# Cost-Effectiveness and Net Benefit of Enhanced Treatment of Depression for Older Adults With Diabetes and Depression

WAYNE KATON, MD[1]
JÜRGEN UNÜTZER, MD, MPH[1]
MING-YU FAN, PHD[1]
JOHN W. WILLIAMS, JR., MD, MHS[2]
MICHAEL SCHOENBAUM, PHD[3]
ELIZABETH H.B. LIN, MD, MPH[4]
ENID M. HUNKELER, MA[5]

**OBJECTIVE** — To determine the incremental cost-effectiveness and net benefit of a depression collaborative care program compared with usual care for patients with diabetes and depression.

**RESEARCH DESIGN AND METHODS** — This article describes a preplanned subgroup analysis of patients with diabetes from the Improving Mood-Promoting Access to Collaborative (IMPACT) randomized controlled trial. The setting for the study included 18 primary care clinics from eight health care organizations in five states. A total of 418 of 1,801 patients randomized to the IMPACT intervention ($n = 204$) versus usual care ($n = 214$) had coexisting diabetes. A depression care manager offered education, behavioral activation, and a choice of problem-solving treatment or support of antidepressant management by the primary care physician. The main outcomes were incremental cost-effectiveness and net benefit of the program compared with usual care.

**RESULTS** — Relative to usual care, intervention patients experienced 115 (95% CI 72–159) more depression-free days over 24 months. Total outpatient costs were $25 (95% CI −1,638 to 1,689) higher during this same period. The incremental cost per depression-free day was 25 cents (−$14 to $15) and the incremental cost per quality-adjusted life year ranged from $198 (144–316) to $397 (287–641). An incremental net benefit of $1,129 (692–1,572) was found.

**CONCLUSIONS** — The IMPACT intervention is a high-value investment for older adults with diabetes; it is associated with high clinical benefits at no greater cost than usual care.

*Diabetes Care* **29:265–270, 2006**

Patients with diabetes have a high rate of major depression, estimated at 11–15% (1). Depression in patients with diabetes is associated with higher medical symptom burden (2), additive functional impairment (3,4), poor self-care (adherence to diet, exercise, cessation of smoking, and medications) (5), a higher number of cardiac risk factors (6), increased macrovascular and microvascular complications, and higher mortality (7).

Given the adverse effects of depression on medical symptom burden and self-care of diabetes, it is not surprising that patients with depression and diabetes have significantly higher medical costs than patients with diabetes alone after controlling for severity of diabetes and medical comorbidity (8). Although several trials have shown that depression can be adequately treated in patients with comorbid diabetes and depression (9,10), there is only one study that has reported the incremental cost-effectiveness of improving depression care in patients with diabetes compared with those treated in usual primary care (11). This study showed a high probability that the increased costs of improving care of depression were associated with larger savings in medical costs (i.e., a cost offset effect) (11). However, this trial occurred in one large HMO in one geographic area of the country, and the findings need to be replicated.

The Improving Mood-Promoting Access to Collaborative (IMPACT) trial recently reported the incremental cost-effectiveness of providing a nurse collaborative care depression intervention compared with usual primary care for 1,801 elderly depressed patients enrolled in 18 primary care clinics from eight diverse health care organizations in five states (12). This randomized controlled study showed a large increase in depression-free days associated with this intervention while increasing total medical costs slightly, compared with patients treated in usual care, over a 2-year period (12). Earlier findings showed that the IMPACT model was substantially more effective at reducing depression compared with usual care in the 418 study participants who had both depression and diabetes (13). In this article, we report the incremental cost-effectiveness of enhanced depression treatment as well as the net benefit of such improvements in care in this sample of 418 older adults with diabetes and depression. Such information is important to examine the value of improving depression care in patients with diabetes and to replicate the one prior study reporting favorable cost-effectiveness of enhanced depression treatment in diabetic patients with de-

From the [1]Department of Psychiatry, University of Washington School of Medicine, Seattle, Washington; the [2]Department of Medicine, Durham Veterans Administration Medical Hospital, Durham, North Carolina; [3]RAND, Arlington, Virginia; the [4]Center for Health Studies, Group Health Cooperative of Puget Sound, Seattle, Washington; and [5]Kaiser Permanente, Oakland, California.

