



Recent epidemiologic studies have found that most patients with mental illness are seen exclusively in primary care medicine. These patients often present with medically unexplained somatic symptoms and utilize at least twice as many health care visits as controls. There has been an exponential growth in studies in this interface between primary care and psychiatry in the last 10 years. This special section, edited by **Wayne J. Katon, MD.**, will publish informative research articles that address primary care-psychiatric issues.

## Improving depression outcomes in older adults with comorbid medical illness

Linda H. Harpole, M.D., M.P.H.<sup>a,\*</sup>, John W. Williams Jr., M.D., M.H.S.<sup>a,b</sup>,  
Maren K. Olsen, Ph.D.<sup>b,c</sup>, Karen M. Stechuchak, M.S.<sup>b</sup>, Eugene Oddone, M.D., M.H.S.<sup>a,b</sup>,  
Christopher M. Callahan, M.D.<sup>d</sup>, Wayne J. Katon, M.D.<sup>e,f</sup>, Elizabeth H. Lin, M.D., M.P.H.<sup>f</sup>,  
Lydia M. Grypma, M.D.<sup>g</sup>, Jürgen Unützer, M.D., M.P.H.<sup>e</sup>

<sup>a</sup>Department of Medicine, Duke University Medical Center, Durham, NC 27709, USA

<sup>b</sup>Center for Health Services Research in Primary Care, Durham Veterans Affairs Medical Center, Durham, NC 27705, USA

<sup>c</sup>Department of Biostatistics and Bioinformatics, Duke University Medical Center, Durham, NC 27705, USA

<sup>d</sup>Indiana University Center for Aging Research, Regenstrief Institute Inc., Indianapolis, IN 46202, USA

<sup>e</sup>Department of Psychiatry, University of Washington, Seattle, WA 98195, USA

<sup>f</sup>Center for Health Studies, Group Health Cooperative, Seattle, WA 98101, USA

<sup>g</sup>Kaiser Permanente of Southern California, San Diego, CA 92120, USA

Received 19 April 2004; accepted 8 September 2004

### Abstract

**Background:** Depression is common in older adults and often coexists with multiple chronic diseases, which may complicate its diagnosis and treatment.

**Objective:** To determine whether or not the presence of multiple comorbid medical illnesses affects patient response to a multidisciplinary depression treatment program.

**Design, Setting and Participants:** Preplanned analyses of Improving Mood-Promoting Access to Collaborative Treatment (IMPACT), a randomized controlled trial of 1801 depressed older adults ( $\geq 60$  years), which was performed at 18 primary care clinics from eight health care organizations in five states across the United States from July 1999 to August 2001.

**Intervention:** Intervention patients had access for up to 12 months to a depression care manager, supervised by a psychiatrist and a primary care expert, who offered education, care management and support of antidepressant management by the patient's primary care physician, or provided brief psychotherapy (Problem-Solving Treatment in Primary Care).

**Measurements:** Depression, quality of life (QOL; scale of 0–10) and mental health component score (MCS) of the Short-Form 12 assessed at baseline, 3, 6 and 12 months.

**Results:** Patients suffered from an average of 3.8 chronic medical conditions. Although patients with more chronic medical conditions had higher depression severity at baseline, the number of chronic diseases did not affect the likelihood of response to the IMPACT intervention when compared to care as usual. Intervention patients experienced significantly lower depression during all follow-up time points as compared with patients in usual care independent of other comorbid illnesses ( $P < .001$ ). Intervention patients were also more likely to experience substantial response (at least a 50% reduction in depressive symptoms) regardless of the number of comorbidities, to experience improved MCS-12 scores at 3 and 12 months, and to experience improved QOL.

**Conclusions:** The presence of multiple comorbid medical illnesses did not affect patient response to a multidisciplinary depression treatment program. The IMPACT collaborative care model was equally effective for depressed older adults with or without comorbid medical illnesses. Published by Elsevier Inc.

**Keywords:** Depression; Comorbidity; Primary care

\* Corresponding author. Tel.: +1 919 483 7434; fax: +1 919 315 0984.

E-mail address: [Linda.h.harpole@gsk.com](mailto:Linda.h.harpole@gsk.com) (L.H. Harpole).

## 1. Introduction

Major depression and dysthymia affect between 5% and 10% of older adults who are seen in the outpatient setting [1–3]. As compared with younger patients, older adults often suffer from multiple coexisting chronic diseases, which can complicate the diagnosis and treatment of depression in the elderly. The adverse effects of depression and chronic medical conditions on functioning are additive [4] and are associated with increased health care costs [5].

It is well established that depression adversely affects outcomes from chronic medical conditions. Patients with coronary artery disease and comorbid depression have functional disability [6], poorer outcomes following coronary artery bypass surgery [7], a worse prognosis following an episode of unstable angina [8] and increased mortality [9] as compared to those without depression. The biologic rationale for increased vulnerability of depressed patients with coronary artery disease is thought to be a manifestation of hypothalamic–pituitary–adrenocortical axis hyperactivity, decreased heart rate variability and changes in platelet receptor function [10]. Depression is also associated with worse glycemic control in diabetics [11] and is a risk factor for the development of stroke [12].

Although prior research had suggested that treatment of depression in late life is not very effective [13], recent studies have demonstrated that depression symptomatology can be successfully treated in older adults [14,15]. How effective treatment is in older patients with medical comorbid illnesses is not clear. Many trials of antidepressants in psychiatric settings have explicitly excluded patients with significant medical and psychiatry comorbidity [16], or accepted those with only stable chronic disease [14]. The few studies, which have included patients with comorbid medical illness, have suggested that treatment for depression may be less effective than for those without comorbid medical illness [17–21].

