with respect to the need for company-based initiatives that bolster the diagnosis, detection, and treatment of depression.[10-12] To date, various organizational and individual "barriers" have been cited as the primary reasons. Organizational barriers have included the lack of evidence affirming depression initiatives as an investment rather than an additional expense; the fact that the costs in lost productivity stem mostly from sources that are mainly invisible (absenteeism and presenteeism); and confusion over the employer role in depression management. Cited individual barriers have included stigma, inertia, and lack of knowledge about treatment options.[13]

Could it be, however, that an additional factor is at work: a lack of information on the full range of depression's impact when the condition is considered in its broader context? What are the links between depression and employee health and productivity across the continuum of severity of the condition? Does depression need to be at clinically diagnosed

TABLE 1 Study Measures

Variable	N	Range	Mean (SD) or Percentage	Meaning of High Score
I. Depression				
1. Depression symptom severity (PHQ-9)	39 097	0,27	2.96 (4.05)	Severe depressed symptoms
2. Mild	39 097	0,1	15.76%	Yes
3. Moderate to severe	39 097	0,1	4.28%	Yes
II. Disease & Health Risks				
4. Major diseases (count)	39 097	0,4	0.12 (0.35)	Has heart disease, asthma, bronchitis, or kidney disease
5. Metabolic syndrome/pre-diabetes	38 769	0,1	30.94%	Has either/both conditions
6. Health risks (count)	39 097	0,8	1.93 (1.34)	8 risks (eg, smoking, overweight, stress)
III. Stress				
7. Predisposition toward stress	39 097	-2,24	8.93 (4.68)	Predisposed to greater stress
8. Organizational stressors	28 363	0,7	1.19 (1.47)	More stressors
IV. Job Characteristics				
9. Works outside of normal hours	25 415	0,3	0.97 (1.04)	Normally works overtime
10. Works nights	18 149	0,1	18.51%	Yes
11. Job requires high physicality	30 230	0,1	21.22%	Yes
12. Job exposure risk–minimal stimulation	30 229	0,100	65.69 (33.02)	Greater exposure to risk
13. Stress-satisfaction offset	37239	-2,2	-0.74 (1.22)	Much more stressful than satisfactory
V. Employee Characteristics				
14. Age	39 095	18,82	40.66 (10.72)	Older
15. Male	39 097	0,1	40.85%	Male
16. Blue-collar	16 468	0,1	24.38%	Yes
17. Industrial (type; vs service = 0)	21 273	0,1	74.89%	Yes
VI. Regional				
18. Europe	38 656	0,1	20.60%	Yes
19. Canada	38 656	0,1	28.67%	Yes
20. Latin America	38 656	0,1	5.36%	Yes
21. US	38 656	0,1	45.35%	Yes

levels for its impact to register, or are its effects operative even at preclinical levels?

Furthermore, what factors co-occur with depression? Do these factors vary across the levels of severity of the condition? Answers to such questions could lead more employers to strive for greater clarity as to how they are being affected by depression. Such answers could also provide the impetus for participation in efforts to better define and tackle the priorities that need to be addressed for intervention.

We undertook this study to explore the insights that an international database of administrations of a comprehensive health risk assessment (HRA), the Wellness Checkpoint, could bring to this issue. Two objectives shaped our approach, both designed to take full advantage of the broad set of self-reports that this HRA elicits on health in the broader context of work, mental well-being, and the demands of organizational and family life:

1. What can be learned about the prediction of health and productivity loss by depression? How does depression compare with other health and non-health factors? Does its impact vary across levels of depression severity?

2. What can be learned about the prediction of workplace depression itself? Does the predictive profile of depression differ across different levels of depression severity? If so, what are the implications for employer strategies for augmenting efforts to reduce the burden of the condition?

The discussion below highlights the portions of the study that focused on these 2 objectives. For more details on the methods and results for the overall study, see Allen, Hyworon, and Colombi (2010).[14]

METHODS

To address these objectives, we obtained an extract drawn from a database by InfoTech Inc, located in Winnipeg, Manitoba, Canada, and the developer of the Wellness Checkpoint. This extract contained the most recently completed HRAs of 198 785 respondents spanning some 60 countries, with 27% coming from Europe, 43% from Canada, 26% from the United States, and 4% from Latin America.

Of the 60% to 90% (depending on the metric) of

TABLE 1 Study Measures *(cont)*

Variable	N	Range	Mean (SD) or Percentage	Meaning of High Score
VII. Work-Life Imbalance				
22. Reduce stress at work	23185	1,5	3.94 (0.92)	Very important
23. Reduce stress at home	23185	1,5	3.76 (1.05)	Very important
24. Better work-life balance	23184	1,5	3.93 (0.93)	Very important
Scale: Work-life imbalance (items 22-24)	23185	0,100	71.96 (19.58)	Worse balance
VIII. Personal Life Impact				
25. Effect: Work on personal life	23633	1,5	2.70 (1.08)	Strongly negative
26. Effect: Personal life on work	23632	1,5	2.47 (0.92)	Strongly negative
27. Stability of personal life	22765	1,4	1.77 (0.70)	Totally unstable
Scale: Adverse personal life impact (items 25-27)	23262	0,100	36.08 (18.76)	Worse impact
IV. Financial Concerns				
28. Financial concerns: Job-related	19137	1,4	2.11 (0.93)	Major concern
29. Financial concerns: Health-related	19137	1,4	1.76 (0.86)	Major concern
30. Financial concerns: Home-related	19137	1,4	2.14 (0.97)	Major concern
Scale: Financial concerns (items 38-30)	19137	0,100	33.40 (25.19)	Worse concerns
X. General Health				
31. Health status	38588	0,100	37.00 (21.70)	Poor
XI. Presenteeism (WLQ Short Form)				
32. Meeting physical work demands	37842	0,100	11.40 (22.27)	Very limited by health
33. Meeting mental work demands	37719	0,100	7.84 (14.66)	Very limited by health
34. Meeting time work demands	38833	0,100	8.98 (16.64)	Very limited by health
35. Meeting output work demands	38814	0,100	7.93 (15.82)	Very limited by health
Scale: Presenteeism (items 32-35)	39097	0,100	9.10 (13.14)	More limitations
XII. Absenteeism				
36. Average days missed due to health, per year	30217	1,4	1.57 (0.71)	10+ days
37. Full days missed due to health, last 2 weeks	39026	0,8	0.20 (0.83)	More days (count)
38. Part days missed due to health, last 2 weeks	39018	0,8	0.16 (0.67)	More days (count)
39. Short- and/or long-term disability	30214	0,3	0.15 (0.41)	Had >=1 STD & >=1 LTD episodes, last 2 years
Scale: Absenteeism (items 36-39)	39072	0,100	4.53 (8.46)	More time away

Abbreviations: LTD, long-term disability; PHQ-9, Patient Health Questionnaire-9; STD, short-term disability; WLQ, Work Limitations Questionnaire.

the sample for whom non-missing data were available, some 25% had blue-collar positions, while 63% were linked to industrial (as opposed to service) companies.

SAMPLE

To focus the study, our analyses identified only those respondents whose observations included responses to the instrument's measures of depression and job performance. These measures in both cases had been selected based on extensive work assessing construct, criterion, and predictive validity conducted elsewhere. The depression measure was the Patient Health Questionnaire-9 (PHQ-9) depression symptom scale, which assesses the 9 criteria on which the diagnosis of the *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) depressive disorders is based.[15] The measure of job performance was the 8-item short-form version of the Work Limitations Questionnaire (WLQ), which elicits self-reports on the extent to which health limits capacity to meet the physical, mental, time, and output demands of work.[16]

Respondents who did not provide non-missing responses to either item set were dropped. A total of 67016 had non-missing PHQ-9 scores, while 43865 had non-missing WLQ scale scores. A total of 39097 respondents had both sets of scores recorded and thus constituted the sample for this analysis.

