Available online at www.sciencedirect.com
SCIENCE DIRECT
General Hospital Psychiatry 27 (2005) 237–243
General Hospital Psychiatry

Medical illness and response to treatment in primary care panic disorder

Peter Roy-Byrne, M.D.[a,*], Murray B. Stein, M.D., M.P.H.[b,c], Joan Russo, Ph.D.[a], Michelle Craske, Ph.D.[d], Wayne Katon, M.D.[e], Greer Sullivan, M.D., M.S.P.H.[f,g], Cathy Sherbourne, M.D.[h]

[a]*Department of Psychiatry and Behavioral Science, University of Washington School of Medicine at Harborview Medical Center, WA 98104, USA*
[b]*Department of Psychiatry, University of California, San Diego, CA, USA*
[c]*Department of Family and Preventive Medicine, University of California, San Diego, CA, USA*
[d]*Department of Psychology, University of California, Los Angeles, CA, USA*
[e]*Department of Psychiatry and Behavioral Science, University of Washington School of Medicine, Seattle, WA 98104, USA*
[f]*VA South Central Mental Illness Research Education and Clinical Center (MIRECC), Little Rock, AR, USA*
[g]*University of Arkansas for Medical Science, Little Rock, AR, USA*
[h]*The RAND Corporation, Santa Monica, CA, USA*

Received 9 February 2005; received in revised form 16 March 2005; accepted 21 March 2005

Abstract

Objective: Although studies have suggested that comorbid medical illness can affect the outcome of patients with depression, little is known about whether medical illness comorbidity affects treatment outcome in patients with anxiety.
Method: Primary care patients with panic disorder ($n=232$), participating in a randomized collaborative care intervention of CBT and pharmacology, were divided into those above ($n=125$) and below ($n=107$) the median for burden of chronic medical illness and assessed at 3, 6, 9 and 12 months.
Results: Subjects with a greater burden of medical illness were more psychiatrically ill at baseline, with greater anxiety symptom severity, greater disability and more psychiatric comorbidity. The intervention produced significant and similar increases in amount of evidence-based care, and reductions in clinical symptoms and disability that were comparable in the more and less medically ill groups.
Conclusions: The comparable response of individuals with more severe medical illness suggests that CBT and pharmacotherapy for panic disorder work equally well regardless of medical illness comorbidity. However, the more severe psychiatric illness both at baseline and follow-up in these same individuals suggest that treatment programs may need to be extended in time to optimize treatment outcome.

Keywords: Panic disorder; Medical illness; Outcome; Primary care

1. Introduction

Accumulating evidence over the past decade has documented important associations between specific medical illnesses and major depression. Studies have demonstrated an increased prevalence of major depression in a variety of chronic medical illnesses including cancer [1], cardiac disease [2], stroke [3], diabetes [4] and HIV disease [5]. Moreover, an adverse effect of comorbid major depression on the course and outcome of several of these same illnesses [6], and an association between comorbid major depression and increased medical costs [7,8], has been observed. Most recently, some [9–11], though not all [12–14], studies have suggested that comorbid medical illness severity may have an adverse impact on response to treatment in patients with major depression. Variations in type and severity of medical illness, other subject characteristics, type of treatment and mode of treatment delivery/study design (efficacy vs. effectiveness) might be accounting for some of these differences. However, despite an equally high prevalence of comorbid medical illness in patients with anxiety disorders, and evidence that anxiety disorders are associated with increased medical costs [15,16], no studies have examined the potential impact of comorbid medical illness on treatment response in patients with anxiety disorders.

* Corresponding author. Tel.: +1 206 341 4201; fax: +1 206 731 3236.
E-mail address: roybyrne@u.washignton.edu (P. Roy-Byrne).

