ORIGINAL ARTICLE

Cost-effectiveness of Systematic Depression Treatment Among People With Diabetes Mellitus

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Context: Depression co-occurring with diabetes mellitus is associated with higher health services costs, suggesting that more effective depression treatment might reduce use of other medical services.

Objective: To evaluate the incremental cost and cost-effectiveness of a systematic depression treatment program among outpatients with diabetes.

Design: Randomized controlled trial comparing systematic depression treatment program with care as usual.

Setting: Primary care clinics of group-model prepaid health plan.

Patients: A 2-stage screening process identified 329 adults with diabetes and current depressive disorder.

Intervention: Specialized nurses delivered a 12-month, stepped-care depression treatment program beginning with either problem-solving treatment psychotherapy or a structured antidepressant pharmacotherapy program. Subsequent treatment (combining psychotherapy and medication, adjustments to medication, and specialty referral) was adjusted according to clinical response.

Main Outcome Measures: Depressive symptoms were assessed by blinded telephone assessments at 3, 6, 12, and 24 months. Health service costs were assessed using health plan accounting records.

Results: Over 24 months, patients assigned to the intervention accumulated a mean of 61 additional days free of depression (95% confidence interval [CI], 11 to 82 days) and had outpatient health services costs that averaged $314 less (95% CI, $1007 less to $379 more) compared with patients continuing in usual care. When an additional day free of depression is valued at $10, the net economic benefit of the intervention is $952 per patient treated (95% CI, $244 to $1660).

Conclusions: For adults with diabetes, systematic depression treatment significantly increases time free of depression and appears to have significant economic benefits from the health plan perspective. Depression screening and systematic depression treatment should become routine components of diabetes care.

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ABUNDANT RESEARCH[1-3] DEMonstrates a strong and consistent association between depression and increased use of health services. Total health care costs for outpatients with current depression are 50% to 100% higher than for those without depressive disorder.[1-3] Increased costs are overwhelmingly due to greater use of general medical services rather than use of depression treatment,[1-3] and these differences persist after attempting to account for comorbid chronic medical illness.[1-3] Improvement in depression is followed by decreases in use of general medical care.[4,5] The consistent association between depression and increased health care costs suggests the possibility that any costs of improved depression treatment could be offset by decreases in other costs of care.

Over the last decade, a series of randomized trials have demonstrated the effectiveness of systematic programs to improve care for depression.[6-12] While these successful programs have varied in intensity and exact content, core elements have been similar: systematic application of evidence-based guidelines, active follow-up to promote treatment adherence, and adjustment of treatment according to clinical outcomes.

Randomized trials in several primary care samples have typically found that systematic depression treatment programs lead to significant improvement in severity of depression and moderate increases in direct health care costs.[10,13-20] Added

costs range from $100 to $1000 over 6 to 12 months, with added cost roughly proportional to the gain in days free of depression. One quarter to one half of cost increases are typically due to increased use of antidepressant medication with the remainder due to increased depression care visits or telephone contacts. Some short-term depression treatment studies[15,19] have suggested decreases in costs of general medical care. Those differences were not statistically significant, however, and increased spending on depression treatment exceeded any savings in general medical care.

We describe herein the incremental cost and incremental cost-effectiveness of a systematic depression treatment program for outpatients with co-occurring diabetes mellitus and depression. Previous research demonstrates that depression co-occurring with diabetes is associated with greater somatic distress,[21] greater functional impairment or disability,[22,23] and increased health services costs.[24-27] Given this pattern of effects, improved depression care might reduce use of general medical services and overall health care costs. Among older adults with diabetes in the IMPACT trial,[28] systematic depression treatment had significant clinical benefit with no increase in overall health care costs. The public health importance of this question is underscored by the increasing prevalence of diabetes[29] and the consistent finding that depression is twice as common among people with diabetes as in the general population.[30]

Questions regarding the cost-effectiveness of depression treatment are broadly relevant to the substantial number of patients with co-occurring depression and chronic medical illness.[31] Older adults with depression typically have 3 or more co-occurring chronic illnesses.[9] In these high-cost patients, the 50% to 100% increase in cost associated with depression has a much greater dollar impact than in the general population.[1,32] Consequently, the potential economic benefit of improved depression treatment may be greatest in patients with multiple chronic conditions and high levels of health service use.