Address correspondence and reprint requests to Wayne Katon, MD, Department of Psychiatry and Behavioral Sciences, Box 356560, University of Washington School of Medicine, 1959 NE Pacific St., Seattle, WA 98195-6560. E-mail: wkaton@u.washington.edu.

Received for publication 22 August 2005 and accepted in revised form 15 October 2005.

E.M.H. has received grant/research support from Eli Lilly, Wyeth, Solvay, Merck, and GlaxoSmithKline.

**Abbreviations:** DCM, depression care manager; HSCL-20, Hopkins Symptom Checklist 20 Depression Scale; IMPACT, Improving Mood-Promoting Access to Collaborative; PST-PC, problem-solving treatment developed for primary care; QALY, quality-adjusted life year.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

pression (11). Because depression adversely affects the complex self-care activities necessary for diabetes control (changing diet, increasing exercise, checking blood glucose, and adherence to medications) and the potential adverse neurobiologic effects of depression on diabetes (14), we hypothesized that improved depression care for this high-cost group of older adults would be particularly cost-effective.

## RESEARCH DESIGN AND METHODS

— Detailed information on the methodology and clinical outcomes of the IMPACT trial have been described elsewhere (15). This trial was conducted in 18 primary care clinics belonging to eight diverse health care organizations in five states. The institutional review boards from each participating organization and the study coordinating center approved all study procedures, and all patients signed written informed consent.

Patients were either identified by systematic screening (two-item depression screen) (16) or referred by their primary care physician. Inclusion criteria included age >60 years, meeting criteria for major depression and/or dysthymia on the Structured Clinical Interview for the DSM-IV (17), and a plan to continue to use the same primary care clinic over the next year. Exclusion criteria included severe cognitive impairment, current alcohol abuse, a history of bipolar disorder, or acute risk of suicide. Recruitment occurred from July 1999 to August 2001. Patients who met eligibility criteria and signed written informed consent were randomized to either the IMPACT intervention or usual care.

### Intervention

The IMPACT intervention was a stepped collaborative care program that was delivered by a depression care manager (in most organizations this was a nurse). The depression care manager (DCM) provided a behavioral activation intervention to all patients (i.e., structured positive activities like exercise) and an initial choice of problem-solving treatment developed for primary care (PST-PC) (18,19) or enhanced treatment with antidepressant medication prescribed by the primary care physician. PST-PC is a six- to eight-session manualized psychotherapy program shown to be as effective as antidepressant medication in primary care patients with major depression (18,19). DCMs received initial training on pharmacotherapy and PST-PC during a 2-day workshop and were required to complete at least five videotaped training cases of PST-PC supervised by a psychologist. The DCMs received weekly supervision by a psychiatrist and primary care physician with geriatric expertise in order to monitor progress of treatment and adjust treatment plans based on clinical response. Initial medication treatment would be augmented with PST-PC based on partial or nonresponse and vice versa. The DCMs followed patients in person or by telephone approximately every 2 weeks over the acute treatment phase (3–6 months) and approximately once a month in the continuation phase (6–12 months).

### Usual care

In patients assigned to usual care, primary care physicians were notified about the patient's depressive diagnosis and could provide antidepressant medication and/or referral to mental health specialty care.

### Outcome measures

Patients had an in-person baseline interview before randomization and were then interviewed by a centralized telephone survey team at 3-, 6-, 12-, 18- and 24-month follow-ups. The primary health outcome was the Hopkins Symptom Checklist 20 Depression Scale (HSCL-20) (20). Adapting the method developed by Lave et al. (21), the HSCL-20 depression scores from baseline and follow-up assessments were used to estimate the number of depression-free days during the 24-month follow-up period. This method uses consecutive depression severity measures to estimate depression severity for each day during the interval using linear interpolation (21). Based on prior work (22), a score of <0.5 on the HSCL-20 was used to indicate remission, and a score of >1.7 was used to indicate the patients was fully symptomatic. Days with intermediate severity scores were assigned a value between depression free and fully symptomatic by linear interpolation. Estimates for each follow-up period were then added to yield to total number of depression-free days during the 24-month follow-up period.