A recent study [22,23] of a disease management model for the treatment of depression in 1801 older adults in the primary care setting was successful at improving outcomes. Because enrollment criteria did not exclude patients with multiple medical illnesses, we have a unique opportunity to determine whether or not comorbid medical illness modulates the effectiveness of depression treatment in this intervention trial. To address the effect of comorbid medical illness on patient outcomes, we analyzed data from the Improving Mood–Promoting Access to Collaborative Treatment (IMPACT) trial of collaborative care management of depression to assess if increasing comorbid medical illness negatively affects response to a successful depression intervention.

## 2. Methods

The IMPACT study was conducted at 18 participating primary care clinics belonging to seven study sites across

the United States. At one site, two different healthcare organizations participated in the study, resulting in a total of eight different health care organizations. Participating organizations include two staff-model health maintenance organizations (HMOs), two regions of a large group-model HMO, the Department of Veterans Affairs, two university-affiliated primary care systems and one private practice physician group. Each institution's review board approved the study procedures and all participants gave written informed consent. A total of 1801 participants were enrolled in the study. A detailed description of the sites, recruitment procedures, overall sample and intervention outcomes are described in early publications [22,23].

Study inclusion criteria include age of 60 years or older, current major depression or dysthymia diagnosed by a Structured Clinical Interview based upon the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (SCID) [24,25], and plans to use one participating primary care clinic as the main source of general medical services for the coming year. Exclusion criteria include history of bipolar disorder or psychosis, ongoing treatment by a psychiatrist, current drinking problems [26], severe cognitive impairment [27] or acute risk of suicide. Baseline, 3-, 6- and 12-month data were utilized for the preplanned analyses described in this paper.

### 2.1. Intervention

Intervention participants received depression care management by a depression clinical specialist (DCS) who was either a nurse or psychologist working in the primary care setting, who collaborated with the patient, his primary care physician, a liaison primary care expert and a psychiatrist. The DCS conducted a psychosocial history, provided education and behavioral activation and helped patients identify treatment preferences. Treatment options included antidepressant medications prescribed by the patients' primary care provider, or six to eight sessions of psychotherapy designed for primary care, namely, Problem-Solving Treatment [28–32], which was delivered by the DCS. A stepped-care algorithm was utilized to guide treatment [23]. The DCS met weekly with the supervising psychiatrist and the liaison primary care physician to monitor progress and adjust treatment plans as needed. Patients had either weekly or biweekly contact with the DCS during the acute treatment phase and less frequently (monthly) once symptoms remitted. Contacts were either in person or by telephone.

### 2.2. Data collection

Baseline interviews were conducted by trained lay interviewers using structured computerized interviews. Follow-up interviews were conducted by a trained telephone survey research group using computer-assisted telephone interviews. All interviewers were blind to study assignment. Survey response rates were 90% at 3 months, 87% at 6 months, and 83% at 12 months.

Baseline interviews captured sociodemographic characteristics, severity of depressive symptoms via the mean score of the 20 depression items from the Symptom Checklist-90 (SCL-20) [33], SCID [24,25] diagnosis of major depression or dysthymia, overall quality of life (QOL) on a 0–10 scale and the mental component score (MCS) of the Short-Form 12 (SF12) [34]. The component scores range from 0 to 100 with lower scores indicating poorer functional status. Cognitive impairment was assessed using a six-item cognitive screener derived from the minimal status examination [27]. The presence of panic attacks in the past 4 weeks was measured [35] as was neuroticism with a subscale of the NEO [36]. Additional questions were asked about the use of antidepressant medication, counseling or psychotherapy in the 3 months prior to enrollment.

A history of diagnosis or treatment for common chronic medical problems over the prior 3 years was determined by the baseline survey. Conditions were collapsed into 11 general categories that were selected to represent the most common or significant chronic medical conditions in older adults. These included asthma, emphysema or chronic bronchitis (chronic lung disease); high blood pressure or hypertension (hypertension); high blood sugar or diabetes (diabetes); arthritis or rheumatism (arthritis); loss of hearing or vision (sensory deficit); cancer — excluding skin cancer (cancer); neurological condition such as epilepsy, seizures, Parkinson's disease or stroke (neurological disease); heart disease such as angina, heart failure or valve problems

(cardiac disease); chronic back problems, headache or other chronic pain problems (chronic pain); stomach ulcer, chronic inflamed bowel, enteritis or colitis (gastrointestinal disease); chronic problems with urination, chronic bladder infections or prostate problems, incontinence or inability to hold your urine (urologic). Skin cancer was excluded from the total count due to presumptive lack of chronicity. A summary score was created for each participant representing the total number of chronic diseases.

Additionally, we calculated a chronic disease score (CDS) [37,38], which is based upon the number of prescribed medications. This score increases with the number of different chronic diseases inferred from the subject's medication profile. In this study, we utilized two different weighting systems, one that predicted health care costs and one that predicted mortality [39]. The two weighting systems of the CDS essentially produced the same result as the simple disease count; therefore, for ease of interpretation and adaptability to clinical scenarios, we chose to present the results utilizing simple disease counts.

### 2.3. Outcomes examined

In this study, we examined five different outcomes. The continuous outcomes included the SCL-20, the MCS, and the QOL. All were assessed at baseline, 3, 6 and 12 months. The dichotomous outcomes included complete remission of depressive symptoms (SCL score <0.5) [40] and treatment response ( $\geq 50\%$  decrease in SCL-20 from baseline). Remission was assessed at all four time points while