0163-8343/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.genhosppsych.2005.03.007

The Collaborative Care for Anxiety and Panic (CCAP) study is a three site primary care study that sought to examine the clinical and cost effectiveness of a combined CBT and medication intervention compared with care as usual in six University-based primary care clinics in three West Coast cities [17,18]. Because the effectiveness design of this study allowed inclusion of subjects with a variety of medical illnesses of different severities, this study provides an opportunity to examine the association between comorbid medical illness and treatment outcome in anxiety. The effectiveness design of the study, where all patients were followed and assessed regardless of treatment uptake, also allows us to ask the secondary question of whether comorbid medical illness affected the uptake of treatment in either intervention or usual care patients. These two question are important in determining whether patients with comorbid medical illness may be more or less likely to initiate and sustain treatment for panic disorder and whether that treatment is more or less likely to be utilized and to be effective than in patients without medical comorbidity.

2. Method

2.1. Setting and subjects

Patients between the ages of 18 and 70 years, meeting *DSM-IV* criteria for panic disorder, with psychiatric and medical comorbidities that were not life threatening (i.e., suicidal ideation, terminal medical illness) or likely to interfere with participation (psychosis, dementia, severe substance abuse), were recruited from six university-affiliated primary care clinics in Seattle, San Diego and Los Angeles. The study was approved by the Institutional Review Boards of all three universities (University of Washington, University of California, Los Angeles, and University of California, San Diego).

2.2. Procedure

More detailed descriptions of the assessments and interventions for the CCAP study have been previously published [17–19]. After baseline assessment, subjects were randomized to intervention or usual care conditions. The intervention utilized a master's level behavioral health specialist (BHS) to deliver six sessions of CBT for panic disorder and related depression and anxiety symptoms [20,21], and to coordinate care, which included medication managed by the primary care physician (PCP) using a medication algorithm [22]. Specific medication recommendations for individual subjects were relayed as needed from a consulting psychiatrist to the PCP via the BHS, who informed the psychiatrist about subject clinical status and received feedback at weekly meetings. Subjects had to complete the six CBT sessions within the first 3 months of the study. Six follow-up telephone booster sessions, each lasting from 15 to 30 min, were scheduled through the rest of the year at 6- to 12-week intervals, to monitor clinical status, reinforce proper medication use and cognitive behavioral skills and make further medication recommendations if necessary. Usual care subjects received pharmacotherapy from their PCP without psychiatric consultation, and possible referral to specialty mental health providers.

Assessments were derived from telephone interviewer-administered questionnaires, queried by interviewers blind to subject intervention status, at baseline and every 3 months during the course of the study.

Medical illness comorbidity was assessed by constructing RxRisk-V scores [23] for each study participant based on their self-reports of prescription medications used during the course of the study, and from a list of self-reported chronic diseases previously used in the Partners in Care Study [24]. Rx-Risk-V scores provide a reliable and valid method for understanding the burden of chronic disease based on automated pharmacy data, age and gender [23,25]. This index does as well as other diagnosis-based measures in predicting costs of care and providing risk adjustment for chronic disease [25]. To construct the index, all medications are categorized into diagnostic categories. In 21 patients who were missing medication information, self-reported chronic disease information was utilized instead of medication to place the patient in the appropriate diagnostic category. These categories are then weighted and summed. In addition, age, gender and a constant are given weights and added to the sum. Because we were interested in medical comorbidity, diagnostic categories involving mental health were removed from the creation of the RxRisk-V score (alcohol dependence, anxiety and tension, bipolar disorder, depression, and psychotic illness).

This analysis focused on dimensional outcome measures of panic/anxiety, depression and functional disability utilizing the Anxiety Sensitivity Index (ASI) [26], a scale that measures the cognitions that underlie panic-related somatization, but is also sensitive to the frequency of recent panic attacks [27]; the CES-D, a scale measuring severity of depression [28]; and five items selected from the larger WHO Disability Scale [29]. We also measured intervention effects on subject-reported use of antianxiety pharmacotherapy (guideline-concordant antipanic medication at a sufficient dose for at least 6 weeks [22,30]) and psychotherapy (attending a minimum of three sessions that contained a minimum of four of seven key components considered characteristic of CBT [31]).