The primary dependent cost variable was total outpatient costs (mental health and nonmental health costs). We will also describe inpatient costs. The intent was to describe the costs of medical and mental health services provided and paid for by the eight participating health care organizations. In capitated systems (HMOs), this was computed from cost-accounting data, and in fee-for-services systems it was estimated by the actual revenue (not charges) generated for the services provided.

The value of the collaborative care intervention was assessed using measurable direct health care costs, improvement in depression symptoms, and patient willingness to pay for improved depressive symptoms. We will describe the incremental cost effectiveness ratio (the incremental cost of the intervention compared with usual care divided by the incremental benefit) and the incremental net benefit (23). The net benefit approach combines both incremental cost and clinical benefit into a single measure (23) and has been recommended when there is a possibility of a negative incremental cost-effectiveness ratio because of the difficulty interpreting negative incremental cost-effectiveness ratios (23). This measure has the advantage of including an estimate of the degree to which patients value treatment of depression (incremental days free of depression multiplied by willingness to pay for each additional day less incremental cost) (23). Because the dollar value of clinical benefit (i.e., days free of depression) is not clearly established, we used data that has been developed from a recent primary care study on patients' willingness to pay for an additional day free of depression (24).

Outpatient mental health costs were defined as estimated costs of all antidepressant medications, all intervention specific costs, and all outpatient specialty mental health care. We estimated the costs of providing the IMPACT intervention based on detailed records of all patients contacts (in-person and telephone), mean salary and benefit costs of depression care managers plus 30% overhead costs, the cost of supervision by psychiatrists and primary care experts with geriatric expertise at each site plus 30% overhead costs, and the cost of providing intervention educational materials (videotapes and pamphlets).

Outpatient medical costs were defined as the costs of all primary care, specialty, urgent care and emergency visits, nonantidepressant prescriptions, laboratory and X-rays, and costs for other outpatient medical care that were provided or paid for by participating health care organizations. Total outpatient costs were

**Table 1—*Patient characteristics***

| Characteristic | Diabetes subgroup | |
|---|---|---|
| | Usual care ($n$ = 214) | Intervention ($n$ = 204) |
| Female | 112 (52) | 111 (54) |
| Mean age (years) | 70.2 ± 0.5 | 70.1 ± 0.5 |
| Married or living with partner | 103 (48) | 93 (46) |
| Ethnic group | | |
| White | 136 (64) | 132 (65) |
| African American | 39 (18) | 46 (23) |
| Hispanic | 33 (15) | 21 (10) |
| Other | 6 (3) | 5 (2) |
| At least high school graduate | 160 (75) | 150 (74) |
| Mean annual income (in $1000s) | 26.0 (1.7) | 27.5 (2.4) |
| Depression status (SCID diagnosis) | | |
| Major depression | 27 (13) | 24 (12) |
| Dysthymia | 61 (28) | 59 (29) |
| Major depression and dysthymia | 126 (59) | 121 (59) |
| Mean HSCL-20 depression score (range 0–4) (±SE) | 1.7 ± 0.04 | 1.7 ± 0.01 |
| Mean chronic disease score | 7.9 ± 0.3 | 7.5 ± 0.3 |
| Mean duration of diabetes | 11.6 ± 0.7 | 10.5 ± 0.7 |
| Diabetes treatment | | |
| Diet only | 26 (12) | 36 (18) |
| Oral hypoglycemic agents only | 110 (51) | 96 (47) |
| Insulin only | 50 (23) | 46 (23) |
| Oral hypoglycemic agents and insulin | 28 (13) | 26 (13) |
| Mean A1C level* | 7.3 ± 0.1 | 7.3 ± 0.1 |

Data are means ± SD or *n* (%), unless otherwise indicated. *$n$ = 293 for A1C results: 147 usual care and 146 intervention. SCID, structured clinical interview for DSM-IV.

defined as the sum of the total ambulatory medical and mental health costs.

Inpatient mental health costs were defined as the sum of costs for all inpatient substance abuse and mental health treatment. Total inpatient medical costs were defined as the sum of costs for all medical/surgical admissions.