METHODS

The Pathways Study was a randomized trial of a systematic depression treatment program for people with comorbid depression and diabetes. Participants were identified by a population-based depression screening program. Study methods are described in detail elsewhere[33,34] and will be summarized herein.

The study was conducted at 9 primary care clinics of Group Health Cooperative (GHC), a mixed-model prepaid health plan serving 500 000 members in Washington and Idaho. Study procedures were reviewed and approved by institutional review boards at GHC and the University of Washington. The GHC membership is representative of the area population[35] and includes Medicare, Medicaid, and other low-income enrollees.

Computerized records were used to identify all adult GHC members at participating clinics with evidence of diabetes according to visit diagnoses or laboratory data (n=9063). These potential participants were mailed a paper-and-pencil survey including the 9-item Patient Health Questionnaire,[36] a self-report measure of depression symptoms based on the American Psychiatric Association *DSM-IV*[37] criteria for diagnosis of a major depressive episode. Of those mailed questionnaires, 1222 were later found to be ineligible (because of erroneous diagnosis, death, and disenrollment, for example) and 4389 (56% of those eligible) returned completed questionnaires. Respondents with a Patient Health Questionnaire score of 10 or more (n=1038) were contacted for a second telephone screening approximately 2 weeks later, and 851 (82% of those invited) completed that second screen. At the second screening, 348 participants were excluded because of low depression scores and an additional 153 were excluded because of recent psychiatric treatment, indications of a bipolar or psychotic disorder, cognitive impairment, or plans to move or disenroll from the health plan. The remaining 375 participants with a Hopkins Symptom Checklist (SCL)[38] depression score of 1.1 or greater at the second screening (indicating at least moderate depressive symptoms) were invited to an in-person baseline visit during the next 2 weeks. Three hundred twenty-nine (88% of those invited) attended the baseline visit and agreed to enroll in the randomized trial. Potential participants provided either written or documented oral consent at each step in the screening process. All randomized trial participants provided written informed consent prior to enrollment and randomization. Additional details regarding the screening and recruitment process were published previously.[34]

Eligible and consenting participants were randomly assigned to continued usual care or a multicomponent depression management program based in the primary care clinic. All intervention services were provided by 3 registered nurses. Based on previous research in this setting and elsewhere,[9,39] we anticipated that a significant proportion of patients with depression identified by screening would have recently received some depression treatment—typically brief or low-dose antidepressant treatment from a primary care physician. Consequently, the intervention was designed to serve those remaining depressed despite primary care treatment as well as those with previously unrecognized depression. The intervention followed a stepped-care model with the step 1 treatment being either antidepressant pharmacotherapy or structured psychotherapy,[40,41] depending on each patient's preference. For patients already using antidepressant medication at baseline, step 1 might include either medication adjustment or addition of structured psychotherapy. For patients not responding to step 1 treatment (ie, Patient Health Questionnaire score failed to decrease at least 50% by 12 weeks), step 2 included addition of a second treatment modality (eg, adding pharmacotherapy for those beginning with psychotherapy) and/or medication adjustment (eg, dose change, medication switch, or augmentation). For those not responding after an additional 12 weeks, step 3 included in-person consultation with one of the study psychiatrists and/or referral for ongoing specialty mental health care within GHC.

The study protocol called for an initial 60-minute visit with a depression nurse specialist followed by 30-minute in-person or telephone contacts approximately twice per month during acute-phase treatment. Frequency of later contacts depended on clinical response, decreasing to once every 2 months for patients in remission. In many cases, active and persistent telephone outreach was required. Intervention contacts and active monitoring continued for 12 months after randomization.