2.3. Statistical analysis

All analyses were intent-to-treat, with all randomized patients used in all analyses. The sample was dichotomized into two medical comorbidity groups based on the psychiatric diagnosis-free RxRisk-V score: RxRisk− (RxRisk-V scores below the median, $n=107$) and RxRisk+ (RxRisk-V scores above or equal to the median, $n=125$). A median split was used after consultation with the author of the RxRisk instrument because no cutoff has previously been developed for this scale and because a median split is the most effective

way to compare people within a sample. Eighteen patients had the median RxRisk-V score, resulting in the slightly uneven sample sizes in the two groups. We reran the analysis with these people in both groups and there was no difference. χ^2 with corrections for continuity and t tests were used to compare the RxRisk groups on demographics, baseline psychiatric characteristics, disability, functioning and treatment characteristics. To determine if the treatment response was modified by chronic disease comorbidity, random coefficient hierarchical models were fit to the data. Models were tested for each dependent outcome variable, the ASI, CES-D, WHO and quality of care variables for both pharmacotherapy and CBT received over the baseline, 3-, 6-, 9- and 12-month course of the study. For continuous variables, mixed effect linear regressions were used, and for the dichotomous outcomes, mixed effect ordinal regressions based on a logistic model were used. In all models, the intercept (subjects) was considered random, and all other effects were considered fixed. Time and time-squared terms were included in all models to account for the curvilinear nature of the outcome responses over time. If chronic physical disease modified the treatment effect over time, then we would expect a significant three-way interaction of RxRisk-V group by treatment group (intervention vs. controls), by time, indicating that the pattern of change in outcome over time due to the intervention depended upon level of physical comorbidity. A full model was fit containing the three-way interaction, the three two-way interactions necessary to support the three-way interaction, the main effects of time, treatment group and RxRisk-V groups, and covariates. The covariates used were those demographic factors that were significantly different between the chronic disease groups (age, gender, income, employment and categorical variables indicating study site) in order to show the independent effect of medical comorbidity. The two California sites were combined because of their similar case mix, which differed significantly from the Seattle site. In the event of a nonsignificant three-way interaction, the model was refit without the three-way interaction. Insignificant two-way interactions were eliminated individually until only significant two-way interactions were retained in the final models. In accordance with our previous reported findings [17], we expect the time by treatment group interaction to be significant in all models. No interactions of RxRisk with treatment or time would indicate that the pattern of response is not dependent upon chronic comorbidity status. In the absence of an RxRisk interaction, a significant main effect of RxRisk would indicate that the chronic disease affects the severity of outcomes, but not affect the treatment groups differentially. Post hoc t test and χ^2 with corrections for continuity were used to elucidate significant findings. Sensitivity analyses were conducted without the use of any covariates.