The incremental quality-adjusted life years (QALYs) associated with the IMPACT intervention were also estimated. Prior literature (25–30) has suggested that going from fully symptomatic to full remission of depression is associated with an increase in quality of life from 0.2 to 0.4 on a scale of 0 (no quality) to 1 (full quality). To determine the incremental QALYs associated with the intervention, we divided the 2-year difference in depression-free days by 365 and then multiplied by the lower (0.2) and upper (0.4) bound increases in QALYs associated with full remission of depression in the literature (25–30). The resulting range of QALYs was then divided into the point estimate for incremental total outpatient costs to estimate costs per QALY associated with the intervention versus usual care.

### Statistical analysis

We conducted intent-to-treat analyses of our dependent variables (depression-free days and costs) over 2 years. To deal with missing data, we used 25 imputed datasets that had been previously imputed using SOLAS 3.2 (31), with propensity score based on Rubin's method (32). Details of this imputation strategy have been provided elsewhere (12). All statistics were first computed within each imputed dataset and were then combined according to Rubin's formula (32). All demographic and clinical characteristics were balanced between the two groups at baseline. Thus, we present the unadjusted means of depression-free days and health care costs in each cost category comparing intervention and usual care patients. CIs for the differences are also provided.

The variance of the incremental cost-effectiveness ratio (incremental cost per depression-free day) was approximated following Taylor's expansion and combined by applying Rubin's rule (32). The CI for incremental cost per depression-free day was then constructed based on normal theory.

We estimated the probabilities of the intervention being associated with increased clinical benefit at lower health care costs compared with usual care by means of bootstrapping procedures with 1,000 replications. This bootstrapping procedure and probability estimation were carried out for each of the 25 imputed datasets. The final probabilities reported were obtained by averaging over the 25 estimates.

**RESULTS** — The enrolled sample of 418 patients with diabetes and depression was sociodemographically and clinically diverse (Table 1). The mean age was ~70 years, about half were women, and approximately one-third were from ethnic/racial minority groups. Over half met criteria for double depression (dysthymia and major depression), and the mean HSCL-20 depression score was 1.7 ± 0.6, indicating moderate to severe depression. The mean duration of diabetes was ~10–11 years, and about one-third were treated with insulin alone or insulin and an oral hypoglycemic agent. The mean $HbA_{1c}$ (A1C) level was 7.3 ± 0.1%.

The mean number of additional depression-free days associated with the intervention in the first 12 months was 59.4 (95% CI 37.3–81.4) and in the second 12 months was 56.1 (31.8–80.4), resulting in 115.4 (71.7–159.1) additional depression-free days for intervention patients compared with those treated in usual care over 2 years.

Table 2 describes the costs of health services during the 24-month period. The average cost of the intervention program was $597. Antidepressant medication costs were $471 higher among intervention compared with usual care patients, but costs of specialty mental health care were $50 lower in intervention patients. Total mental health costs (intervention program, specialty mental health, and antidepressant costs) were $1,019 higher in intervention compared with usual care patients. On the other hand, nonmental health medication costs were $271 lower and other outpatient costs were $722 lower in intervention patients, suggesting a substantial medical cost offset in non–mental health–related ambulatory care services. Our primary cost outcome, total outpatient services, was only $25 (95% CI −1,638 to 1,689) higher in intervention compared with usual care patients. The incremental cost-effectiveness ratio based on this cost outcome was 25 cents (−$14 to $15) per depression-free day.