Antidepressant pharmacotherapy was prescribed by the primary care physician, closely monitored by the depression nurse specialists, and supported by supervision and advice from the study psychiatrists. Treatment followed the protocol developed for the IMPACT late-life depression trial[9] with specific guidance regarding medication selection, dosing, and criteria for dose adjustment or medication change.

The structured psychotherapy, problem-solving treatment followed the model developed by Mynors-Wallis et al[40,41] and adapted by Hegel et al[42] for use in the IMPACT clinical trial.[9] This structured depression-specific psychotherapy focuses on

development of more effective problem-solving skills and includes structured between-session homework assignments. Each nurse received 1 week of initial training and demonstrated proficiency in problem-solving treatment during treatment of 4 practice cases.

During weekly supervision with us (W. J. K., G. E. S., E. J. L., E. H. B. L.), each nurse identified cases for clinical review according to specific criteria (eg, failure to respond to treatment, overdue for treatment contact). Following these meetings, nurses provided specific feedback to treating primary care physicians regarding recommended adjustments in medication management.

Participants in the intervention and usual care groups were contacted by telephone for blinded assessment of clinical outcome (SCL depression scale) at approximately 3, 6, 12, and 24 months after randomization. The proportions of randomized participants completing follow-up assessments were 89% at 6 months, 88% at 12 months, and 85% at 24 months. Intervention and usual care participants did not differ in rates of follow-up participation. Effectiveness was defined as the number of "depression-free days" during follow-up as originally calculated by Lave et al.[43] This method integrates depression symptom scores over time to estimate days during follow-up free of significant depressive symptoms. As in our previous studies,[15,16] depression-free days were calculated using an SCL depression threshold of 0.5 to define depression free and a threshold of 2.0 to define fully symptomatic depression. Thresholds were selected using data from previous research[44] indicating that SCL depression scores of 0.5 and 2.0 were roughly equivalent to the Hamilton depression scores of 7 and 22 used originally by Lave et al.[43] Sensitivity analyses varying the SCL score thresholds for depression free (between 0.3 and 0.7) and fully symptomatic (between 1.7 and 2.3) had no meaningful impact on our estimates of incremental depression-free days (details available on request).

Use and cost of health services provided by GHC were measured using the health plan's computerized cost accounting records. This system uses general ledger costs to calculate actual budget-based cost (not charges) for all services provided or purchased by GHC. Costs for intervention services provided by study staff (including supervision) were calculated using actual salary and fringe benefit rates plus a 30% overhead rate (eg, space, administrative support). Resulting unit costs were $79 for each in-person nurse visit (typically 30 minutes) and $31 for each telephone contact (typically 10-15 minutes). These estimates included time required for outreach efforts and record keeping (eg, approximately 45 minutes of nurse time was allowed for each 10- to 15-minute telephone contact). Intervention costs also included a fixed $57 for each participant assigned to the intervention program for costs of supervision and information system support.

Our hypotheses focused on outpatient costs, defined as outpatient services provided or purchased by GHC as well as all services provided by intervention staff. The sample size was not sufficient to support accurate comparisons of inpatient health services costs, so those are presented as secondary analyses only. Complete cost data were only available for participants remaining enrolled in the GHC health plan.

All analyses were based on original treatment assignment regardless of treatment received. Primary analyses compared effectiveness and cost for the full 24-month follow-up period, but we also present data for the first and second years separately to facilitate comparison with previous studies. Primary analyses computed incremental effectiveness, incremental cost, and incremental cost-effectiveness ratio for participants contributing any follow-up data (ie, completed at least 1 blinded outcome assessment or remained enrolled for at least 3 months). These analyses used repeated observations for depression symptoms and costs based on each interview period, with individuals included in the study until either cost or effectiveness information was missing.[45,46] Individuals who died during follow-up (5% of the sample) had complete cost data but incomplete effectiveness data. Because people died between interviews, this approach excluded costs accrued between the final interview and the date of death. Individuals who disenrolled from the health plan but continued blinded follow-up assessments had incomplete cost data. Individuals who discontinued follow-up assessments but remained enrolled in the health plan contributed incomplete effectiveness data. Secondary analyses included only participants with complete follow-up data (ie, completed the 24-month outcome assessment or remained enrolled for 24 months).