Table 1
Baseline characteristics of the medically comorbid groups

Characteristic	Below RxRisk, median ($N=107$)	Above RxRisk, median ($N=125$)	$\chi^2(1)$ or $t(230)$
	N (%) or mean (S.D.)	N (%) or mean (S.D.)	
Demographics			
Site			
Washington	41 (38.3)	77 (61.6)	11.59*
California	66 (61.7)	48 (38.4%)	
Women	64 (59.8)	92 (73.6)	4.37**
White	71 (66.4)	83 (66.4)	0.00
Low income	25 (23.6)	47 (37.6)	4.62***
At least some college	83 (77.6)	94 (75.2)	0.07
Employed	77 (72.0)	52 (41.6)	20.32*
Married	31 (29.2)	29 (23.2)	0.80
Age in years	33.7 (8.4)	47.7 (9.2)	11.99*
Baseline psychiatric characteristics			
Comorbid psychiatric conditions			
Social Phobia	44 (41.5)	50 (40.3)	0.03
PTSD	26 (24.5)	42 (33.6)	1.86
Depression	51 (48.1)	77 (61.6)	3.70**
CES-Depression Scale	23.1 (13.2)	31.1 (13.7)	4.49*
Full panic attack frequency	1.0 (1.9)	1.8 (4.8)	1.61
Limited symptom panic attack frequency	2.9 (4.6)	2.9 (3.6)	0.06
Anticipatory anxiety (0-4 range)	1.7 (1.2)	1.9 (1.1)	1.66
Anxiety Sensitivity Scale	31.1 (11.8)	35.3 (12.4)	2.64***
Fear Q Scale	27.7 (17.6)	38.1 (19.0)	4.32*
Agoraphobia Fear subscale	10.9 (9.6)	17.2 (11.3)	4.50*
Social Phobia Scale	16.8 (10.0)	21.0 (10.1)	3.17***
NEO Neuroticism Scale	2.2 (0.8)	2.5 (0.8)	3.03***
Baseline functioning and disability			
WHO Disability Scale	10.1 (4.2)	13.7 (4.4)	6.36*
SF-12 Physical Health Component Score	50.4 (10.3)	37.5 (12.3)	8.57*
SF-12 Mental Health Component Score	38.6 (11.5)	35.4 (10.6)	2.19**
Baseline treatment characteristics (past 3 months)			
Received any mental health specialty care	20 (18.9)	35 (28.0)	2.16
Received three or more counseling sessions with at least four CBT components	3 (2.8)	6 (4.8)	0.20
Received any appropriate antipanic medication for 6+ weeks	21 (20.0)	44 (35.2)	5.78**

* $P<.001$.
** $P<.05$.
*** $P<.01$.

3. Results

There were significant and substantial differences between subjects above (RxRisk+, $n=125$) and below (RxRisk−, $n=107$) the median chronic disease score at baseline (Table 1). Subjects with greater severity of medical illness were older, more often female, poorer, less likely to be employed and more likely to be from the Washington site. The RxRisk+ group also had significantly higher rates

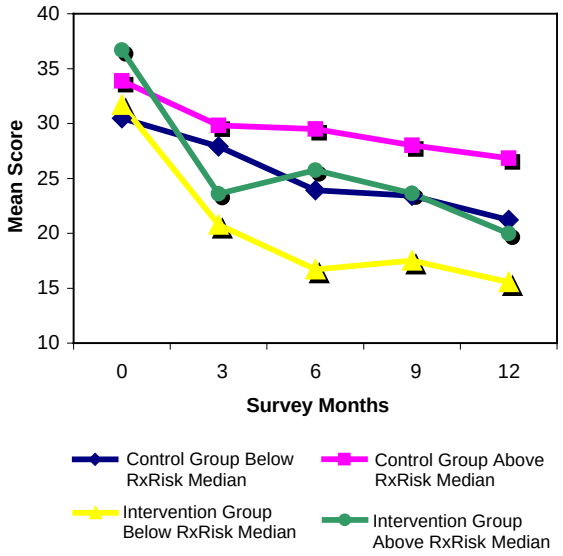

Fig. 1. Anxiety Sensitivity Index Scale by intervention and RxRisk groups.

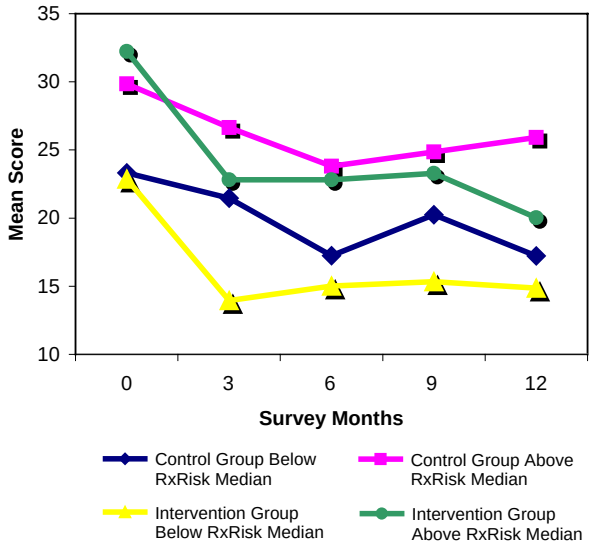

Fig. 3. CES-D Scale by intervention and RxRisk groups.