In the 1st year, there was a $665 (95%

**Table 2—*Twenty-four month health care costs***

| | Intervention | Usual care | Difference (95% CI) |
|---|---|---|---|
| Intervention costs | $597 (560–635) | $0 (0–0) | $597 (560–635) |
| Median | $553 | 0 | |
| Antidepressant medications | $933 (794–1072) | $462 (363–560) | $471 (306–636) |
| Median | $805 | $240 | |
| Outpatient mental health | $293 (163–422) | $342 (198–487) | −$50 (−244 to 145) |
| Median | $0 | $0 | |
| Total mental health | $1,823 (1,614–2,032) | $804 (613–995) | $1,019 (739–1,299) |
| Median | $1,527 | $392 | |
| Other medications | $3,245 (3,848, 3,642) | $3,516 (3,100, 3,933) | −$271 (−832 to 289) |
| Median | $2,782 | $2,881 | |
| Other outpatient mean | $7,846 (6,951–8,740) | $8,568 (7,460–9,675) | −$722 (−2,134 to 689) |
| Median | $6,360 | $6,821 | |
| Total outpatient | $12,913 (11,800, 14,026) | $12,888 (16,605, 14,170) | $25 (−1,638 to 1,689) |
| Median | $11,561 | $11,381 | |
| Inpatient mental health | $10 (−9 to 29) | $52 (−50 to 154) | −$42 (−146 to 62) |
| Median | $0 | $0 | |
| Inpatient medical costs | $5,112 (3,651–6,574) | $5,992 (3,337–8,647) | −$880 (−3,826 to 2,066) |
| Median | $0 | $144 | |
| Grand total | $18,035 (15,948–20,123) | $18,932 (15,860–22,004) | −$896 (−4,549 to 2,755) |
| Median | $14,400 | $14,184 | |

Data are means (95% CI), unless otherwise indicated.

CI −340 to 1,670) increase in total outpatient costs associated with the intervention group, and in the 2nd year (during which no intervention services were provided), there was a $639 (−1,714 to 435) cost savings in total outpatient costs in intervention compared with usual care patients.

When total medical costs (inpatient and outpatient) are included, in the 1st year there was an increased cost of $515 (95% CI −2,136 to 3,165), while in the 2nd year there was a cost savings of $1,411 (−3,821 to 998). Over 2 years, the grand total of health care costs (inpatient and outpatient) was $896 (−4,549 to 2,755) lower in intervention compared with usual care patients.

Based on available estimates of depression and QALYs (25–30), the increase in depression-free days of 115.4 was associated with the IMPACT intervention corresponds to an estimate of 0.063 (95% CI 0.039–0.087) to 0.126 (0.079–0.174) QALYs. Combining the QALY estimates with the point estimate for incremental outpatient costs yields a cost per QALY range of $198 (95% CI 144–316) to $397 (287–641) associated with the IMPACT intervention.

Based on total outpatient costs, the probability that the intervention improved outcomes and saved money was estimated by bootstrapping procedures to be 50.3%. When total costs (inpatient and outpatient) are included, the probability that the intervention improved outcomes and saved money was 67.3%. In all estimates, the intervention showed greater clinical effectiveness than usual care.

Another way to determine the value of the intervention is the incremental net benefit, which includes patients' willingness to pay for treatment to relieve depressive symptoms, estimated to be approximately $10 per day in our prior research (24). Given the finding of 115.4 incremental depression-free days associated with the IMPACT intervention at an incremental total ambulatory cost of $25, this translates into an incremental net benefit of $1,129 (95% CI 692–1,572). A sensitivity analysis that lowered the willingness to pay to $5 per day found an incremental net benefit of $552 (334–771).

**CONCLUSIONS** — We found that a stepped collaborative care intervention for patients with diabetes and depression was associated with ~115 more depression-free days over a 24-month period. The increased mental health costs in the intervention group were essentially balanced by lower ambulatory medical costs in this group. Health care plan investments of $665 in outpatient costs in year 1 were balanced by cost-savings of a similar amount in year 2. These data suggest the potential of continuing to accrue clinical and monetary benefits after year 2 that are not captured by our analysis. These findings are more favorable than prior trials that have tested depression quality improvement interventions versus usual primary care in young to middle-aged populations of patients with depression, which have found a range of 13–58 increased depression-free days with and a moderate increase in outpatient costs of approximately $150 to $800 over a 1-year period compared with usual primary care (22). The only other cost-effectiveness analysis of an intervention aimed at improving care of depression in a mixed-age group of primary care patients with depression and diabetes from one large HMO also found an increased benefit in intervention compared with usual care patients of 69 depression-free days and a $600 cost savings over a 2-year period (33).