MEASURES

A review of the extract identified 39 pertinent measures comprising 12 categories. Table 1 introduces these categories (by roman numerals) and measures (by numbers). Grouping the variables into these categories helps to facilitate the discussion that follows.

Two categories were descriptors of productivity loss: presenteeism as a function of the health of the employee respondents (4 measures) and absenteeism as a function of the health of the employee

respondents (4 measures). A third category included a single measure describing general health (the 5-level excellent-to-poor item). A fourth category consisted of variables that flagged 2 levels of depression symptom severity (mild; moderate to severe) as well as the overall PHQ-9 depression symptom scale. A fifth category was composed of the study's other measures of health, including health risks and 2 measures of disease.

The remaining categories each included a set of contextual characteristics that were plausible predictors of depression, health, and productivity loss: work-life imbalance (3 measures); personal life impact (3 measures); financial concerns (3 measures); stress (2 measures); job characteristics (5 measures); employee characteristics (4 measures); and geographic region (4 measures: Europe, Canada, Latin America, and the US).

Results from factor analyses supported the use of 5 summary scales—presenteeism, absenteeism, work-life imbalance, financial concerns, and adverse personal life impact, each composed from their corresponding sets of items as introduced above—in the results that follow.

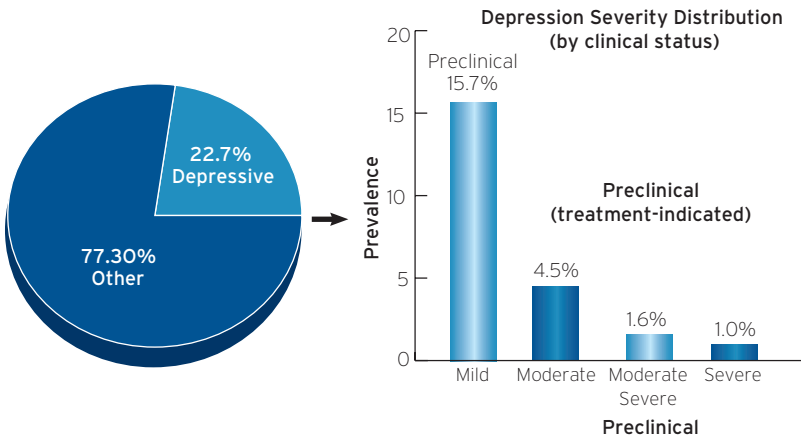
ANALYTIC APPROACH

Our first objective was to differentiate in descriptive terms those respondents who reported depressive symptoms from those who did not. Comparisons based on the study's contextual characteristics were used for this purpose.

Next we focused on depression as an independent variable. For our second step, we used the PHQ-9 classification scheme to examine the impact of depression on health and productivity loss stratified by level of severity. These analyses focused on depression by itself, with no adjustments made for potentially confounding factors, and included preliminary estimates of aggregated dollars lost by severity category. Next, depression was pitted against other health and non-health factors in direct tests of the prediction of health and productivity loss that controlled for potentially confounding factors.

The final step focused on depression as a dependent variable. Here we again took advantage of the capacity of the PHQ-9 scale to stratify depressed respondents by level of severity to compare those who reported mild (ie, preclinical) symptoms vs those who reported moderate to severe symptoms indicative of a clinical diagnosis. These latter tests were framed to contrast the prediction of both groups by each contextual characteristic.

FIGURE 1 Distribution of Depressive Symptoms in Employee Study Sample



RESULTS

SAMPLE CHARACTERISTICS

Just under 23% of this sample reported depressive symptoms in the mild to severe range (Figure 1 and Table 2). Younger, female respondents were more likely to record these symptoms. Also, those with more diseases and more risk behaviors were more likely to report depressive symptoms, as were those who reported less job satisfaction, who worked beyond normal hours, and who worked in minimal-stimulation jobs. Similarly, those who recorded a greater predisposition toward stress and greater exposure to environmental stressors as well as those who reported greater work-life imbalance, negative personal life impact, and more financial concerns all exhibited a greater likelihood of depression.

On the other hand, those in blue-collar positions, who worked in industrial companies, whose jobs required high physicality, and whose jobs entailed working nights were less likely to report depressive symptoms. While Canadian and European respondents were more likely to report depressive symptoms, Latin American and US respondents were less likely to do so.

IMPACT OF DEPRESSION BY ITSELF

Considered by itself, depression exerted impacts on health and productivity that were large and in the expected direction. When the depression group was stratified by the 4 levels of severity delineated by the PHQ-9 measure and compared with those with symptom responses in the normal range, the more severe the symptoms, the greater the deficits observed (Table 3). This held true not only for general health but also for presenteeism and absenteeism.

Of particular interest was the relative aggregate

productivity loss expressed in dollars that was estimated for each severity group (Table 4 and Figure 2). This aggregate loss was computed by multiplying each group's prevalence (per 1000 employee population) by its average per patient symptom impact, and then multiplying the result by an assumed average annual compensation of $50 000 per employee. The mild group's deficits proved the largest by a significant margin on both measures of productivity loss. In fact, it generated an aggregate dollar loss estimate that was more than 33% greater than the total loss estimate for the other 3 severity levels combined.

PREDICTING HEALTH AND PRODUCTIVITY LOSS FROM DEPRESSION IN CONTEXT

When adjustments were made for potential confounds, females, blue-collar workers, service employees, those with more health risks and more diseases, and those with greater financial concerns and adverse personal life impact recorded poorer general health (Table 5). Likewise, those holding minimal-stimulation jobs and with stressful (vs satisfactory) jobs reported poorer general health, as did those in each of the 3 regions relative to the US. On the other hand, those who worked outside normal hours and those with jobs requiring high physicality reported better general health. Yet with all of these significant controls, depression symptoms showed a highly significant linkage to poor general health—in fact, the third largest of the predictors in the analysis.

Turning to productivity loss, those with poor general health, who were male, and who had more work/life imbalance, greater financial concerns, and more adverse personal life impact all reported greater levels of presenteeism (Table 5). Greater predisposition toward stress and more exposure to environmental stressors were also linked to more presenteeism, as did being employed by firms in each of 3 regions measured relative to the US. Similarly, having a stressful job or a job that required more physicality or involved minimal stimulation also led to greater presenteeism. In contrast, having a metabolic/pre-diabetic condition and working nights were linked to less, not more, presenteeism. Yet even with adjustments for all of these influences, depression symptoms exerted a highly significant effect—in fact, posting the largest of all predictors tested.

On the other hand, being younger or female, being in a blue-collar position, having more major diseases,

TABLE 2 Describing Depression in the Study Sample

Characteristic	Normal (n=33066) (77.3%)	Reported Depression Symptoms n=10331 (22.7%)	T (p)
Age	41.1	39.2	14.8 (.00)
Male	42.9%	33.7%	15.6 (.00)
Blue-collar	25.5%	20.7%	6.0 (.00)
Industrial	79.2%	61.0%	26.5 (.00)
Major diseases (count)	0.10	0.17	17.5 (.00)
Metabolic syndrome/pre-diabetes	28.6%	38.9%	18.3 (.00)
Health risks (count)	1.7	2.6	59.2 (.00)
Work-life imbalance	69.9	78.1	28.4 (.00)
Financial concerns	29.2	45.5	40.6 (.00)
Adverse personal life impact	32.3	47.1	56.3 (.00)
Predisposition toward stress	7.8	12.1	82.7 (.00)
Organizational stressors	1.1	1.3	7.9 (.00)
Works outside of normal hours	0.95	1.0	6.2 (.00)
Works nights	19.5%	15.3%	6.0 (.00)
Job requires high physicality	21.8%	19.1%	4.8 (.00)
Job exposure–minimal stimulation	63.7	72.9	20.1 (.00)
Stress-satisfaction offset	-0.96	0.02	69.8 (.00)
Europe	19.9%	23.0%	6.3 (.00)
Canada	26.5%	36.3%	17.9 (.00)
Latin America	6.1%	3.0%	11.3 (.00)
US	47.6%	37.8%	16.3 (.00)