Estimated incremental cost was adjusted for age, sex, outpatient costs during the 6 months prior to baseline, and baseline medical comorbidity (assessed using a modified version of the RxRisk score[47]). For this adjustment, distribution of prior costs was truncated at the 95th percentile to reduce influence of extreme outliers. Estimated gain in depression-free days was adjusted for age, sex, and baseline depression score. Primary analyses used linear regression with confidence intervals (CIs) for incremental cost and incremental cost-effectiveness ratios based on the Fieller Theorem.[48] Given the skewed distribution of cost data, secondary analyses were conducted using gamma regression with a log link. This method allowed us to assess sensitivity of the linear model to skewness in cost outcomes and should have provided less biased estimates of mean differences than would comparison of log-transformed costs.[49]

Value of the intervention program was assessed using incremental cost, incremental benefit, and incremental net benefit.[45,50] The net benefit approach combines both incremental cost and benefit into a single measure. Because the dollar value of clinical benefit (in this case, days free of depression) is not clearly established, net benefit depends on willingness to pay for an additional day free of depression. Net benefit is therefore equal to incremental benefit (incremental days free of depression multiplied by willingness to pay for each additional day) less incremental cost. Because net benefit is a sum rather than a ratio, this approach avoids some of the difficulties that may arise in computing the ratio of incremental cost to incremental effectiveness. For example, 2 identical negative cost-effectiveness ratios can have opposite meaning, implying either that a new intervention is clearly dominant or clearly inferior to standard care. In some cases, the CI for a cost-effectiveness ratio can include both possibilities (ie, CI extends from one negative number to another but actually includes all possible positive values as well).

RESULTS

As presented in **Table 1**, participants assigned to the intervention and usual care groups were generally comparable in demographic characteristics and baseline clinical characteristics. Nearly all participants had type 2 diabetes. Baseline SCL scores indicated a moderate level of depression. Approximately half were already using an antidepressant prescribed by the primary care physician at time of enrollment. Usual care participants had higher costs prior to enrollment and higher RxRisk scores (suggesting greater medical comorbidity), but these differences were not significant at the 5% level.

Of 329 patients enrolled, 278 contributed complete clinical outcome data (completed all blinded outcome assessments), 41 contributed partial clinical data (com-

Table 1. Baseline Characteristics of Participants Assigned to Intervention and Usual Care Groups

	Intervention (n = 165)	Usual Care (n = 164)	Test Statistic
Age, y, mean (SD)	58 (12)	57 (12)	$t_{324} = 0.5$; $P = .63$
Female, No. (%)	57 (35)	56 (34)	$\chi^2_1 = 0.01$; $P = .91$
White, No. (%)	115 (71)	131 (80)	$\chi^2_1 = 4.24$; $P = .04$
>1 y College, No. (%)	50 (31)	36 (22)	$\chi^2_1 = 3.10$; $P = .08$
Type 2 diabetes mellitus, No. (%)	157 (96)	156 (96)	$\chi^2_1 = 0.08$; $P = .77$
Years since diabetes diagnosis, mean (SD)	10.2 (10.1)	9.6 (8.7)	$t_{327} = 0.58$; $P = .56$
SCL[38] depression score, mean (SD)	1.71 (0.51)	1.63 (0.46)	$t_{327} = 1.39$; $P = .17$
Already using antidepressant, No. (%)	86 (53)	99 (61)	$\chi^2_1 = 2.11$; $P = .15$
RxRisk[47] score, mean (SD)	3366 (3020)	3937 (4019)	$t_{327} = 1.90$; $P = .059$
Costs in prior 6 mo, $, mean (SD)	3665 (4583)	5045 (8120)	$t_{327} = 1.46$; $P = .15$

Abbreviation: SCL, Hopkins Symptom Checklist.