Thus, there are now two trials with a combined sample of ~750 patients with diabetes and depression that have shown a marked increase in benefits of a similar nurse collaborative care program. In these two studies, an increase in outpatient mental health costs of ~$900 to $1,000 (i.e., cost of mental health visits, psychopharmacologic treatment, and psychiatric supervision) in the intervention group were balanced by lower total medical care costs. Multiple studies have shown that depression in primary care patients is as-

sociated with increased medical costs in every category measured compared with patients without depression, including non–mental health primary care visits, medical specialty visits, emergency room visits, laboratory tests, X-rays, procedures, and pharmacy costs (34,35). The data from these two recent trials demonstrate that improving the quality of depression care and the resulting improvement over 2 years in depression outcomes translates into a cost savings in each of these categories.

Why have we seen more favorable cost-effectiveness of improved quality of depression care among patients with diabetes compared with trials of depression quality improvement in younger and/or healthier populations? Our previous studies suggest that patients with comorbid depression and diabetes compared with those with diabetes alone have a higher probability of experiencing all ten diabetes symptoms from a standard diabetes symptom checklist even when controlling for A1C levels and diabetes complications (2). This increase in diabetes symptoms could lead to increased medical visits and testing and resulting non–mental health costs. Epidemiologic studies have also shown that depression in patients with diabetes is associated with poor self-care, including lack of adherence to diet, exercise, smoking cessation, and three disease control medications (i.e., antihypertensives, lipid-lowering, and oral hypoglycemic agents) (5). This poor adherence associated with depression could lead to increased complications of diabetes and raise medical costs. Depression is also associated with neurobiologic changes that could worsen the course of diabetes (14). Several recent longitudinal studies (7,36,37) have shown that patients with diabetes and depression compared with those with diabetes alone developed significantly more macrovascular and microvascular complications and had increased mortality over several years of follow-up.

When total health care (inpatient and outpatient) costs are considered, the intervention group had lower total health care costs over a 2-year period compared with the group receiving care as usual, resulting in a net savings of ~$896 (although the CIs include zero). The probability that the intervention was associated with lower total health care costs and higher benefits than usual care was 67.3%.

When considering the patient's perspective using a net benefit analysis, the IMPACT intervention was associated with an incremental net benefit compared with usual care of $1,129 (95% CI 692–1,572). The advantage of the net benefit approach is that it includes both a measure of the value to the patient of effective depression treatment as well as cost to the medical system. The CI for the net benefit approach does not include zero. This suggests that by including patient value as expressed by willingness to pay for relief of depression symptoms, the intervention has unequivocal net benefit. A sensitivity analysis that decreased willingness to pay for relief of depressive symptoms by half continued to show unequivocal net benefit.

Limitations of this study include the narrow focus on the outcomes of depression (improved depression care also produces other health benefits such as improved functioning and quality of life) (13) and direct medical costs as well as the fact that we combined health care data from eight diverse health care organizations that use somewhat different methods to capture such data. Including net benefit analysis added a patient perspective on the perceived value of treatment. Future studies should focus on other potential benefits such as benefits to employers and families in terms of improved productivity, reduced absenteeism, and decreased family burden for care. CIs using both ambulatory and total medical cost data in the incremental cost-effectiveness ratios include zero, indicating limited power given the available sample sizes. Another limitation is the need for imputation based on the missing cost data. A final limitation was that the estimate of QALYs from HSCL-20–based depression-free days has not been independently validated against other measures of QALYs (i.e., time trade-off or standard gamble).

Our estimates of costs/QALYs suggest programs that aim to improve care for populations of diabetic patients should strongly consider including quality improvement programs for depression such as IMPACT in their disease management efforts for diabetes. Generally, treatments that show cost-effectiveness ratios <$20,000 per QALY are recommended for rapid dissemination into health care systems (38). Federal and private health insurers should cover such evidence-based treatments for depression (39).

**Acknowledgments**— John A. Hartford Foundation no. 98297-G and California Health Care Foundation no. 98-3138B (to J.U.), National Institutes of Mental Health no. 1 K24 MH 069471-01 (to W.J.K.), and Robert Wood Johnson, Hogg Foundation (J.W.W.)