TABLE 3 Health and Productivity Loss Stratified by Depression Symptom Severity

	Level of Depression Symptom Severity							
	Normal (77.3%)	Mild (15.8%)	Moderate (4.3%)	Moderately Severe (1.6%)	Severe (1.0%)	F	df	P
General health	33.37	47.05	55.13	57.41	60.76	1128.1	4,38533	0.00
Presenteeism	6.1	16.0	23.0	29.7	39.3	2866.6	4,39092	0.00
Absenteeism	3.6	6.4	9.0	12.1	15.9	636.0	4,39067	0.00

TABLE 4 Annual Productivity Dollars Lost to Depression per 1000 Employees, by Symptom Severity

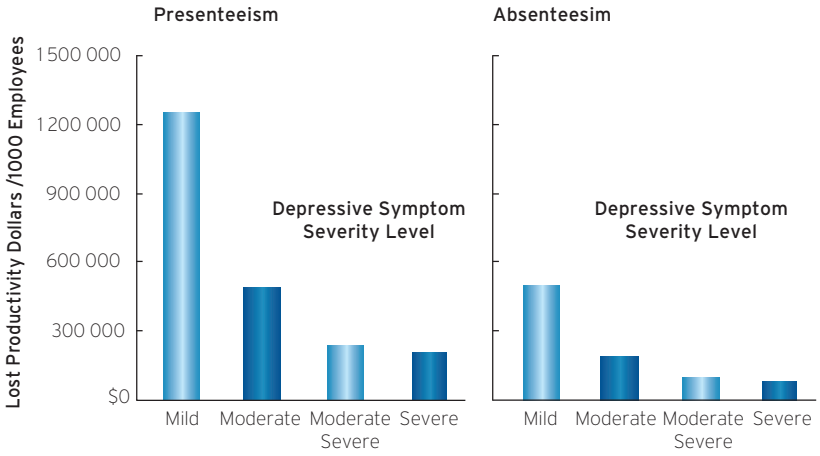
Component	Level of Depression Symptom Severity			
	Mild	Moderate	Moderately Severe	Severe
Prevalence	158	43	16	10
Individual component loss[a]				
Presenteeism (dollars per 1000 employees)	1260 800	492 200	239 085	204 360
Absenteeism (dollars per 1000 employees)	504 320	192 600	97405	82 680
Total productivity loss[a]				
Presenteeism + absenteeism (dollars per 1000 employees)	1 765 120	684 800	339 490	287 040

[a]Assumes an average annual compensation of $50 000 per employee.

having health risks, and being in poorer general health all led to ties to more time away from work (Table 5). More financial concerns and more adverse personal life impact were likewise linked to more absenteeism, as was greater exposure to environmental stressors and working at a European or Canadian firm (relative to a US firm). Conversely, having a greater predisposition toward stress, holding a job requiring greater physicality, and working more "beyond normal" hours were tied to less absenteeism. Depression symptoms, however, posted the greatest influence when all these factors were controlled.

These analyses accounted for 28%, 32%, and 12% of the variance in general health, presenteeism, and absenteeism, respectively—each an exemplary level of explanation achieved, especially in view of the size and varied nature of the sample.

FIGURE 2 Productivity Dollars Lost to Depression, by Symptom Severity



PREDICTING SEVERITY-STRATIFIED DEPRESSION IN CONTEXT

When controls were made for potential confounds, the presence of depressive symptoms was tied to each of the following (Table 6): younger age; female; working in a service job; having more diseases and more health risks; greater work-life imbalance, more financial concerns, and more adverse personal life impact; greater predisposition toward stress and more exposure to organizational stressors; working in jobs with normal hours only or working in jobs that were stressful; and working for firms in any of 3 regions examined (relative to the US).

When stratification was made for severity, more health risks, being female, having a minimal-stimulation job, and holding a position with a European firm all better predicted mild depression than moderate to severe depression. Conversely, adverse personal impact significantly better predicted moderate to severe depression than mild depression. Most striking here was the significant contrast in the relative prediction by adverse personal impact vs health risk count for the 2 severity categories (Figure 3). Again, the level of explanation achieved was exemplary: 12% for mild depression and 18% for moderate to severe depression.

TABLE 5 Health and Productivity Loss as a Function of Depression in Context

Predictor	General Health		Presenteeism		Absenteeism	
	B[a]	Z[b]	B	Z	B	Z
General health	-	-	0.06	9.6@	0.09	14.0@
Depression symptom severity	0.15	2.6@	0.35	40.9@	0.17	16.2@
Age	-0.01	-1.3	0.00	0.5	-0.02	-3.7@
Male	-0.01	-2.1@	0.01	1.1	-0.07	-10.9@
Blue-collar	0.04	4.2@	0.02	1.7	0.06	4.9@
Industrial	-0.04	05.0@	0.01	1.4	-0.01	-0.6
Major diseases (count)	0.07	14.2@	0.02	4.4@	0.07	8.8@
Metabolic syndrome/pre-diabetes	0.12	22.3@	-0.01	-2.2@	0.02	2.5@
Health risks (count)	0.27	47.7@	-0.00	-0.7	0.02	3.0@
Work-life imbalance	0.00	0.3	0.02	3.2@	0.02	1.9
Financial concerns	0.08	9.7@	0.08	9.9@	0.05	5.5@
Adverse personal life impact	0.12	14.6@	0.09	11.2@	0.04	4.4@
Predisposition toward stress	-0.02	-3.5@	0.02	3.2@	-0.07	-10.4@
Organizational stressors	0.02	3.5@	0.02	2.2@	0.02	2.9@
Works outside of normal hours	-0.02	-3.8@	0.02	3.2@	-0.04	-5.6@
Works nights	-0.00	-0.0	-0.03	-3.4@	0.01	1.3
Job requires high physicality	-0.02	-3.4@	0.03	5.3@	0.03	-4.2@
Job exposure–minimal stimulation	0.04	5.9@	0.02	2.9@	0.04	5.6@
Stress-satisfaction offset	0.03	4.7@	0.11	19.9@	0.03	4.3@
Europe (vs US)	0.18	31.0@	0.12	20.5@	0.12	16.7@
Canada (vs US)	0.06	11.0@	0.11	18.8@	0.08	12.5@
Latin America (vs US)	0.08	12.4@	0.07	9.3@	0.01	1.5
R^2	0.28	0.32	0.12			

@ $p < .05$ [a] Standardized beta. [b] Z score.

DISCUSSION

These results augment and sharpen the business case for continuing—indeed expanding—employer efforts to promote better management of depression. They do so both by refining what is understood about the nature of the burden depression generates on

employee health and productivity and by differentiating the predictive profile across levels of severity of the condition.

First, not only did depression exert a huge impact on employee health and productivity across a wide variety of demographic and health characteristics, personal circumstances, job types, and geographic regions, but, in the first comparisons of which we are aware, it also ranked at or near the top in terms of the burden it fosters relative to non-health as well as other health characteristics. These findings replicate our earlier study, conducted on a previous version of the data extract used for this study, which showed depression to be the strongest among a set of health drivers of presenteeism and a significant driver of absenteeism.[17,18]

TABLE 6 Differentiating the Prediction of Mild vs Moderate to Severe Depression in Context