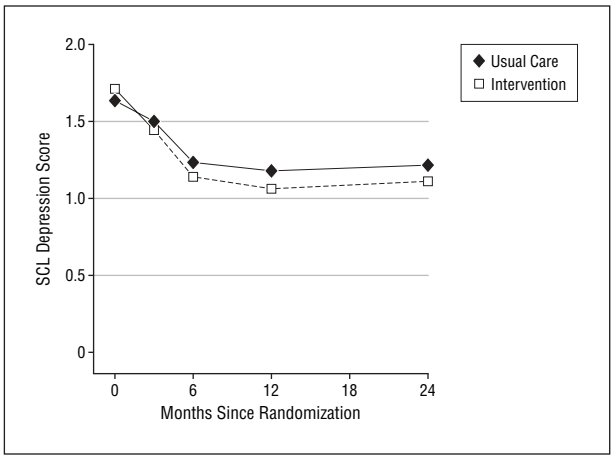

Figure 1. Severity of depression over time for participants assigned to intervention and usual care groups.

Table 2. Depression-Free Days During Follow-up for Participants Assigned to Intervention and Usual Care Groups (Includes Participants Completing Both 12- and 24-Month Follow-up Assessments)*

	Intervention (n = 135)	Usual Care (n = 143)	Difference (95% CI)
Year 1	186 (97)	166 (97)	20 (–2 to 42)
Year 2	226 (118)	193 (117)	33 (5 to 61)
Total	412 (202)	359 (207)	53 (0 to 97)

Abbreviation: CI, confidence interval.
*Values are expressed as mean (SD).

pleted at least 1 blinded outcome assessment), and 10 were missing all clinical outcome data. Compared with participants with complete clinical outcome data, those with any missing clinical outcomes had higher RxRisk scores (4876 vs 3428; $P = .008$), indicating greater severity of chronic medical illness. Otherwise, those with complete and incomplete clinical outcome data did not differ significantly in treatment group assignment or in any of the baseline demographic or clinical variables described in Table 1. Of those enrolled, 288 contributed complete cost data (remained enrolled in the health plan the full 24 months), 35 contributed partial cost data (died or disenrolled between 3 and 24 months), and 6 contributed no cost data (disenrolled prior to the first follow-up assessment). Those with complete and incomplete cost data did not differ significantly in treatment group assignment or in any of the baseline demographic or clinical variables described in Table 1.

The course of SCL depression scores over time is shown in **Figure 1**. As previously reported, mean depression scores were significantly lower in the intervention group at 6 and 12 months after adjustment for baseline values. This significant difference was maintained at 24 months (1.10 vs 1.22; $F_{1,273} = 3.95$; $P = .048$). As presented in **Table 2**, participants assigned to the intervention group accumulated approximately 20 more depression-free days in the first year compared with the usual care group, with an additional increment of 33 days in the second year.

As previously reported, the intervention program had no significant effect on mean hemoglobin A_{1c} levels at 6 or 12 months. After adjustment for baseline values, no significant difference was observed at 24 months (7.87% in intervention group vs 7.82% in usual care; $F_{1,264} = 0.17$; $P = .68$).

As presented in **Table 3**, outpatient depression treatment costs were approximately $700 higher in the intervention group during the first year, with most of this difference due to the direct cost of intervention services. General medical outpatient costs during year 1 were somewhat lower in the intervention group so that total outpatient costs in the 2 groups were approximately equal. During the second year of follow-up, outpatient depression treatment costs were approximately $100 higher in the intervention group, but total outpatient costs were approximately $1400 lower. As shown by standard deviations in Table 3, the distribution of outpatient costs was highly skewed. The usual care group did include a larger number of high-cost outliers. Median outpatient costs during the second year were approximately $600 lower for the intervention group than for the usual care group. Secondary analyses examined total health services costs (inpatient and outpatient services) over 2 years, finding mean (SD) costs of $21 148 ($27 548) for the intervention group and $22 258 ($35 607) for those assigned to usual care.