Table 1  
Patient characteristics

Sample characteristics	All (N=1801)	Usual care (n=895)	Intervention (n=906)	Group test P value
Female	1168 (64.9)	587 (65.6)	581 (64.1)	.52
Mean (S.D.) age, years	71.2 (7.5)	71.4 (7.6)	71.0 (7.4)	.33
Marital status				.23
Married or living with partner	834 (46.3)	432 (48.3)	401 (44.3)	
Divorced/separated/never married	521 (28.9)	248 (27.7)	273 (30.1)	
Widowed	446 (24.8)	215 (24.0)	232 (25.6)	
Ethnic background				.16
Caucasian/White	1388 (77.1)	679 (75.9)	709 (78.2)	
African American/Black	222 (12.3)	108 (12.1)	114 (12.6)	
Other	191 (10.6)	107 (12.0)	83 (9.2)	
Education				.34
Less than high school graduate	347 (19.2)	170 (18.9)	177 (19.5)	
High school graduate or GED	408 (22.7)	209 (23.4)	199 (22.0)	
Some college	637 (35.4)	327 (36.6)	309 (34.2)	
College graduate/graduate degree	409 (22.7)	189 (21.1)	221 (24.3)	
Depression status (SCID diagnosis)				.35
Major depression	306 (17.0)	146 (16.3)	160 (17.7)	
Dysthymia	542 (30.1)	283 (31.6)	259 (28.6)	
Major depression and dysthymia	953 (52.9)	466 (52.1)	487 (53.7)	
Two or more prior episodes of depression	1274 (70.7)	632 (70.6)	642 (70.9)	.90
Mean (S.D.) SCL-20 depression score (range, 0–4)	1.7 (0.6)	1.7 (0.6)	1.7 (0.6)	.75
Positive result on anxiety screener	518 (28.7)	260 (29.0)	258 (28.5)	.79
Mean (S.D.) NEO neuroticism scale	22.5 (5.2)	22.5 (5.3)	22.5 (5.2)	.88
Mean (S.D.) physical component score (PCS-12)	40.3 (7.4)	40.1 (7.4)	40.4 (7.4)	.35
Any depression treatment in lifetime	1189 (66.0)	577 (64.5)	611 (67.5)	.19

Values are N (%) unless otherwise indicated.

The numbers presented in this table are based on the multiple imputed data sets and are subject to rounding discrepancies.

response is only examined at the three follow-up time points because it reflects a change at each point from baseline.

#### 2.4. Analyses

We conducted *t* tests or chi-square tests to compare demographic and clinical characteristics of intervention and usual-care patients at baseline (Table 1) and to compare frequency of chronic medical illnesses between the groups (Table 2). Analysis of variance was used to test the association between the numbers of medical comorbidities and depression status by diagnosis. For all continuous outcome variables, we fit linear mixed-effects models (PROC MIXED in SAS) including fixed and random effects. In all of the mixed-effects models, we treated time as a categorical variable, and we used an unstructured covariance to account for the within-subject correlation over time. Unadjusted models simply included the fixed effects of time, treatment group, number of chronic diseases as well as all two-way and the three-way interaction term. We used predicted values from the model to examine the relationship between treatment group, number of chronic diseases and time. We plotted expected SCL-20, MCS-12 and QOL trajectories for

patients with either two or five chronic diseases, as these represented the first and third quartiles of this variable. Adjusted models included a number of other covariates of interest, including site, age, race, gender, education, marital status, type of depression, anxiety, NEO neuroticism score, physical component score of the SF12 (PCS-12) and any depression treatment in lifetime. For each of these covariates we explored their interactions with time and included those higher-level terms if they were statistically significant.

For the two dichotomous outcomes, we utilized a population-average generalized estimating equation (GEE) model, with an unstructured covariance matrix. Similar to the mixed-effects models, we ran both unadjusted and adjusted models. Adjusted models included the baseline effects of age, race, gender, education, marital status, type of depression, anxiety, NEO neuroticism score, PCS-12 and any depression treatment in lifetime. All GEE models were fit using PROC GENMOD in SAS version 8.2 (SAS Institute, Cary, NC).

In this study, missing data occurred at both the item and subject level. We used an extended hot deck multiple imputation technique that modifies the predictive mean matching method to impute item-level missing data [41–43]. Rates of item-level missing data were less than 2% for all variables discussed in this paper. Although there were no significant differences in the completion rate of follow-up interviews between the intervention and usual-care groups, we found somewhat different predictors of follow-up response in intervention and usual-care patients. We used an approximate Bayesian bootstrap multiple imputation method [44] to impute subject-level missing data at baseline and each follow-up. Imputations were conducted separately in the intervention and usual-care groups. Using Rubin's [43] rules, the results across five imputed data sets were combined by averaging, and standard errors were adjusted to reflect both within-imputation variability and between-imputation variability.

Table 2  
Self-report of chronic medical conditions treated or diagnosed within past 3 years

	Usual care <sup>a</sup>	Intervention <sup>a</sup>	<i>P</i> value <sup>b</sup>
Mean number of comorbidities <sup>c</sup> (S.D.)	3.8 (1.9)	3.7 (1.9)	.65
Asthma, emphysema or chronic bronchitis	188 (21.0)	232 (25.6)	.02
High blood pressure or hypertension	516 (57.6)	527 (58.2)	.82
High blood sugar or diabetes	214 (23.9)	204 (22.5)	.50
Arthritis or rheumatism	495 (55.4)	506 (55.8)	.83
Loss of hearing or vision	511 (57.1)	484 (53.4)	.12
Cancer diagnosed or treated in the last 3 years (excluding skin cancer)	47 (5.3)	58 (6.4)	.31
A neurological condition such as epilepsy, seizures, Parkinson's disease or stroke	67 (7.5)	84 (9.3)	.18
Heart disease such as angina, heart failure or valve problems	261 (29.1)	236 (26.0)	.15
Chronic back problems, headache or other chronic pain problems	517 (57.7)	506 (55.9)	.43
Stomach ulcer, chronic inflamed bowel, enteritis or colitis	197 (22.0)	180 (19.9)	.28
Chronic problems with urination, chronic bladder infections (prostate problems), incontinence or inability to hold your urine	349 (39.0)	348 (38.5)	.80

<sup>a</sup> Unless otherwise indicated, data reported are the percentage of usual care (intervention) subjects having the specified comorbidity.