**References**

1. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ: The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 24:1069–1078, 2001
2. Ludman EJ, Katon W, Russo J, Von Korff M, Simon G, Ciechanowski P, Lin E, Bush T, Walker E, Young B: Depression and diabetes symptom burden. *Gen Hosp Psychiatry* 26:430–436, 2004
3. Von Korff M, Katon W, Lin EH, Simon G, Ludman E, Oliver M, Ciechanowski P, Rutter C, Bush T: Potentially modifiable factors associated with disability among people with diabetes. *Psychosom Med* 67: 233–240, 2005
4. Von Korff M, Katon W, Lin EH, Simon G, Ciechanowski P, Ludman E, Oliver M, Rutter C, Young B: Work disability among individuals with diabetes. *Diabetes Care* 28:1326–1332, 2005
5. Lin EH, Katon W, Von Korff M, Rutter C, Simon GE, Oliver M, Ciechanowski P, Ludman EJ, Bush T, Young B: Relationship of depression and diabetes self-care, medication adherence, and preventive care. *Diabetes Care* 27:2154–2160, 2004
6. Katon WJ, Lin EH, Russo J, Von Korff M, Ciechanowski P, Simon G, Ludman E, Bush T, Young B: Cardiac risk factors in patients with diabetes mellitus and major depression. *J Gen Intern Med* 19:1192–1199, 2004
7. Black SA, Markides KS, Ray LA: Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes. *Diabetes Care* 26:2822–2828, 2003
8. Simon G, Katon W, Lin E, Ludman E, Von Korff M, Ciechanowski P, Young B: Diabetes complications and depression as predictors of health care costs. *Gen Hosp Psychiatry* 27:344–351, 2005
9. Lustman PJ, Griffith LS, Freedland KE, Kissel SS, Clouse RE: Cognitive behavior therapy for depression in type 2 diabetes mellitus: a randomized, controlled trial. *Ann Intern Med* 129:613–621, 1998
10. Lustman PJ, Freedland KE, Griffith LS, Clouse RE: Fluoxetine for depression in diabetes: a randomized double-blind placebo-controlled trial. *Diabetes Care* 23: 618–623, 2000
11. Katon W, Simon G, Unutzer J, Fan M, Schoenbaum M, Von Korff M, Williams J Jr, Lin EHB, Rutter C, Ciechanowski P, Ludman E: Cost-effectiveness and probability of cost-offset of a stepped care inter-