of major depression, but only slightly higher rates of PTSD and social phobia. At baseline, the RxRisk+ group also reported significantly more severe symptoms of depression, anxiety sensitivity, agoraphobia, social phobia and neuroticism, poorer physical and mental functioning on the SF-12 and greater overall disability on the WHO scale. The groups did not differ on panic attack frequency, limited symptom panic attack frequency or anticipatory anxiety. Lastly, in the 3 months prior to the study, the RxRisk+ group was more likely to receive an appropriate antipanic medication for six or more weeks than the RxRisk− group. Although the RxRisk+ group had slightly higher rates of receiving any mental health specialty care or receiving three or more counseling sessions with at least four CBT components, these differences did not reach statistical significance.

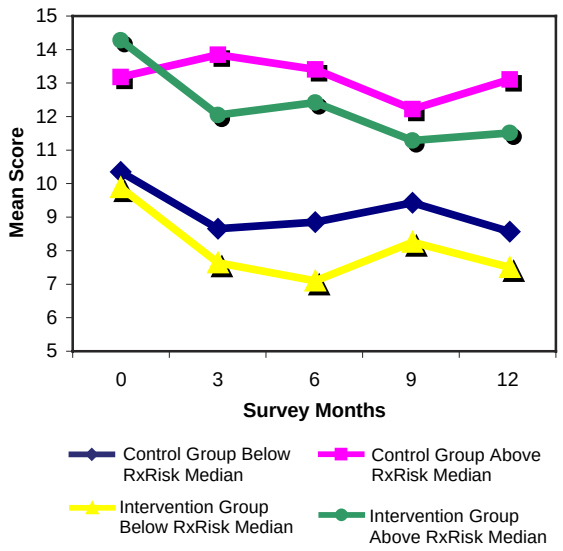

Fig. 2. WHO scale by intervention and RxRisk groups.

3.1. Outcome effects

Effects on the various outcome measures are illustrated in Figs. 1–3. Consistent with the baseline data reviewed above, the two medical illness groups significantly differed on all three measures at baseline (intercept), with more severely medically ill patients doing more poorly. Chronic disease status did not mediate the treatment effects on these measures over time (no significant three-way interactions were observed). As was previously shown [17], all the time by treatment interactions were statistically significant (significant intervention vs. control effects on anxiety sensitivity, depression and WHO disability), but there were no significant three-way interactions with RxRisk. The main effect of RxRisk was significant in all three models in the presence of the covariates: ASI (z=4.44, P=.02), CES-D (z=5.74, P=.002) and WHO Disability Total (z=1.89, P<.001). Removing the covariates (age, gender,

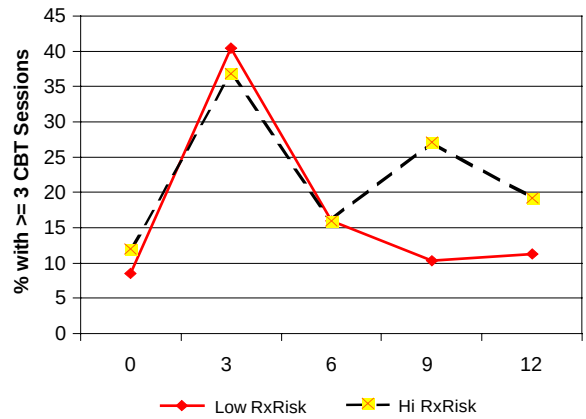

Fig. 4. Received 3+ sessions counseling plus at least four of seven CBT techniques.

income, site and employment) increased the significance of RxRisk as a predictor of outcome over time for all three variables ($P<.0001$).