<sup>b</sup> Comparing differences across intervention conditions for multiple imputed data sets.

<sup>c</sup> Number of comorbidities excludes cancer if it was skin cancer.

### 3. Results

The enrolled sample of 1801 patients was ethnically and clinically diverse (Table 1). The majority of patients had suffered from two or more prior episodes of depression in the past and had received depression treatment in the past. Evaluation of intervention and control groups demonstrated no statistically significant difference between the two groups at baseline. On average, patients suffered from 3.8 chronic medical conditions, in addition to depression (Table 2). The average number comorbidities for those with major depression only, dysthymia only and major depression and dysthymia was 3.4, 3.6 and 3.9, respectively ( $P < .0001$ ). More than 50% of patients suffered from high blood pressure, arthritis, loss of hearing or vision, or chronic pain. Although the overall mean number of comorbidities was equivalent between intervention and control patients, intervention patients were more likely to suffer from lung disease in the past 3 years.

Table 3  
Clinical outcomes

	Unadjusted model estimates				Adjusted analysis for intervention vs. usual care			
	Usual care		Intervention		Between-group difference		T	P value <sup>c</sup>
	Number of comorbidities		Number of comorbidities		Number of comorbidities			
	Low	High	Low	High	Low <sup>a</sup>	High <sup>b</sup>		
SCL-20 depression score (range, 0–4)								
Baseline	1.57	1.75	1.62	1.73	0.02	−0.01	−0.74	.46
3-Month follow-up	1.34	1.54	1.11	1.23	−0.25	−0.29	−0.39	.69
6-Month follow-up	1.10	1.28	0.87	0.98	−0.25	−0.29	−0.23	.82
12-Month follow-up	1.29	1.46	0.90	1.06	−0.40	−0.38	0.76	.45
MCS-12 (SF12 mental health component score)								
Baseline	42.49	41.93	42.74	42.13	0.42	0.30	−0.24	.81
3-Month follow-up	44.45	44.38	46.04	45.82	1.63	1.43	−0.11	.91
6-Month follow-up	45.13	45.07	45.76	45.10	0.56	0.09	−0.51	.61
12-Month follow-up	45.03	44.56	46.55	45.90	1.57	1.29	−0.21	.83
Overall QOL in past month (range, 0–10)								
Baseline	5.70	5.08	5.50	5.24	−0.16	0.16	2.28	.02
3-Month follow-up	6.10	5.49	6.56	5.97	0.49	0.48	−1.65	.10
6-Month follow-up	6.17	5.57	6.51	6.00	0.35	0.42	−1.31	.19
12-Month follow-up	6.15	5.92	6.80	6.40	0.67	0.47	−2.58	.01

Linear mixed-effects regression was used to fit all models presented in this table. Number of comorbidities is a simple count of chronic medical conditions in the past 3 years excluding cancer if the type of cancer was skin. In the adjusted analysis, additional covariates included site, age, race, gender, education, marital status, type of depression, anxiety, NEO neuroticism score, PCS-12 and any depression treatment in lifetime.

<sup>a</sup> Estimate of treatment group difference for low comorbidities; note that low number of comorbidities is defined in this table as the first quartile, which is two chronic medical conditions.

<sup>b</sup> Estimate of treatment group difference for high comorbidities; note that high number of comorbidities is defined in this table as the third quartile, which is five chronic medical conditions.

<sup>c</sup> Represents the test at each time point of whether the treatment group differences are the same for different numbers of comorbidities. (This is not a test of treatment group differences for the specific levels of two and five chronic medical conditions.)

### 3.1. Clinical outcomes

Table 3 presents unadjusted and adjusted model results for all continuous outcome variables. Adjusted models operationalize the covariates as they are reported in Table 1. Site is operationalized as a categorical variable with eight levels. At baseline, patients with higher numbers of chronic

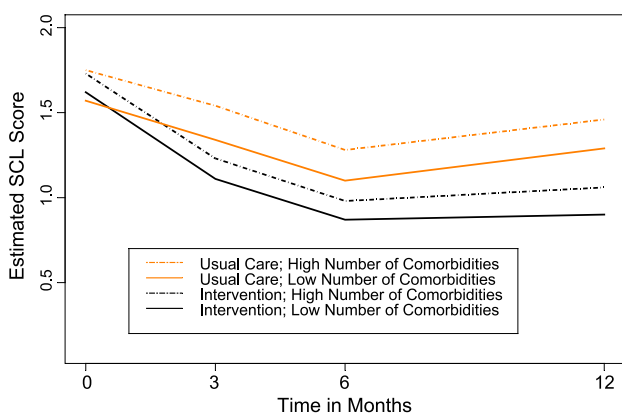


Fig. 1. Estimated mean SCL-20 scores over time for subjects receiving usual care with high and low numbers of comorbidities and for subjects receiving intervention with high and low numbers of comorbidities. High number of comorbidities is defined as the third quartile, which is five chronic medical conditions. Low number of comorbidities is defined as the first quartile, which is two chronic medical conditions.

diseases had worse predicted depression severity (measured by SCL-20 depression scores) than those with fewer chronic diseases ( $P < .01$ ). The number of chronic diseases, however, did not alter the change in depression severity over time. Regardless of the number of chronic diseases, intervention patients had significantly lower depression severity during all follow-up assessments ( $P < .001$ ) as compared with patients in usual care. This is graphically demonstrated in Fig. 1 (unadjusted results) where within treatment groups, the two comorbid illness groups have parallel trajectories. These results were similar to the adjusted model. Columns 1 and 2 in Table 3 demonstrate that in the adjusted analysis, intervention vs. control differences were essentially the same for those with low vs. high numbers of comorbidities. A subgroup analysis evaluating the potential impact of gender upon outcome demonstrated that males and females followed similar patterns over time (results not shown).