vention in patients with diabetes and depression. Presented at the 18th annual NIMH conference on Mental Health Services Research, Bethesda, Maryland, 18–19 July 2005
12. Katon W, Schoenbaum M, Fan M, Callahan C, Williams JJ, Hunkeler E, Harpole L, Zhou Z, Langston C, Unützer J, the Impact Investigators: Cost-effectiveness of an intervention (IMPACT) to improve depression care in the elderly. *Arch Gen Psychiatry*. 62:1313–1320, 2005
13. Williams JW Jr, Katon W, Lin EH, Noel PH, Worchel J, Cornell J, Harpole L, Fultz BA, Hunkeler E, Mika VS, Unützer J: The effectiveness of depression care management on diabetes-related outcomes in older patients. *Ann Intern Med* 140:1015–1024, 2004
14. Musselman DL, Betan E, Larsen H, Phillips LS: Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. *Biol Psychiatry* 54: 317–329, 2003
15. Unützer J, Katon W, Williams JW, Jr, Callahan CM, Harpole L, Hunkeler EM, Hoffing M, Arean P, Hegel MT, Schoenbaum M, Oishi SM, Langston CA: Improving primary care for depression in late life: the design of a multicenter randomized trial. *Med Care* 39:785–799, 2001
16. Kroenke K, Spitzer RL, Williams JB: The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 16:606–613, 2001
17. First MD, Spitzer RL, Gibbon M, Williams JBW: Structured Clinical Interview for DSM-IV Axis I Disorders (SCID). Clinical Version. Washington, DC, American Psychiatric Press, 1996
18. Mynors-Wallis LM, Gath DH, Lloyd-Thomas AR, Tomlinson D: Randomised controlled trial comparing problem solving treatment with amitriptyline and placebo for major depression in primary care. *BMJ* 310:441–445, 1995
19. Hegel M, Arean P: *Problem-Solving Treatment for Primary Care (PST-PC): A Treatment Manual for Depression*. Dartmouth, NH, Project IMPACT, 2003
20. Derogatis LR, Lipman RS, Rickels K, Uhlenhuth EH, Covi L: The Hopkins Symptom Checklist (HSCL): a measure of primary symptom dimensions. *Mod Probl Pharmacopsychiatry* 7:79–110, 1974
21. Lave JR, Frank RG, Schulberg HC, Kamlet MS: Cost-effectiveness of treatments for major depression in primary care practice. *Arch Gen Psychiatry* 55:645–651, 1998
22. Simon GE, Katon WJ, VonKorff M, Unützer J, Lin EH, Walker EA, Bush T, Rutter C, Ludman E: Cost-effectiveness of a collaborative care program for primary care patients with persistent depression. *Am J Psychiatry* 158:1638–1644, 2001
23. Stinnett AA, Mullahy J: Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. *Med Decis Making* 18:S68–80, 1998
24. Unützer J, Katon WJ, Russo J, Simon G, von Korff M, Lin E, Walker E, Ludman E, Bush T: Willingness to pay for depression treatment in primary care. *Psychiatr Serv* 54:340–345, 2003
25. Wells KB, Sherbourne CD: Functioning and utility for current health of patients with depression or chronic medical conditions in managed, primary care practices. *Arch Gen Psychiatry* 56:897–904, 1999
26. Unützer J, Patrick DL, Diehr P, Simon G, Grembowski D, Katon W: Quality adjusted life years in older adults with depressive symptoms and chronic medical disorders. *Int Psychogeriatr* 12:15–33, 2000
27. Revicki DA, Wood M: Patient-assigned health state utilities for depression-related outcomes: differences by depression severity and antidepressant medications. *J Affect Disord* 48:25–36, 1998
28. Kaplan R: Health-related quality of life in mental health services evaluation. In *Cost-Effectiveness of Psychotherapy: A Guide for Practitioners, Researchers, and Policy-Makers*. Miller N, Magruder K, Eds. New York, Oxford University Press, 1999, p. 213–228
29. Fryback DG, Dasbach EJ, Klein R, Klein BE, Dorn N, Peterson K, Martin PA: The Beaver Dam Health Outcomes Study: initial catalog of health-state quality factors. *Med Decis Making* 13:89–102, 1993
30. Pyne JM, Patterson TL, Kaplan RM, Ho S, Gillin JC, Golshan S, Grant I: Preliminary longitudinal assessment of quality of life in patients with major depression. *Psychopharmacol Bull* 33:23–29, 1997
31. O'Callahan F: Multiple imputation using SOLAS for missing data analysis. *Mag Stud Statistics* 0:3–7, 2001
32. Rubin DB: *Multiple Imputation for Nonresponse in Surveys*. New York, John Wiley & Sons, 1987
33. Simon GE, Manning WG, Katzelnick DJ, Pearson SD, Henk HJ, Helstad CS: Cost-effectiveness of systematic depression treatment for high utilizers of general medical care. *Arch Gen Psychiatry* 58:181–187, 2001
34. Katon WJ, Lin E, Russo J, Unützer J: Increased medical costs of a population-based sample of depressed elderly patients. *Arch Gen Psychiatry* 60:897–903, 2003
35. Unützer J, Patrick DL, Simon G, Grembowski D, Walker E, Rutter C, Katon W: Depressive symptoms and the cost of health services in HMO patients aged 65 years and older: a 4-year prospective study. *JAMA* 277:1618–1623, 1997
36. Katon W, Rutter C, Simon G, Lin E, Ludman E, Ciechanowski P, Kinder L, Young B, Von Korff M: The association of comorbid depression with mortality in patients with type 2 diabetes. *Diabetes Care* 28: 2668–2672, 2005
37. Zhang X, Norris SL, Gregg EW, Cheng YJ, Beckles G, Kahn HS: Depressive symptoms and mortality among persons with and without diabetes. *Am J Epidemiol* 161: 652–660, 2005
38. Gold M, Siegel J, Russel L, Weinstein M: *Cost-Effectiveness in Health and Medicine*. New York, Oxford University Press, 1996
39. Unützer J, Schoenbaum M, Druss B, Katon W: Transforming mental health care at the interface with general medicine: report for the President's New Freedom Commission for Mental Health. *Psychiatr Serv*. In press