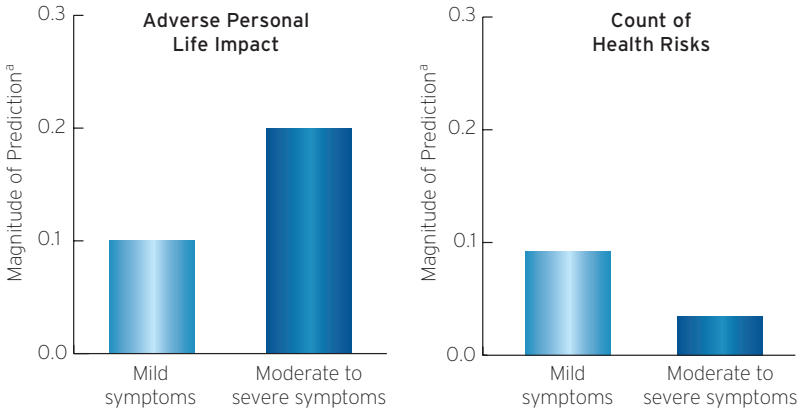
	Mild		Moderate to Severe		Mild vs. Moderate to Severe	
Predictor	B[a]	Z[b]	B	Z	X^2	P
Age	-0.02	-4.2@	0.00	0.6	17.5	0.00@
Male	-0.05	-7.6@	-0.06	-9.3@	0.2	0.65
Blue-collar	-0.00	-0.0	0.00	0.2	0.1	0.70
Industrial	-006	-6.8@	-0.07	-7.8@	1.7	0.20
Major diseases (count)	0.02	2.6@	0.03	4.3@	1.1	0.30
Metabolic syndrome/pre-diabetes	0.02	2.6@	0.03	4.9@	0.2	0.63
Health risks (count)	0.09	13.7@	0.03	5.0@	70.7	0.00@
Work-life imbalance	0.05	6.7@	0.04	5.3@	1.8	0.18
Financial concerns	0.07	8.2@	0.12	12.8@	2.1	0.15
Adverse personal life impact	0.10	10.9@	0.20	20.6@	18.1	0.00@
Predisposition toward stress	0.12	16.9@	0.15	20.3@	0.4	0.51
Organizational stressors	0.02	2.7@	0.03	4.3@	3.3	0.07
Works outside of normal hours	-0.02	-2.3@	-0.10	-1.7	0.4	0.52
Works nights	-001	-1.1	-0.00	-0.4	1.9	0.17
Job requires high physicality	-000	-0.5	-0.00	-0.5	0.1	0.74
Job exposure–minimal stimulation	0.01	1.7	-0.01	-2.1	19.6	0.00@
Stress-satisfaction offset	0.08	11.1@	0.07	10.5@	2.7	0.10
Europe (vs US)	0.07	10.6@	0.06	8.9@	28.3	0.00@
Canada (vs US)	0.02	3.2@	0.03	5.6@	0.0	0.90
Latin America (vs US)	0.02	3.2@	0.06	9.2@	1.2	0.28
R^2	0.12		0.18			

@ $p < .05$ [a] Standardized beta. [b] Z score. Note: The X^2 test for each predictor had 1 degree of freedom and was calculated using forward stepwise regression with controls for all other predictors in the column.

Furthermore, depression's reach extends beyond those whose symptoms are indicative of a clinical diagnosis to include those whose symptoms can be characterized as preclinical—ie, present but not at a level that is likely to elicit a clinical diagnosis of depression. In fact, mild depression exerted an aggregate burden in lost productivity dollars that was more than a third greater than the loss associated with moderate to severe depression combined, because of its greater prevalence and the nontrivial impact it registered on those affected.

Second, the presence of depression was predicted by a variety of contextual characteristics ranging from demographic and personal characteristics to various job attributes. But the evidence here indicated that the mix of these predictors varied across levels of severity. Adverse personal impact—itself an inner-focused measure indicative of potentially deep-seated issues involving home, work, and personal life that may merit clinical intervention—was the more potent predictor of moderate to severe depression. In contrast, health risks—factors more directly amenable to employer health promotion efforts—better predicted mild depression.

FIGURE 3 Differentiating the Prediction of Depressive Symptoms: The Impact of 2 Contextual Characteristics by Severity Level, by Severity of Depressive Symptoms



[a] Prediction entry for each severity level is the standardized beta coefficient calculated from the regression of the severity level on the contextual characteristic with controls for demographic, personal, job, and employer characteristics (range: -1.0 to 1.0).

For employers seeking to improve workforce performance, these findings point to the need to ensure that depression is given top priority. Programs and policies for upgrading the diagnosis, detection, and treatment of depression need to be added to the list of any investments being made in education, training, and other forms of human capital. Benefit

designs are an example. These findings underscore the need for parity in mental and physical health coverage.[19-20] It is in the interest of employers to realize this objective in the coverages provided to their employees.

It is also squarely within the employers' interest to pursue expansion of outreach, education, and treatment efforts targeting depression. To date, employees with a clinical diagnosis have typically comprised the main target of the programs and policies that employers have in place for managing depression. Our findings support the calls that have been made for interventions that build upon improvements in medical care, especially ones that address workplace environment issues and provide job-coaching services.[21] They strongly suggest the need to broaden these efforts to include those who are symptomatic but not diagnosed with the condition. They in fact call for the allocation of available resources that is proportionate across the entire spectrum of depression severity. While more severe episodes need proper referral to professional care, mild depression can be addressed by employer-sponsored efforts such as employee assistance programs and stress-reduction programs that focus on individual coping skills as well as organizational issues.

Screening for depression with HRAs like the one used in this study can serve to streamline this resource allocation. When obtained via processes that properly safeguard privacy and confidentiality, standardized depression symptom assessment can provide a vehicle for optimizing system entry, for facilitating the integrated management of depression, and for improving the quality of care and creating effective interfaces among fragmented components in the delivery system.[22,23]

This study illustrates the considerable potential that standardized symptom assessment offers for managing workplace depression. Future work can build on this potential with methodological improvements that incorporate complementary data from other sources (eg, claims) in the context of evaluation designs that follow respondents over time. Future work is also needed to refine the preliminary estimates of dollar loss reported here. These estimates did a reasonable job of conveying relative magnitude, but more refinement on the various components (eg, individual compensation vs average compensation) is needed before the actual magnitude of these estimates can be treated as an actionable basis for policy and program initiatives.

These limitations notwithstanding, this study underscores the importance of coming to grips with and managing the burden of depression across the full continuum of severity of the condition. Future research that serves to facilitate this objective will substantially advance workforce health and productivity.•

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

Sean Nicholson, PhD; Matthew Sweeney, MS; Jennifer Whiteley, EdD, MSc, MA; James Harnett, PharmD, MS

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.

AUTHOR AFFILIATIONS
Cornell University, Ithaca, New York (Dr Nicholson and Mr Sweeney); and Pfizer Inc, New York, New York (Drs Whiteley and Harnett).

CORRESPONDING AUTHOR Sean Nicholson, PhD, Cornell University, 123 MVR Hall, Ithaca, NY 14853 (sn243@cornell.edu).

KEYWORDS health and productivity; absences; presenteeism; business case

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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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Economic Costs of Work and Productivity Losses in Employees With Osteoarthritis

Ariel Berger, MPH; Craig Hartrick, MD, DABPM, FIPP; John Edelsberg, MD, MPH; Alesia Sadosky, PhD; Gerry Oster, PhD

ABSTRACT

OBJECTIVE To examine the economic costs of work and productivity loss among workers with osteoarthritis (OA).

METHODS Using a large US longitudinal database from a number of self-insured employers containing information on work loss, we identified all employed persons aged ≥18 years with ≥1 health care encounters for OA during calendar year (CY) 2007. Persons not enrolled for all of CY2007 were dropped. We examined total days and costs of work loss due to illness, including total paid claims for short-term disability and workers' compensation, and the total cost of absenteeism, estimated as hours of work loss due to illness (excluding short-term disability and workers' compensation) multiplied by mean hourly earnings of US workers in CY2007. We examined all workers with OA and subgroups thereof defined based on medication use (ie, opioids, nonsteroidal anti-inflammatory drugs [NSAIDs], injectable corticosteroids) and selected comorbidities.

RESULTS We identified a total of 2399 persons with OA. Mean (SD) age was 53 (7) years; 62% were men. Study subjects averaged 39.2 (SD=61.2) days of work loss due to illness (ie, exclusive of recreation/leave). The mean total cost of short-term disability, workers' compensation, and absenteeism combined was $5002 among all OA patients, and ranged from $7133 among those with long-term use of opioids to $4719 among those who received injectable corticosteroids; it ranged from $6247 among those with comorbid diabetes to $4941 among those with cancer.