3.2. Effects of intervention on guideline concordant care

We have previously reported that for the entire population included in this study, our intervention did not result in different rates of guideline-concordant pharmacotherapy compared to usual care, but did result in increased rates of CBT treatment at the 3-month time point compared to usual care [17]. The analyses of the rates of CBT treatment revealed no effect modification by medical illness (nonsignificant three-way interaction). As previously demonstrated, there was a significant time by treatment effect, indicating that the intervention group had a greater percentage of patients in CBT treatment over time. There was also a significant RxRisk group by time interaction ($z=2.02$, $P=.04$), which increased in statistical significance when the covariates were removed. Fig. 4 displays these results. The significant interaction is a result of the significant difference of the RxRisk groups at 9 months; 27.1% of those in the RxRisk+ group were receiving therapy, in contrast to only 10.3% of the RxRisk− group [$\chi^2(1)=5.72$, $P<.02$]. The RxRisk groups did not differ statistically at any other time point. Across time, although both RxRisk groups showed decreases in the percentage of patients receiving therapy, more subjects in the more medically ill group were maintained in therapy.

The analyses performed on the rates of guideline-concordant pharmacotherapy revealed a nonsignificant three-way interaction. As previously reported, there were also a nonsignificant time by treatment effect and treatment effect. However, there was a significant time by RxRisk group interaction ($z=2.60$, $P=.009$). This result was also significant when the covariates were removed. Fig. 5 presents the results of these analyses. The interaction was due to the finding that patients in the RxRisk+ group had significantly higher rates of use of guideline-concordant medication at all time points ($P<.001$), except for 3 months, when they did not differ significantly.

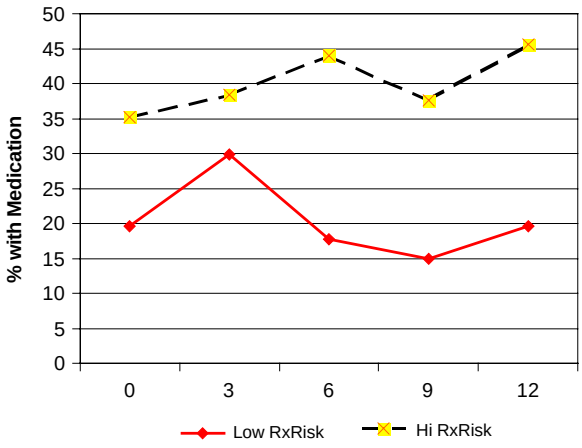

Fig. 5. Received appropriate antipanic pharmacotherapy for at least 6 weeks by RxRisk over time.

4. Discussion

This analysis confirms prior findings that psychiatric patients with depression and anxiety who have a greater burden of comorbid medical illness have more severe symptoms and functional disability associated with their illness [6]. Similar to a recent primary care-based effectiveness trial, differences between intervention and control were similar in both lower and higher severity of medical illness groups. However, outcomes of both intervention and usual care patients with higher medical illness severity continued to lag behind those with less or no medical illness burden [12]. Because our sample of panic disorder patients with more medical illness had more severe symptoms of anxiety, phobia and depression, and also more associated physical disability at baseline, it cannot be determined whether these findings are due to the medical illness comorbidity itself, or to the more severe psychiatric symptoms associated with it. Other limitations include the use of self-reported illness and medication use data to diagnose medical illness, the post hoc nature of the analysis and the limited generalizability of this selected sample.

Prior models examining relationships between depression and medical illness have suggested bidirectional effects where each condition can exacerbate the other by affecting self-care, biobehavioral risk factors for chronic disease and common underlying biological substrates of both illnesses [4]. In contrast to the mutually reinforcing interactions in this model, we did not find that there was an interaction between treatment of panic disorder and the presence of greater or lesser severity of medical illness. While those with more severe medical illness remained more symptomatic after treatment, this was totally attributable to their initially greater severity of illness at baseline.