Overall estimates for incremental effectiveness, incremental costs, and incremental cost-effectiveness ratio in-

Table 3. Health Services Costs for Participants Assigned to Intervention and Usual Care Groups*

	Year 1		Year 2	
	Intervention (n = 156)	Usual Care (n = 154)	Intervention (n = 139)	Usual Care (n = 145)
Total outpatient depression treatment costs	1202 (1102)	448 (667)	542 (825)	446 (733)
Antidepressant prescriptions	259 (364)	173 (308)	281 (454)	221 (454)
Specialty mental health visits	240 (783)	162 (484)	158 (534)	118 (345)
Primary care mental health visits	131 (225)	130 (86)	101 (225)	106 (235)
Intervention services	545 (222)	0	0	0
Screening costs†	27 (0)	27 (0)	0	0
Total outpatient nondepression costs	6361 (6129)	7089 (7035)	6527 (7104)	8027 (8971)
Other prescriptions	1856 (1542)	2390 (3032)	1698 (1614)	2546 (3226)
Other primary care visits	1120 (1080)	1133 (1196)	1139 (1312)	1174 (999)
Emergency department/urgent care	392 (1112)	371 (1105)	436 (1131)	536 (1466)
Other medical visits	1169 (1170)	1775 (3173)	1160 (1633)	1454 (2228)
Diagnostic services	745 (987)	792 (995)	641 (820)	887 (1635)
Other outpatient services	1079 (3483)	628 (2056)	1453 (4159)	1430 (4196)
Total outpatient costs	7563 (6730)	7537 (7550)	7070 (7256)	8474 (9325)

*Values are expressed as mean (SD) in US dollars. Figures for each year include all participants remaining enrolled throughout that year.
†Total screening costs divided by number of eligible patients identified.

Table 4. Incremental Effectiveness, Outpatient Cost, and Cost-effectiveness of Intervention Program Compared With Usual Care*

	Incremental Depression-Free Days	Incremental Outpatient Cost, $	Incremental Cost per Depression-Free Day, $
All available data, unadjusted	48 (23 to 73)	–856 (–1656 to –55)	–17.8 (–39.2 to 3.6)
All available data, adjusted†	61 (11 to 82)	–314 (–1007 to 379)	–5.2 (–17.6 to 7.2)

*Values are expressed as mean (95% confidence interval).
†Depression-free days are adjusted for age, sex, and baseline depression severity. Costs are adjusted for age, sex, costs prior to randomization, and RxRisk[47] score.

cluded participants with any available follow-up data (ie, completed at least 1 blinded follow-up assessment or remained enrolled in the health plan for at least 3 months). As presented in **Table 4**, adjustment for baseline differences increased the benefit in depression-free days from 48 to 61 days, with the CI clearly excluding zero. Adjustment decreased the estimate of cost savings from approximately $850 to approximately $300, with the CI clearly including the possibility of a moderate cost increase. Point estimates for the cost-effectiveness ratio were in the dominant range (intervention had lower cost and greater effectiveness) but CIs clearly included the possibility that the intervention increased outpatient costs. Sensitivity analyses including only participants with complete follow-up data (ie, completed the 24-month assessment and remained in the health plan for 24 months) yielded identical results for incremental effectiveness; adjusted cost savings was somewhat greater (–$605 [95% CI, –$1766 to $566]). Additional secondary analyses using gamma regression yielded an incremental cost estimate of –$443 compared with –$605 for the linear model.

Because we find both clinical benefit and cost savings, the traditional cost-effectiveness ratio does not accurately indicate the value of the intervention. Rather than examining the ratio of costs to benefits, we should estimate the sum of benefits and savings. Incremental net benefit[45] is one method for representing that sum. The economic value of clinical benefit is assigned a dollar value according to our willingness to pay for each unit of clinical improvement. **Figure 2** illustrates the relationship between willingness to pay and incremental net benefit. If we attach no value (ie, willingness to pay = $0) to a day free of depression, then the incremental net benefit of the intervention program is equal to cost savings alone, approximately $300 per patient treated. Incremental net benefit increases as we attach greater benefit to a day free of depression: approximately $630 per patient if we value an additional day free of depression at $5, approximately $950 for a value of $10, and approximately $1600 for a value of $20. The 95% CI for incremental net benefit excludes zero for any value of willingness to pay greater than $8 per additional depression-free day.