CONCLUSION Economic costs of work and productivity loss are high among workers with OA, and vary in relation to medication use and comorbidities.

AUTHOR AFFILIATIONS
Policy Analysis Inc (PAI), Brookline, Massachusetts (Ms Berger and Drs Edelsberg and Oster); Oakland University William Beaumont School of Medicine, Rochester, Michigan (Dr Hartrick); and Pfizer Inc, New York, New York (Dr Sadosky).

CORRESPONDING AUTHOR Ariel Berger, MPH, Policy Analysis Inc (PAI), 4 Davis Court, Brookline, MA 02445 (aberger@pai2.com).

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KEYWORDS osteoarthritis; utilization; health care costs; absenteeism; expenditures, indirect

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INTRODUCTION

Approximately 27 million persons in the US aged 25 years or older have osteoarthritis (OA). Prevalence increases with age, ranging from about 2% among persons under 45 years of age to over 80% among those aged 75 years and older.[1,2] Among persons under the age of 45 years, OA is more prevalent among men; among those aged 45 years and older, it is more prevalent among women.[3] OA occurs most often in the knees, hips, feet, ankles, cervical spine, lower back, and fingers/thumbs.

While pharmacotherapy—primarily analgesics and anti-inflammatories—is the mainstay of treatment for OA, synovectomy and/or arthroscopic debridement also may provide some measure of relief in patients with comparatively early disease; exercise, weight loss, activity modification, and physical therapy also are used as treatment for OA. For patients with advanced disease in whom these treatments are no longer effective, arthroplasty (eg, total knee replacement [TKR], total hip replacement [THR]) is indicated. Almost 500 000 THRs and 700 000 TKRs are performed annually in the US,[4] the great majority of which are for OA. TKR and THR typically restore function, provide pain relief, and improve quality of life in patients with advanced OA[5-11]; however, relative to the period immediately prior to TKR/THR, total health care costs tend to increase in the years following arthroplasty.[12,13]

Several recent studies have provided estimates of work loss among persons with OA. Based on data from the Medical Expenditure Panel Survey (MEPS), a nationally representative database that relies on

self-reported OA and work loss, Kotlarz and colleagues estimated that persons with OA averaged 9 days of work loss annually.[14] Using administrative data from self-insured companies, White and colleagues estimated the mean work loss of employees with health care encounters for OA to be 25.7 days annually, while the corresponding estimate of Kleinman and colleagues was 19.8 days annually.[15,16] In the latter study, mean annual indirect costs among persons with OA were estimated to be $2034 (expressed in terms of calendar year [CY] 2008 dollars); in the former study, they were estimated to be $2537 (in CY2005 dollars). In another study based on similar data to those used by White et al, mean annual indirect costs of OA were estimated to be $4603 (in CY2005 dollars).[17] Sadosky et al used self-reported information to estimate mean annual indirect costs of employed persons with mild, moderate, and severe OA; their estimates were $6096, $13 251, and $17 214, respectively (in CY2008 dollars).[18] While these studies suggest that levels of work and productivity loss are generally high among employed persons with OA, relatively little is known concerning the degree to which they vary among subgroups of this population, including those with and without evidence of receipt of specific medications recommended for OA (eg, nonsteroidal anti-inflammatory drugs [NSAIDs], opioids), and those with and without specific comorbidities (eg, back pain). To address this and related issues, we utilized a large US electronic database containing information on medical care costs as well as absenteeism, short-term disability, and disability payments.

METHODS

DATA SOURCE

Data for this study were obtained from the Medstat MarketScan Health and Productivity Management (HPM) Database, which is a subset of the MarketScan Commercial Database. The HPM Database comprises information from enrollment files and medical and outpatient pharmacy claims from a variety of private insurers that provide health care coverage to their employees. All person-identifying information in the database has been fully encrypted, and the database is fully compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

The database contains health care claims for all employees and their dependents. Information available for each facility and professional-service (ie, medical) claim includes date and place of service, diagnosis (in International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] format), procedures (in ICD-9-CM [selected plans only], Current Procedure Terminology, 4th Edition [CPT-4], and Healthcare Common Procedural Coding System [HCPCS] formats), provider specialty, and charged and paid amounts. Information available for each retail pharmacy claim includes the drug dispensed (in National Drug Code [NDC] format), the dispensing date, charged and paid amounts, and the quantity dispensed and number of days of therapy supplied. For all employees, the database also includes information on short-term disability (eg, case days, total payments), as well as dates and times of work absences and reasons (eg, vacation, disability, sickness).

Demographic and eligibility data also are available for all persons, including age, gender, geographic region, coverage type, and the start (and end, if appropriate) dates of eligibility for plan benefits. All data can be arrayed longitudinally to provide a detailed profile of all medical and pharmacy services used by each person over time.

Data for this study spanned the period January 1, 2007, to December 31, 2007 (CY2007), which represented the most recent period for which complete information was available ("study period") at the time of project initiation.

STUDY SAMPLE

We identified all employed persons (aged ≥18 years) in the HPM Database who, during CY2007, had evidence of OA, which we defined as 2 or more outpatient encounters on different days, or 1 or more inpatient stays, with mention of OA (ICD-9-CM diagnosis code 715.XX) ("OA patients"). All pharmacy, professional-service, and facility claims, as well as all information on disability and work loss, were then compiled over CY2007 for all identified employed persons with OA.

We excluded those who (1) were not continuously enrolled in the database for all of CY2007; (2) were aged ≤18 years; (3) were not listed as the primary beneficiary; (4) were Medicaid beneficiaries; (5) were aged ≥65 years and enrolled in a Medicare supplemental or fee-for-service plan; (6) did not have both medical and drug coverage; and (7) were deemed ineligible for short-term disability, workers' compensation, or work absences.

All information on disability and work loss was then compiled for all remaining persons for all of the study period.

MEASURES AND ANALYSES

We examined the demographic and clinical characteristics of employed persons with OA, including

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TABLE 1 Sample Selection

Inclusion/Exclusion Criteria	
Number of patients with:	
>2 outpatient claims on different days with diagnoses of OA during CY2007 or	16986
1 inpatient claim with diagnosis of OA during CY2007	18534
Total of above who:	
Are primary beneficiaries and	14675
Have medical and drug coverage during CY2007 and	14675
Are not Medicaid enrollees and	14675
Are aged 18-64 years or	14675
Are aged >65 and not enrolled in Medicare supplemental/fee-for-service plans and	14675
Are employed by a company that contributes data on absenteeism and	3692
Are employed by a company that contributes data on short-term disability and	2725
Are employed by a company that contributes data on workers' compensation and	2589
Were enrolled in the database for all of CY2007	2399

Abbreviations: CY, calendar year; OA, osteoarthritis.

their age, sex, plan type, geographic region, and prevalence of selected comorbidities; study subjects were assumed to have a particular comorbidity if they had either 1 or more hospitalizations, or 2 or more outpatient claims at least 30 days apart, during CY2007 with a corresponding diagnosis code/prescription. All measures were characterized on the basis of information during CY2007.