The effects of individual comorbid illnesses were examined in separate models (results not shown). Although the presence of arthritis, urologic problems, lung disease, chronic pain and diabetes were associated with worse depression scores at baseline, the presence or absence of these chronic illnesses did not alter the expected change in SCL-20 score over time.

This relationship between number of comorbid medical illnesses and the MCS-12 score was also evaluated (Table 3).

Table 4  
Clinical outcomes

	Expected probabilities — unadjusted model				Adjusted analysis for intervention vs. usual care			
	Usual care		Intervention		Between-group difference			
	Number of comorbidities		Number of comorbidities		Number of comorbidities		<i>T</i>	<i>P</i> value <sup>c</sup>
	Low	High	Low	High	Low <sup>a</sup>	High <sup>b</sup>		
Complete remission of depression symptoms (SCL-20 score <0.5)								
3-Month follow-up	0.07	0.03	0.18	0.14	3.03	5.58	1.22	.22
6-Month follow-up	0.20	0.14	0.31	0.29	1.94	2.65	0.91	.36
12-Month follow-up	0.11	0.06	0.28	0.23	3.37	5.26	1.06	.29
Response (at least 50% decrease in SCL-20 depression score from baseline)								
3-Month follow-up	0.17	0.13	0.32	0.31	2.38	3.02	1.10	.27
6-Month follow-up	0.33	0.29	0.52	0.47	2.15	2.20	−0.76	.45
12-Month follow-up	0.22	0.17	0.49	0.41	3.43	3.49	−0.74	.46

Generalized estimating equation was used to fit all models presented in this table. Number of comorbidities is a simple count of chronic medical conditions in the past 3 years excluding cancer if the type of cancer was skin. In the adjusted analysis, additional covariates included site, age, race, gender, education, marital status, type of depression, anxiety, NEO neuroticism score, PCS-12, and any depression treatment in lifetime.

<sup>a</sup> Odds ratio of treatment group difference for low comorbidities; note that low number of comorbidities is defined in this table as the first quartile, which is two chronic medical conditions.

<sup>b</sup> Odds ratio of treatment group difference for high comorbidities; note that high number of comorbidities is defined in this table as the third quartile, which is five chronic medical conditions.

<sup>c</sup> Represents the test at each time point of whether the treatment group differences are the same for different numbers of comorbidities. (This is not a test of treatment group differences for the specific levels of two and five chronic medical conditions.)

Similar to the SCL-20 results, the number of comorbid illnesses had little impact on MCS-12 scores over time. Patients within the intervention group experienced improved MCS-12 scores as compared with those in the usual-care group, regardless of the number of comorbidities, at 3 and 12 months.

For QOL, patients with higher numbers of chronic disease had worse QOL (lower scores) at baseline as compared with those with fewer comorbid illnesses (Table 3). Again, the number of comorbid illnesses did not alter the intervention vs. usual-care effect. Over time, intervention patients experienced greater improvement in QOL as compared with usual-care patients, regardless of the number of chronic diseases.

Table 4 presents analysis results from the dichotomous clinical outcomes. Intervention patients experienced greater rates of depression remission (defined as SCL-20 score <0.5) and response (defined as at least 50% decrease in SCL-20 score from baseline) regardless of the number of comorbidities. These differences held over the 12-month follow-up period (Table 4). Absolute rates of response and remission in patients were lower in patients with more vs. less comorbid illness. These trends were similar in both the usual care and intervention group.

To address the question of whether or not some of the items that comprise the SCL-20 are in fact measuring symptoms that should be attributed to medical illness instead of depression severity, for example, poor appetite, sleep disturbance and fatigue, we created two modified SCL scores, one which excluded 7 of the 20 items that addressed potential physical complaints, and another which excluded 3, and built unadjusted and adjusted models using the modified SCL scores (results not

shown). Although the differences between patients with fewer vs. more comorbidities were not as striking when using the modified SCL score, the results were still statistically significant and similar to those seen with the original SCL score.

### 3.2. Intensity of intervention

In order to determine whether it took more intervention resources to improve treatment outcomes for patients with more severe medical illness, we compared the measured number of phone visits, number of clinic visits, and number of phone and clinic visits combined to the DCS. Intervention patients averaged 15.3 total visits, with a mean of 9.2 clinic and 6.1 phone visits. The association between the number of comorbid illnesses and the “dose” of the intervention was examined graphically and analytically through Spearman correlations (results not shown). The Spearman correlations between number of chronic diseases and total number of visits, clinic visits, and phone visits were 0.03, −0.03 and 0.06, respectively.

## 4. Discussion

This study demonstrates that a multidisciplinary disease management program for depression in older adults was equally effective for patients with and without multiple chronic comorbid medical diseases. As expected, at baseline, individuals with more chronic medical illnesses had higher rates of depression and lower QOL in both the intervention and control groups. Regardless of the number of chronic diseases, however, depressed individuals who were randomized to the IMPACT intervention program experienced similar rates of response to depression

treatment and remission from depressive symptoms, improved mental health and improved QOL as compared with those in usual care.

This finding is important in that both depression and comorbid medical disorders frequently coexist in the elderly population. It is estimated that 88% of people aged 65 years and older suffer from one or more chronic medical illnesses, and that 25% of them will suffer from more than four chronic diseases [45]. Moreover, comorbid medical illness has been associated with higher rates of depression. A recent longitudinal community-based study in Canada found that 4% of individuals with any long-term medical condition developed major depression, as compared with 2.8% of those without medical conditions [46]. Others [47] have demonstrated that people suffering from one of eight medical disorders had a 41% increase in the risk of having any recent psychiatric disorder compared with those without chronic medical disorders, and that on average, patients with depression suffered from two chronic medical conditions [48].

As compared with many prior studies in which patients with comorbid conditions were excluded [16], patients in this cohort suffered from a mean of 3.8 comorbid illnesses, with 97% of patients having at least one comorbid disease. Moreover, more than 50% of patients suffered from either arthritis, loss of hearing or vision, or chronic pain, suggesting that this population was significantly disabled, and thus fairly representative of older adults in typical primary care practices.