Secondary analyses examined incremental costs and incremental benefits among participants using and not using antidepressant medication at baseline. Among those not using antidepressants prior to enrollment, the gain in depression-free days was 84 (95% CI, 52 to 116) and estimated cost savings were $421 (95% CI, $1324 decrease to $483 increase in cost). Among those already receiving depression treatment, the intervention group experienced 34 (95% CI, 5 to 63) additional days free of depression and a $30 increase in outpatient costs (95% CI, $970 decrease to $1030 increase).

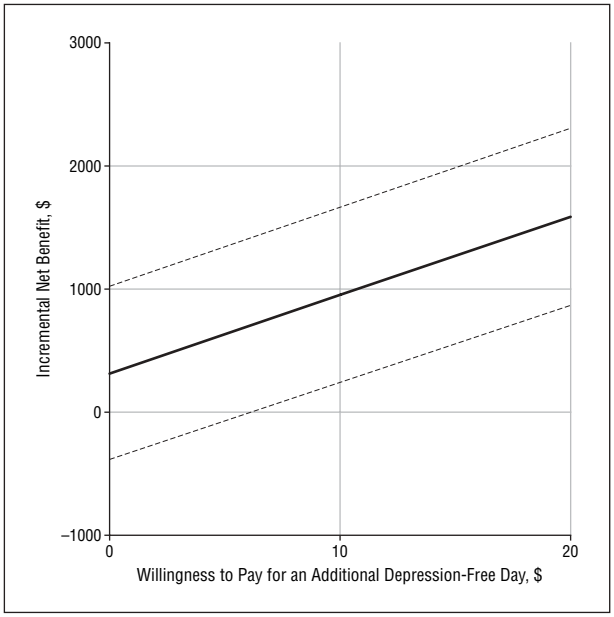

Figure 2. Change in incremental net benefit as a function of willingness to pay for each additional day free of depression shown with 95% confidence intervals (based on total outpatient health care costs). Estimates include all available data and are adjusted for baseline covariates.

COMMENT

Consistent with several other studies of systematic care programs for depression, we find that this collaborative care program for patients with diabetes and comorbid depression produced a significant and sustained increase in days free of depression.[6-12] Over the 2-year follow-up period, we estimate that the intervention reduced outpatient health services costs by approximately $300. An investment of approximately $800 in additional depression treatment costs was offset by a decrease of approximately $1100 in costs of general medical care. The overall economic value of the intervention includes both cost savings and clinical benefits. While there is no generally accepted dollar value for a day free of depression, our previous research[51] suggests that primary care patients entering depression treatment would typically be willing to pay at least $270 per month (in 1997 dollars) for a treatment that completely relieved symptoms of depression. That figure is equivalent to $11 for an additional depression-free day in 2003 dollars. Applying that value to results from this trial yields an overall economic benefit of approximately $1000 per patient treated.

Our previous studies of similar interventions have typically found modest increases in health services costs for patients receiving improved depression care.[14-16] We identify several possible explanations for the finding of cost savings in this sample. Most important, follow-up extended for 24 months so that any long-term benefits of improved depression care could be realized. Second, patients with diabetes may have more consistent patterns of use so that decreased costs associated with recovery from depression might be less hidden in random variability. Third, availability of more generic antidepressant drugs may reduce the direct costs of improved depression treatment. We cannot, however, attribute lower costs in the intervention group to any effect of depression treatment on glycemic control.