Productivity loss was measured using all information in the database on time absent from work. Reason(s) for absenteeism (eg, sickness, recreation) was ascertained based on information in the database. (The term *absenteeism* has been defined differently in several previous studies—namely, as total days of work loss, combining sick leave, short-term disability, and workers' compensation.) Indirect costs were examined in terms of payments for workers' compensation claims and short-term disability, as noted in the database, as well as the estimated cost of absenteeism, which was calculated by multiplying the number of hours absent from work by the mean hourly wage of US full-time civilian employees in CY2007, which was $21.08.[19]

All analyses were undertaken for all employed persons with OA, as well as subgroups therein based on gender, selected comorbidities (ie, other chronic pain-related conditions [ie, migraine, back pain, cervical pain, arthritis other than OA, fibromyalgia, painful neuropathic disorders, gout], neoplasms, depression, diabetes), and type of medication received (ie, opioids, nonsteroidal anti-inflammatory drugs [NSAIDs], injectable corticosteroids). Among the latter, we also stratified according to levels of use of each medication, as follows: "long-term" (receipt of ≥90 days of therapy in CY2007); "short-term" (receipt of between 1 and 90 days of therapy in CY2007); and "none" (no evidence of use of such therapy in CY2007). Simple descriptive statistics (eg, frequency counts, percentages, means, medians, SD, interquartile range [IQR]) were used to describe each measure. Significance testing was not undertaken as there were no *a priori* hypotheses per se (ie, all analyses are descriptive in nature). All analyses were conducted using PC-SAS v.9.1.3.

RESULTS

A total of 2399 persons met all sample selection criteria (Table 1). Mean (SD) age was 53 (7) years; 62% were men (Table 2). A total of 1185 employed persons with OA (50.7%) had other chronic painful conditions; 1266 (52.8%) had "other body/joint pain," 968 (40.4%) had arthritis (other than OA), and 542 (22.6%) had hypertension. A total of 1945 (81.1%) study subjects received NSAIDs during CY2007; use was ≥90 days (ie, long term) for 845 (43.4%) of these patients. Among the 1688 (70.4%) employed persons with OA who received opioids during CY2007, 358 (21.2%) had evidence of use ≥90 days. A total of 1026 (42.8%) study subjects received ≥1 corticosteroid injections during CY2007.

Exclusive of absences attributable to recreation/leave, employed persons with OA averaged 39.6 (SD=61.2) days of work loss in CY2007; corresponding median (IQR) values were 10 (2, 56) days. Mean (SD) days of absenteeism were 40.0 (60.3) among men and 39.0 (62.7) among women. Study subjects who received opioids had more days of work loss than those who had not received these agents (55.9 [74.7] days among long-term users, 48.4 [63.8]

TABLE 2 Demographic and Clinical Characteristics of OA Patients[a]

Characteristic	OA Patients (n=2399)	
Age, Years		
18-24	0	(0.0)
25-34	40	(1.7)
35-44	239	(10.0)
45-54	"1,025"	(42.7)
55-65	"1,088"	(45.4)
≥65	7	(0.3)
Mean (SD)	53.0	(7.0)
Median (IQR)	54	"(49, 58)"
Minimum	25	
Maximum	65	
Gender		
Male	"1,492"	(62.2)
Female	907	(37.8)
Comorbidity		
Neoplasms	226	(9.4)
Hyperlipidemia	384	(16.0)
Diabetes	274	(11.4)
Obesity	52	(2.2)
Depressive disorders	109	(4.5)
Anxiety disorders	52	(2.2)
Migraine	60	(2.5)
Hypertension	542	(22.6)
Ischemic heart disease	64	(2.7)
Valve disease	23	(1.0)
Cardiac dysrhythmias	56	(2.3)
Congestive heart failure	6	(0.3)
Cerebrovascular disease	19	(0.8)

Characteristic	OA Patients (n=2399)	
Comorbidity		
Back pain	162	(6.8)
Cervical pain	112	(4.7)
Arthritis (other than OA)	968	(40.4)
Fibromyalgia	34	(1.4)
Painful neuropathic disorders	207	(8.6)
Gout	18	(0.8)
Other body/joint pain	"1,266"	(52.8)
Other diseases of musculoskeletal system and connective tissue	449	(18.7)
Fatigue	66	(2.8)
Headache	31	(1.3)
Chest pain	79	(3.3)
Abdominal pain	73	(3.0)
Sprains & strains	144	(6.0)
Dislocations & fractures	176	(7.3)
Sleep disorders	109	(4.5)
Payer Type		
PPO	832	(34.7)
POS	"1,219"	(50.8)
Other/unknown	72	(3.0)
Census Region		
Northeast	351	(14.6)
South	423	(17.6)
Midwest	642	(26.8)
West	981	(40.9)
Missing/unknown	2	(0.1)

Abbreviations: CY, calendar year; HMO, health maintenance organization; IQR, interquartile range; OA, osteoarthritis; PPO, point of service.
[a] Unless otherwise specified, all values are number of patients (%).

days among short-term users, and 13.6 [35.4] days among those without evidence of use of opioids). A similar phenomenon was noted among those receiving NSAIDs (47.3 [68.4] days among long-term users, 42.0 [60.4] days among short-term users, and 16.8 [40.1] days among those without evidence of use of NSAIDs) (Table 3). For both opioids and NSAIDs, days of work loss increased with levels of use of these therapies. In contrast, study subjects with evidence of receipt of injectable corticosteroids averaged about 34.5 (57.9) days of work loss, while those who did not receive these injections had 42.7 (63.3) days of work loss.

Exclusive of absences attributable to recreation/leave, work loss was high among those with evidence of comorbid depression (50.1 [74.8] days), other chronic painful conditions (42.9 [65.8] days), cancer (44.5 [63.2] days), and diabetes (52.7 [72.2] days); corresponding values for employed persons with OA who did not have these comorbid conditions were 38.7 (60.4) days, 35.6 (56.1) days, 38.6 (61.0) days, and 37.4 (59.4) days, respectively (Table 4). Levels of absenteeism attributable to leave/vacation were comparable across all subgroups defined by either medication use or comorbidities.

Mean total indirect costs among study subjects were $5002 ($8268); the median (IQR) was $2003 ($675, $5985). Men had nominally higher indirect costs than women ($5241 [$8725] vs $4608 [$7443]).

Indirect costs by medication subgroup are set forth in Figure 1. Mean total indirect costs were $7133 ($10429) among subjects with long-term use of opioids, $5940 ($8540) among those with short-term use of opioids, and $2174 ($5265) among those without evidence of use of these agents; corresponding values for NSAIDs were $6007 ($9304), $5231 ($7982), and $2574 ($6172), respectively. Study subjects who received injectable

TABLE 3 Estimated Productivity Loss Among OA Patients, by Use of Selected Medications During CY2007