The relationship between comorbid medical illness and depression is complex. Medical illness can induce mood disorders through biological pathways, psychosocial stressors and disability. Patients with specific diseases, such as diabetes, coronary artery disease, stroke, cancer, Parkinson's disease and HIV are at increased risk of developing major depression [49–57]. Conversely, depression may also function as an etiologic factor in the onset and course of medical illness, including cardiovascular disease [7–9,58], diabetes [59] and stroke [60–62].

In this cohort, patients with more comorbidities had significantly worse depression at baseline. This is consistent with the conclusions of others that the effects of depression and medical conditions are additive [4,63,64], as both can adversely affect symptom burden, functioning and QOL. Therefore, although patients with multiple comorbid diseases received the same relative benefit from the quality improvement effort, at the end of the intervention, their depression severity, although improved from baseline, was worse than those without as many comorbid illnesses.

The improvement in depression severity realized by patients with multiple comorbid diseases does not appear to have required more intensive intervention on behalf of the DCS. The number of visits with the treating DCS was no different for those with more vs. less comorbid illnesses. This is consistent with the finding of Koike et al [17] who found that depressed patients with comorbid medical illness

tended to have similar rates of treatment but worse depression outcomes than depressed patients without comorbid medical illness.

This finding raises several questions. For example, do patients with multiple comorbid diseases require a more intense intervention for treating depression, or alternatively do they need an intervention that targets treatment not only of their depression but also of their comorbid diseases? In this study, the team treating the patient did attempt to consider other medical factors that were contributing to the patient's depression, and the DCS's were trained in the relationship between chronic pain and depression. However, there were no specific protocols for treating patients with coexisting comorbid diseases.

A potential limitation of this study is our reliance on self-reports of chronic medical conditions. Prior research has suggested that comorbidity can be reasonably measured by questionnaire rather than by medical record review [65]. We also do not have any reason to believe that reporting inaccuracies would differ between those randomized to usual care vs. intervention.

In summary, elderly patients with depression often suffer from multiple comorbid medical conditions. Research suggests that the presence of depression can adversely affect morbidity (i.e., symptom burden, functioning and QOL) and mortality from medical illnesses, and that the combined effects of medical and psychiatric comorbidities are greater than the sum of the effects of the individual illnesses. Effective treatment of these individuals will require attention to not only their medical illnesses but also to their depression. This study demonstrates that a disease management intervention like the one employed in Project IMPACT is successful at improving depression severity in older patients with and without significant comorbid diseases and provides evidence that diagnosing and treating depression in older adults with multiple chronic diseases is both feasible and effective. What remains to be answered is how best to treat patients who suffer from both depression and comorbid diseases so as to experience similar rates of response and remission as seen in those with less comorbidities. In this study, patients received the same intensity of services regardless of their baseline comorbidity status. New research should answer the question if either a more intensive depression care management intervention or one that addresses physical and psychological health could lead to better outcomes in this comorbid group.

### Acknowledgment

This study is supported by grants from the John A. Hartford Foundation, the California Healthcare Foundation, the Hogg Foundation, and the Robert Wood Johnson Foundation.

We would like to acknowledge the contributions and support of patients, primary care providers and staff at the

study coordinating center and at all participating study sites, which include Duke University, Durham, NC; The South Texas Veterans Health Care System, The Central Texas Veterans Health Care System and The San Antonio Preventive and Diagnostic Medicine Clinic; Indiana University School of Medicine, Indianapolis, IN; Health and Hospital Corporation of Marion County; Group Health Cooperative of Puget Sound in cooperation with the University of Washington, Seattle, WA; Kaiser Permanente of Northern California, Oakland and Hayward, CA; Kaiser Permanente of Southern California, San Diego, CA; Desert Medical Group, Palm Springs, CA. This study is the result of work supported in part with patients, resources and the use of facilities at the South Texas Veterans Health Care System and the Central Texas Veterans Health Care System. The views expressed in this paper are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs.

We would also like to acknowledge the contributions of IMPACT study advisory board (Lisa Goodale, A.C.S.W., Richard C. Birkel Ph.D., Howard Goldman, M.D., Ph.D., Thomas Oxman, M.D., Lisa Rubenstein, M.D., M.S.P.H., Cathy Sherbourne Ph.D., Kenneth Wells M.D., M.P.H.) and programming support by Tonya Marmon, M.S.

## Appendix A

The IMPACT Investigators include (in alphabetical order): Patricia Arean, Ph.D. (Co-PI); Thomas R. Belin, Ph.D.; Noreen Bumby, D.O.; Christopher Callahan, M.D. (PI); Paul Ciechanowski, M.D., M.P.H.; Ian Cook, M.D.; Jeffrey Cordes, M.D.; Steven R. Counsell, M.D.; Richard Della Penna, M.D. (Co-PI); Jeanne Dickens, M.D.; Michael Getzell, M.D.; Howard Goldman, M.D., Ph.D.; Lydia Grypma, M.D. (Co-PI); Linda Harpole, M.D., M.P.H. (PI); Mark Hegel, Ph.D.; Hugh Hendrie, M.B., Ch.B., D.Sc. (Co-PI); Polly Hitchcock Noel, Ph.D. (Co-PI); Marc Hoffing, M.D. (PI), M.P.H.; Enid M. Hunkeler, M.A. (PI); Wayne Katon, M.D. (PI); Kurt Kroenke M.D.; Stuart Levine, M.D., M.H.A. (Co-PI); Elizabeth H.B. Lin, M.D., M.P.H. (Co-PI); Tonya Marmon, M.S.; Eugene Oddone, M.D., M.H.Sc. (Co-PI); Sabine Oishi, M.S.P.H.; R. Jerome Rauch, M.D.; Michael Sands, M.D.; Michael Schoenbaum, Ph.D.; Rik Smith, M.D.; David C. Steffens, M.D., M.H.S.; Christopher A. Steinmetz, M.D.; Lingqi Tang, Ph.D.; Iva Timmerman, M.D.; Jürgen Unützer, M.D., M.P.H. (PI); John W. Williams Jr., M.D., M.H.S. (PI); Jason Worchel, M.D.; Mark Zweifach, M.D.