The contrast between results during the first and second years of follow-up is notable for both incremental effectiveness and incremental costs. Regarding incremental effectiveness, the gain in depression-free days in year 2 was 1.5 times as large as in year 1, even though all intervention activities ended at 12 months. Previous trials of systematic care programs for depression have shown mixed results regarding the durability of clinical benefits after added intervention services are withdrawn.[52-54] The sustained benefit seen in this trial probably reflects both the selection of a sample with more chronic depression as well as the intervention's focus on sustained treatment and prevention of relapse. More than two thirds of patients enrolled reported dysthymia or chronic depression, and a high burden of chronic medical illness may have contributed to chronicity of depression. Consequently, the rate of recovery in the usual care comparison group may have been lower in this sample than in some previous intervention trials. The continuation/maintenance phase of the intervention emphasized ongoing monitoring of depressive symptoms, long-term medication adherence, and creation of a long-term self-care plan. This emphasis would be expected to yield sustained benefits of the intervention program over usual care. Regarding incremental cost, the advantages of the intervention program did not appear until the second year. While many previous studies find that systematic depression care programs lead to modest increases in health services costs, analyses were typically limited to 6 or 12 months. The long-term studies published to date have generally reported increasing incremental benefit decreasing incremental costs with longer follow-up.[17,19,20,54]

As the follow-up period lengthens, the proportion of participants who die, disenroll from the health plan, or fail to complete blinded outcome assessment also increases. Our primary analysis uses all available data. Because incremental benefits grow with time and incremental costs concentrate in the early months, including participants with partial outcome data should yield conservative results (underestimating true incremental benefit and overestimating true incremental cost of depression treatment). The proportion of randomized participants contributing no outcome data was relatively low (3% for clinical outcomes, 2% for cost outcomes) and a high proportion of participants contributed complete data (85% for clinical outcomes, 87% for cost outcomes). In addition, those with missing outcome data were generally similar to those with complete data in baseline clinical and demographic characteristics. Still, we cannot exclude the possibility of bias due to missing follow-up data.

Our analyses of incremental costs take the perspective of the health plan or insurer. As would be expected in an older population with chronic medical illness, disenrollment from the health plan was relatively low. Consequently, insurers can actually realize any long-term benefits following short-term investment in improved depression treatment.

Interpretation of these findings should consider some additional limitations. First, findings in a sample of middle-aged and older adults with diabetes might not gen-

eralize to the general population of patients with depression. Second, this integrated depression treatment program might prove more difficult to implement in less organized health care systems. Third, health care use patterns in this sample might differ from those in a health care system with different financing mechanisms and financial incentives. Fourth, we cannot distinguish specific effects of either antidepressant medication or psychotherapy from nonspecific effects of increased contact with supportive health care professionals.

Consistent with previous research, slightly more than half of participants had been recognized as having depression and were prescribed antidepressants in the year prior to enrollment. Secondary analyses found that this previously treated group received less clinical benefit and had less favorable incremental cost. In earlier cost-effectiveness studies, incremental benefit was typically greater when systematic depression treatment programs were compared with untreated comparison groups than when compared with patients recognized and treated in usual primary care.[15] We should emphasize that incremental cost estimates for these subgroups have wide and overlapping confidence limits.

While we estimate that the intervention program led to lower outpatient health services costs over 2 years, we cannot exclude the possibility that outpatient costs might increase by as much as $400. The sample in this study was not large enough to accurately compare inpatient costs or total health services costs. Replication of these findings in other patient samples and other health care systems is clearly needed.

Our findings certainly indicate that future research should examine long-term effectiveness and cost of improved depression treatment. The 6- or 12-month horizon typically used in previous studies may have led to both underestimation of incremental effectiveness and overestimation of incremental costs. We observe that clinical benefits of systematic depression treatment persist long after the end of the formal intervention. Positive effects of depression intervention on use of health services may also not appear for 12 months or more.

The American Diabetes Association now recommends routine screening for depression among people with diabetes.[55] Our findings demonstrate that linking depression screening to a systematic depression management program for people with diabetes yields significant increases in time free of depression as well as reductions in outpatient health services costs. Among people with diabetes, depression is associated with a wide range of burdens, including less effective self-care, more severe physical symptoms, and greater functional impairment and disability. Of course, reducing human suffering remains the most important reason for improving care for depression. If reducing that burden of suffering also reduces costs of care, then depression management programs should be routinely integrated into diabetes care.

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