	NSAIDs			Opioids			Injectable Corticosteroids	
	Long-Term Use (n=845)	Short-Term Use (n=1100)	No Use (n=454)	Long-Term Use (n=358)	Short-Term Use (n=1330)	No Use (n=711)	Any Use (n=1026)	No Use (n=1373)
Absenteeism								
Sickness-related								
Mean (SD)	5.9 (9.1)	6.2 (8.7)	3.9 (5.1)	5.5 (6.7)	6.5 (8.8)	4.2 (8.0)	5.2 (6.5)	6.0 (9.5)
Median (IQR)	5 (0, 8)	5 (0, 10)	2 (0, 6)	5 (0, 8)	5 (0, 10)	2 (0, 7)	4 (0, 8)	5 (0, 9)
Disability-related								
Mean (SD)	2.0 (13.5)	1.5 (10.1)	0.7 (10.2)	1.6 (11.4)	2.1 (12.8)	0.5 (8.3)	1.3 (9.9)	1.7 (12.5)
Median (IQR)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Leave								
Mean (SD)	1.7 (5.3)	1.9 (5.4)	2.1 (5.9)	2.1 (7.0)	1.8 (5.1)	1.8 (5.4)	2.0 (5.6)	1.7 (5.4)
Median (IQR)	0 (0, 1)	0 (0, 2)	0 (0, 2)	0 (0, 1)	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 1)
Recreational-related								
Mean (SD)	22.0 (12.6)	22.0 (12.7)	21.1 (12.8)	20.3 (13.2)	22.3 (12.5)	21.8 (12.7)	21.7 (12.6)	21.9 (12.7)
Median (IQR)	25 (13, 31)	25 (13, 31)	24 (10, 31)	24 (10, 31)	25 (15, 31)	25 (12, 31)	25 (12, 31)	25 (13, 31)
Other/unknown[a]								
Mean (SD)	12.0 (30.4)	10.1 (28.8)	4.4 (19.1)	16.2 (38.8)	11.6 (29.3)	2.9 (14.1)	8.8 (28.6)	10.3 (27.4)
Median (IQR)	0 (0, 8)	0 (0, 6)	0 (0, 1)	0 (0, 14)	0 (0, 9)	0 (0, 1)	0 (0, 3)	0 (0, 6)
All of above								
Mean (SD)	43.5 (36.4)	41.8 (34.2)	32.2 (25.9)	45.8 (41.8)	44.2 (35.3)	31.2 (23.0)	39.2 (33.3)	41.7 (34.3)
Median (IQR)	37 (25, 53)	38 (25, 50)	32 (21, 41)	38 (22, 60)	39 (27, 54)	32 (21, 41)	36 (23, 47)	37 (24, 50)
Short-term disability								
Mean (SD)	23.2 (39.5)	22.1 (40.0)	5.5 (18.6)	26.5 (40.7)	25.5 (41.3)	4.2 (18.7)	17.0 (36.0)	21.1 (38.2)
Median (IQR)	0 (0, 38)	0 (0, 32)	0 (0, 0)	0 (0, 44)	0 (0, 40)	0 (0, 0)	0 (0, 16)	0 (0, 32)
Workers' compensation								
Mean (SD)	5.1 (34.9)	2.6 (25.9)	2.3 (21.1)	6.5 (36.7)	3.5 (30.7)	1.8 (18.1)	2.4 (23.8)	4.2 (31.8)
Median (IQR)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Total number of days absent from work[b]								
Inclusive of leave/recreational-related								
Mean (SD)	70.9 (69.4)	66.1 (62.3)	40.0 (42.5)	78.4 (75.7)	72.4 (65.3)	37.1 (38.5)	58.3 (59.5)	66.3 (64.9)
Median (IQR)	44 (29, 103)	45 (30, 88)	33 (22, 44)	47 (29, 114)	50 (32, 99)	33 (21, 42)	39 (27, 70)	43 (29, 91)
Exclusive of leave/recreational-related								
Mean (SD)	47.3 (68.4)	42.2 (60.4)	16.8 (40.1)	55.9 (74.7)	48.4 (63.8)	13.6 (35.4)	34.5 (57.9)	42.7 (63.3)
Median (IQR)	12 (3, 72)	14 (3, 62)	4 (0, 11)	16 (4, 93)	18 (5, 71)	4 (0, 10)	9 (1, 43)	12 (2, 63)

Abbreviations: CY, calendar year; IQR, interquartile range; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis.
[a] Includes claims without listed cause (ie, sickness, disability, leave, recreation).
[b] Represents sum of absenteeism, short-term disability, and workers' compensation.

corticosteroids during CY2007 averaged $494 less in indirect costs than those who did not receive these injections ($4719 [$8165] vs $5213 [$8340]).

Indirect costs by comorbidity subgroup are displayed in Figure 2. Employed persons with OA and other chronic painful conditions averaged $5488 ($9194) in indirect costs; those with comorbid depression, $5648 ($8127); those with comorbid cancer, $4941 ($7093); and those with comorbid diabetes, $6247 ($9168).

DISCUSSION

Employees with OA miss a substantial number of days of work each year and have associated high indirect costs. In our study, days of work loss and total indirect costs increased with increasing use of opioids and NSAIDs; they also were nominally greater in those with each of the 4 selected comorbidities (depression, other chronic pain-related conditions, cancer, diabetes) compared with those without these conditions. We note that these high

TABLE 4 Estimated Productivity Loss Among OA Patients, by Selected Comorbidity

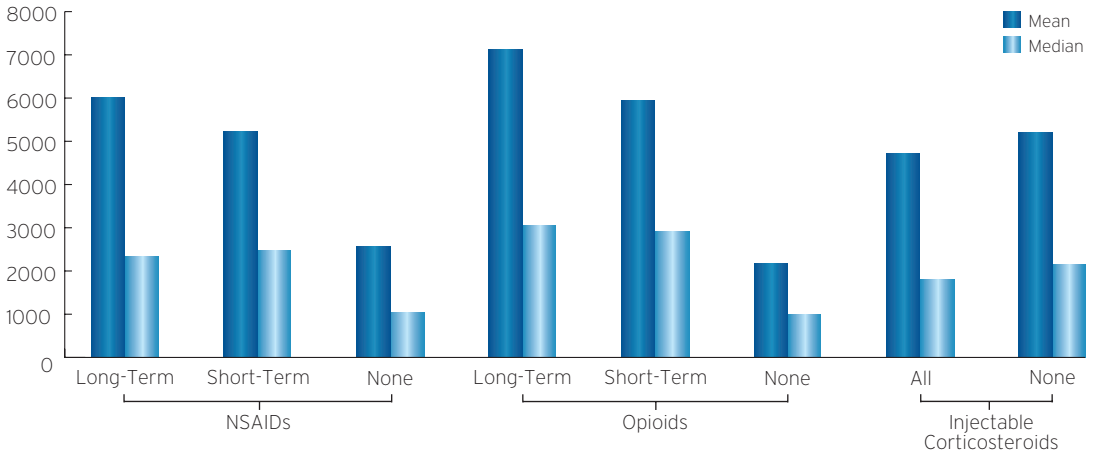
	Depression		Other Chronic Pain-Related Condition[a]		Cancer		Diabetes	
	Yes (n=109)	No (n=2290)	Yes (n=1185)	No (n=1214)	Yes (n=226)	No (n=2173)	Yes (n=274)	No (n=2125)
Absenteeism								
Sickness-related								
Mean (SD)	5.4 (5.8)	5.7 (8.4)	5.8 (8.7)	5.6 (7.9)	6.0 (8.1)	5.7 (8.4)	6.6 (12.6)	5.6 (7.6)
Median (IQR)	5 (0, 10)	5 (0, 9)	5 (0, 9)	4 (0, 8)	5 (0, 9)	5 (0, 8)	5 (0, 9)	4 (0, 9)
Disability-related								
Mean (SD)	1.6 (8.8)	1.5 (11.6)	1.2 (9.0)	1.9 (13.4)	1.2 (10.1)	1.6 (11.6)	3.4 (21.6)	1.3 (9.4)
Median (IQR)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Leave								
Mean (SD)	1.9 (4.9)	1.9 (5.5)	1.8 (5.3)	2.0 (5.6)	2.2 (7.7)	1.8 (5.2)	1.1 (3.3)	2.0 (5.7)
Median (IQR)	0 (0, 2)	0 (0, 1)	0 (0, 1)	0 (0, 2)	0 (0, 1)	0 (0, 2)	0 (0, 0)	0 (0, 2)
Recreational-related								
Mean (SD)	19.8 (13.8)	21.9 (12.6)	21.5 (12.8)	22.1 (12.6)	19.8 (13.3)	22.0 (12.6)	21.0 (12.9)	21.9 (12.7)
Median (IQR)	24 (6, 29)	25 (13, 31)	24 (12, 31)	25 (14, 31)	25 (7, 30)	25 (14, 31)	24 (11, 31)	25 (13, 31)
Other/unknown[b]								
Mean (SD)	8.3 (16.3)	9.7 (28.4)	10.4 (30.2)	8.9 (25.5)	11.3 (30.2)	9.5 (27.7)	14.3 (37.4)	9.1 (26.4)
Median (IQR)	0 (0, 8)	0 (0, 5)	0 (0, 5)	0 (0, 5)	0 (0, 8)	0 (0, 5)	0 (0, 8)	0 (0, 5)
All of above								
Mean (SD)	37.1 (27.0)	40.8 (34.2)	40.7 (34.7)	40.4 (33.0)	40.5 (38.2)	40.6 (33.4)	46.4 (46.2)	39.8 (31.9)
Median (IQR)	36 (23, 49)	37 (24, 48)	36 (24, 48)	37 (24, 48)	36 (16, 49)	37 (25, 48)	36 (22, 53)	37 (24, 48)
Short-term disability								
Mean (SD)	26.4 (50.4)	19.0 (36.6)	21.5 (40.2)	17.2 (34.2)	25.7 (47.2)	18.7 (36.1)	26.1 (42.9)	18.5 (36.5)
Median (IQR)	0 (0, 33)	0 (0, 28)	0 (0, 30)	0 (0, 25)	0 (0, 41)	0 (0, 27)	0 (0, 42)	0 (0, 25)
Workers' compensation								
Mean (SD)	12.1 (61.8)	3.0 (26.0)	4.8 (34.5)	2.1 (21.4)	0.4 (4.8)	3.7 (30.1)	2.3 (21.8)	3.6 (29.4)
Median (IQR)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Total number of days absent from work[c]								
Inclusive of leave/recreational-related								
Mean (SD)	71.9 (77.3)	62.4 (62.0)	66.1 (67.1)	59.7 (58.0)	66.5 (66.2)	62.5 (62.4)	74.8 (73.1)	61.3 (61.2)
Median (IQR)	46 (30, 92)	41 (28, 81)	43 (29, 87)	41 (28, 78)	43 (24, 93)	41 (28, 80)	44 (30, 112)	41 (28, 79)
Exclusive of leave/recreational-related								
Mean (SD)	50.1 (74.8)	38.7 (60.4)	42.9 (65.8)	35.6 (56.1)	44.5 (63.2)	38.6 (61.0)	52.7 (72.2)	37.4 (59.4)
Median (IQR)	17 (4, 72)	10 (2, 56)	12 (2, 61)	10 (1, 52)	12 (1, 67)	10 (2, 55)	14 (4, 81)	10 (1, 52)