## References

- [1] Oxman TE, Barrett JE, Barrett J, et al. Symptomatology of late-life minor depression among primary-care patients. *Psychosomatics* 1990;31:174–80.
- [2] Lyness JM, Caine ED, King DA, et al. Psychiatric disorders in older primary care patients. *J Gen Intern Med* 1999;14:249–54.
- [3] Schulberg HC, Katon WJ, Simon GE, et al. Best clinical practice: guidelines for managing major depression in primary medical care. *J Clin Psychiatry* 1999;60(Suppl 9):19–26.
- [4] Wells KB, Stewart A, Hays RD, et al. The functioning and well-being of depressed patients. Results from the medical outcomes study. *JAMA* 1989;262:914–9.
- [5] Simon GE, VonKorff M, Barlow W. Health care costs of primary care patients with recognized depression. *Arch Gen Psychiatry* 1995;52(10):850–6.
- [6] Steffens DC, O'Connor CM, Jiang WJ, et al. The effect of major depression on functional status in patients with coronary artery disease. *J Am Geriatr Soc* 1999;47:319–22.
- [7] Peterson JC, Charlston ME, Williams-Russo P, et al. New postoperative depressive symptoms and long-term cardiac outcomes after coronary artery bypass surgery. *Am J Geriatr Psychiatry* 2002;10:192–8.
- [8] Lesperance F, Frasure-Smith N, Juneau M, Theroux P. Depression and 1-year prognosis in unstable angina. *Arch Intern Med* 2000;160:1354–60.
- [9] Penninx B, Beekman A, Honig A, et al. Depression and cardiac mortality: results from a community-based longitudinal study. *Arch Gen Psych* 2001;58(3):221–7.
- [10] Musselman DL, Evans DL, Nemeroff CB. The relationship of depression to cardiovascular disease. *Arch Gen Psychiatry* 1998;55:580–92.
- [11] Van Tilburg MAL, McCaskill CC, Lane JD, et al. Depressed mood is a factor in glycemic control in type 1 diabetes. *Psychosom Med* 2001;63(4):551–5.
- [12] Roose SP, Glassman AH, Seidman SN. Relationship between depression and other medical illnesses. *JAMA* 2001;286(14):1687–90.
- [13] Callahan CM, Hendrie HC, Dittus RS, Brater DC, Hui SL, Tierney WM. Improving treatment of late life depression in primary care: a randomized clinical trial. *J Am Geriatr Soc* 1994;42(8):839–46.
- [14] Sheikh JI, Cassidy EL, Doraiswamy PM, et al. Efficacy, safety, and tolerability of sertraline in patients with late-life depression and comorbid medical illness. *J Am Geriatr Soc* 2004;52:86–92.
- [15] Williams JW, Mulrow CD, Chiquette E, et al. A systematic review of newer pharmacotherapies for depression in adults: evidence report summary. *Ann Intern Med* 2000;132:743–56.
- [16] Brown C, Schulberg HC. Diagnosis and treatment of depression in primary medical care practice: the application of research findings to clinical practice. *J Clin Psychol* 1998;54:303–14.
- [17] Koike AK, Unützer J, Wells KB. Improving the care for depression in patients with comorbid medical illness. *Am J Psychiatry* 2002;159:1738–45.
- [18] Katon W, Russo J, Frank E, et al. Predictors of nonresponse to treatment in primary care patients with dysthymia. *Gen Hosp Psychiatry* 2002;24:20–7.
- [19] Cole MG, Bellevance F, Mansour A. Prognosis of depression in elderly community and primary care populations: a systematic review and meta-analysis. *Am J Psychiatry* 1999;156:1182–9.
- [20] Popkin MK, Callies AL, Mackenzie TB. The outcome of antidepressant use in the medically ill. *Arch Gen Psychiatry* 1985;42:1160–3.
- [21] Schulberg HC, McClelland M, Gooding W. Six-month outcomes for medical patients with major depressive disorders. *J Gen Intern Med* 1987;2:312–7.
- [22] Unützer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in the primary care setting. A randomized controlled trial. *JAMA* 2002;288:2836–45.
- [23] Unützer J, Katon W, Williams JW, et al. Improving primary care for depression in late life: the design of a multicenter randomized trial. *Med Care* 2001;38:785–99.
- [24] Williams JB, Gibbon M, First MB, et al. The structured clinical interview for *DSM-III-R* (SCID): multisite test–retest reliability. *Arch Gen Psychiatry* 1992;49:630–6.

- [25] First MB, Spitzer RL, Gibbon M, et al. *Structured Clinical Interview for DSM-IV Axis I Disorders (SCID)*. Washington (DC): American Psychiatry Press, Inc; 1996.
- [26] Mayfield D, McLeod G, Hall P. The CAGE questionnaire: validation of a new alcoholism screening instrument. *Am J Psychiatry* 1974;131:1121–3.
- [27] Callahan CM, Unverzagt FW, Hui SL, et al. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med Care* 2002;40:771–81.
- [28] Hegel MT, Barret JE, Oxman TE, et al. *Problem-solving treatment for primary care (PST-PC): a treatment manual for depression*. Hanover (NH): Dartmouth University; 1999.
- [29] Arean P, Hegel M, Unutzer J. *Problem-solving therapy for older primary care patients: maintenance group manual for Project IMPACT*. Los Angeles: University of California; 1999.
- [30] Arean P, Hegel M, Unutzer J. *Problem-solving treatment in primary care: addendum to PST-PC treatment manual for Project IMPACT*. Los Angeles: University of California; 1999.
- [31] Hegel MT, Barrett JE, Oxman TE. Training therapists in problem-solving treatment of depressive disorders in primary care: lessons learned from the treatment effectiveness project. *Fam Syst Health* 2000;18:133–45.
- [32] Mynors-Wallis LM, Gath DH, Day A, Baker F. Randomized controlled trial of problem solving treatment, antidepressant medication, and combined treatment for major depression in primary care. *BMJ* 2000;320:26–30.
- [33] Derogatis LR, Lipman RS, Covi L. SCL-90: an outpatient psychiatric rating scale. *Psychopharmacol Bull* 1973;9:13–28.
- [34] Ware Jr J, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220–33.
- [35] Rush AJ, Giles DE, Schlessner MA, Fulton CL, Weissenburger J, Burns C. The Inventory for Depressive Symptomatology (IDS): preliminary findings. *Psychiatry Res* 1986;18(10):65–87.
- [36] Costa PT, McCrae RR. *The NEO Personality Inventory Manual*. Odessa (Fla): Psychological Assessment Resources; 1985.
- [37] Von Korff M, Wagner EH, Saunders K. A chronic disease score from automated pharmacy data. *J Clin Epidemiol* 1992;45:197–203.
- [38] Clark DO, Von Korff M, Saunders K, et al. A chronic disease score with empirically derived weights. *Med Care* 1995;33(8):783–95.
- [39] Perkins AJ, Kroenke K, Unutzer J, Katon W, et al. Measuring comorbidity: predictive validity of common measures in a cohort of older adults. *J Clin Epidemiol* 2004 [in press].
- [40] Simon GE, Katon WJ, Von Korff M, et al. Cost-effectiveness of a collaborative care program for primary care patients with persistent depression. *Am J Psychiatry* 2001;158:1639–44.
- [41] Little RJ. Missing data adjustments in large surveys. *J Bus Econ Stat* 1988;6:287–301.
- [42] Bell R. Presentation at Depression PORT Methods Workshop (I). Santa Monica (Calif): Rand; 1999.
- [43] Rubin DB. *Multiple imputation for non-response in surveys*. New York (NY): John Wiley & Sons; 1987.
- [44] Lavori P, Dawson R, Shera D. A multiple imputation strategy for clinical trials with truncation of patient data. *Stat Med* 1995;14:1913–25.
- [45] Hoffman C, Rice D, Sung H. Persons with chronic conditions. Their prevalence and costs. *JAMA* 1996;276:1473–9.
- [46] Patten S. Long-term medical conditions and major depression in a Canadian population study at waves 1 and 2. *J Affect Disord* 2001;63:35–41.
- [47] Wells KB, Golding JM, Burnam MA. Psychiatric disorder in a sample of the general population with and without medical disorder. *Am J Psychiatry* 1988;145:976–81.
- [48] Wells KB, Rogers W, Burnam A, et al. How the medical comorbidity of depression patients differs across health care settings: results from the medical outcomes study. *Am J Psychiatry* 1991;148:1688–96.
- [49] Anderson RJ, Freeland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 2001;24:1069–78.
- [50] Gonzalez M, Snyderman T, Colket J, et al. Depression in patients with coronary artery disease. *Depression* 1996;4:57–62.
- [51] Rugulies R. Depression as a predictor for coronary heart disease: a review and meta-analysis. *Am J Prev Med* 2002;23:51–61.
- [52] Schleifer S, Macari-Hinson M, Coyle D, et al. The nature and course of depression following myocardial infarction. *Arch Intern Med* 1989;149:785–9.
- [53] Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry* 2001;158:725–30.
- [54] Frasure-Smith N, Lesperance F, Talajic M. Depression following myocardial infarction: impact on 6-month survival. *JAMA* 1993;1819–25.
- [55] Whyte E, Mulsant B. Post-stroke depression: epidemiology, pathophysiology and biological treatment. *Biol Psychiatry* 2002;52:253–64.
- [56] Schrag A, Jahanshahi M, Quinn N. What contributes to depression in Parkinson's disease? *Psychol Med* 2001;31:65–73.
- [57] Mayeux R, Williams J, Stern Y, Cote L. Depression and Parkinson's disease. *Adv Neurol* 1984;40:241–51.
- [58] Ferketich AK, Schwartzbaum JA, Frid DJ, et al. Depression as an antecedent to heart disease among women and men in the NHANES I Study. *Arch Intern Med* 2000;160:1261–8.
- [59] Ciechanowski P, Katon W, Russo J, Hirsch I. The relationship of depressive symptoms to symptom reporting, self-care and glucose control in diabetes. *Gen Hosp Psychiatry* 2003;25:246–52.
- [60] Simonsock EM, Wallace RB, Blazer DG, Berkman LF. Depressive symptomatology and hypertension-associated morbidity and mortality in older adults. *Psychosom Med* 1995;57:427–35.
- [61] Morris PLP, Robinson RG, Adrzejewski P, et al. Association of depression with 10-year poststroke mortality. *Am J Psychiatry* 1993;150:124–9.
- [62] Robinson RG, Kubos KL, Starr LB, et al. Mood changes in stroke patients: relationship to lesion location. *Compr Psychiatry* 1993;24:555–66.
- [63] Ormel J, Kempen G, Deeg JH, et al. Functioning, well-being, and health perception in late middle-aged and older people: comparing the effects of depressive symptoms and chronic medical conditions. *J Am Geriatr Soc* 1998;46:39–48.
- [64] Berardi B, Menchetti M, De Ronchi D, et al. Late-life depression in primary care: a nationwide Italian epidemiological survey. *J Am Geriatr Soc* 2002;50:77–83.
- [65] Katz JM, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Med Care* 1996;34:73–84.