Abbreviations: CY, calendar year; IQR, interquartile range; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis.
[a] Comprises migraine, back pain, cervical pain, arthritis (other than OA), fibromyalgia, painful neuropathic disorders, and gout.
[b] Includes claims without listed cause (ie, sickness, disability, leave, recreation).
[c] Represents sum of absenteeism, short-term disability, and workers' compensation.

indirect costs of OA are only in part attributable to OA itself, as persons with OA are more likely to have several costly comorbidities than are persons of similar age and sex without OA. Using data from MEPS, Kotlarz et al estimated in multivariate analyses that only about one-third of days of absenteeism among persons with self-reported OA are attributable to OA.[14]

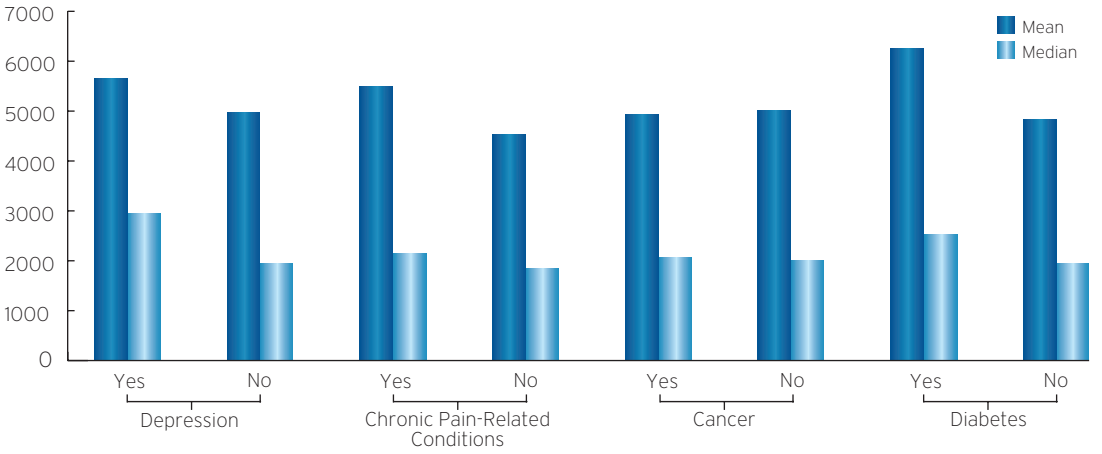
Our estimate of mean work-loss days is higher than those reported in recent studies based on administrative data.[16,17] We believe there are 2 principal reasons for this difference. First, because we required 2 separate outpatient encounters with diagnoses of OA (or a single inpatient stay with this diagnosis), subjects in our study probably had more severe OA than those in the other studies. Both of the other studies required 2 separate diagnoses, but in one study only 1 of the

FIGURE 1 Mean and Median Indirect Costs Among OA Patients, by Medication Received



Abbreviations: OA, osteoarthritis; NSAID, nonsteroidal anti-inflammatory drug.

FIGURE 2 Mean and Median Indirect Costs Among OA Patients, by Comorbidity



Abbreviation: OA, osteoarthritis.

diagnoses had to occur during the study year, and in the other, only 1 had to occur in the 3-year period including the study year. As evidence of greater disease severity, more than 70% of subjects in our study filled prescriptions for opioids; more than 40% received corticosteroid injections. The second reason concerns how we handled a category of absenteeism in the database designated as "other/unknown," which averaged almost 10 days per study subject. Given that estimates of absenteeism due to vacation/leave were comparable across varying levels of use of OA-related pharmacotherapy and the presence/absence of selected comorbidities, we assumed all "other/unknown" days represented leave associated with illness. To the extent that it represented personal leave or vacation days, however, our estimate is inflated.

Our database records instances of days of work loss, but does not account for diminished productivity at work, a phenomenon referred to as *presenteeism*.[17,20,21] Given the chronic and debilitating nature of OA, it is probable that some study subjects were not maximally productive while at work due to their OA or other underlying conditions. Diminished effectiveness on the job may also result from tolerability issues with medications used to treat OA, such as opioid-related side effects. Presenteeism has been estimated to account for a larger share of indirect costs than work-loss days due to illness; in CY2002, it was estimated to comprise 84% of total indirect costs among all active workers with arthritis (ie, an average of 5.2 hours per week in lost productive time).[20] Unfortunately, the degree to which employed persons with OA

in our study sample suffered from "presenteeism" is unknowable given the limitations of the study database; our findings therefore undoubtedly underestimate the magnitude of indirect costs among employed persons with OA.

Several limitations of our study should be noted. First, as in all database studies, there may be errors of omission and commission in coding. Employed persons with OA who did not have this diagnosis entered on an inpatient or ≥2 outpatient claims were not included. In addition, our sample may include persons with ≥2 outpatient visits resulting in a diagnosis of OA that were in fact "rule out" visits for OA. Similar problems with the assignment of comorbidities may have occurred. Second, stratification as to medications received was based on recorded prescription drug dispenses by retail pharmacies. As many OA patients undoubtedly took over-the-counter (OTC) pain-related medications (eg, acetaminophen, ibuprofen) for symptom relief, we may have underestimated levels of NSAID use in study subjects.[22,23] We note, however, that to the degree this occurred, findings from our study likely underestimate differences in absenteeism and indirect costs between long-term users, short-term users, and persons who actually did not use NSAIDs. Third, the database does not contain hourly wage information. Accordingly, we multiplied time absent from work (exclusive of vacation/leave time) by the mean hourly wage of US workers in CY2007 and added to the resulting product information contained in the database on actual payments related to short-term disability and/or workers' compensation. Given the limitations of the database, we cannot determine the degree to which this value corresponds to the actual hourly wage of employees with OA. Finally, the database did not contain direct information concerning the severity of OA. While it seems probable that employed persons with OA with evidence of long-term use of analgesics had more severe disease/were more bothered by their symptoms than those without use of these agents, without more direct information concerning disease severity we could not examine the effect of this parameter on indirect costs.

CONCLUSION

In conclusion, levels of short-term disability, workers' compensation, and absenteeism are high among employees with OA, especially those who receive opioids and/or NSAIDs, or have comorbid depression, other chronic painful conditions, cancer, and/or diabetes.•

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