There were no differences in the effect of our intervention on quality of care in the two medical illness groups. In both groups, the intervention successfully improved exposure to quality CBT during the first 3 months, when CBT sessions were offered to intervention patients. In contrast, the intervention failed to improve the proportion of patients receiving high quality pharmacotherapy, with both intervention and usual care patients in both income groups increasing their exposure to quality pharmacotherapy during the study. However, regardless of intervention, patients with more severe medical illness had higher rates of guideline-concordant pharmacotherapy at 6, 9 and 12 months, consistent with their greater rates at baseline and with recently reported findings linking medical illness morbidity with higher quality of retrospectively reported pharmacotherapy in a larger and more heterogeneous group of anxiety disorder patients [30]. This finding may be related to increased physician visits on the part of these patients with more severe medical illness,

although we have no data to confirm increased visits. Similarly, there was a significant tendency for the patients with more severe medical illness who availed themselves of CBT regardless of intervention status, to maintain CBT treatment longer, something that has not been previously reported, and cannot be attributed to a greater rate of physician visits.

Finally, the intervention had equivalent effects on the various measures of clinical and functional outcome in the two groups. Patients with more severe medical illness started off with more severe symptoms and on average remained more symptomatic than less severely medically ill patients, with both groups showing greater improvement with the intervention compared with usual care. We have previously inferred that benefits of the intervention are predominantly due to the impact of CBT, since rates of quality pharmacotherapy were not influenced by the intervention (Roy-Byrne et al., in press). The current analysis, demonstrating similar intervention response in subjects, regardless of their level of medical illness comorbidity, suggests that CBT as an intervention for panic disorder works equally well in patients with varying burdens of comorbid medical illness.

In conclusion, this analysis shows that patients with panic disorder with a higher burden of comorbid medical illness respond equally well as those with lesser burdens of medical illness to an intervention designed to increase rates of quality antipanic pharmacotherapy and CBT. Because the more severely medically ill patients begin with more severe psychiatric symptoms and disability, they end up after treatment with less complete responses (i.e., a higher level of residual symptoms). This suggests that helping these initially more medically ill patients achieve more complete resolution of their symptoms and functional deficits will require more intensive treatment, characterized either by greater amounts and frequency of the same treatment, or perhaps additional "stepped-care," which would deliver either adjunctive medications or behavioral treatments targeted toward residual symptoms. In addition, the bidirectional effect between psychiatric and medical illness suggests that additional interventions may be required to address the poor health habits and medical illness adherence in these patients, which if unaddressed, will serve to sustain medical illness severity and in turn exacerbate anxiety symptom severity. These hypotheses should be tested in future controlled studies.

Acknowledgments

This study was supported by NIH grants MH57835 and MH64122 (Murray B. Stein, M.D., M.P.H.), MH57858 and MH065324 (Peter Roy-Byrne, M.D.) and MH58915-03 (Michelle Craske, Ph.D.).

References

[1] McDaniel JS, Musselman DL, Porter MR, Reed DA, Nemeroff CB. Depression in patients with cancer. Diagnosis, biology, and treatment. Arch Gen Psychiatry 1995;52:89–99.

[2] Rudisch B, Nemeroff CB. Epidemiology of comorbid coronary artery disease and depression. Biol Psychiatry 2003;54:227–40.

[3] Robinson RG. Poststroke depression: prevalence, diagnosis, treatment, and disease progression. Biol Psychiatry 2003;54:376–87.

[4] Katon W, von Korff M, Ciechanowski P, et al. Behavioral and clinical factors associated with depression among individuals with diabetes. Diabetes Care 2004;27:914–20.

[5] Petitto JM, Evans DL. Depression in cancer and HIV infection: research findings and implications of effective antidepressant treatment. Depress Anxiety 1998;8(Suppl 1):80–4.

[6] Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. Biol Psychiatry 2003;54:216–26.

[7] Simon GE. Social and economic burden of mood disorders. Biol Psychiatry 2003;54:208–15.

[8] Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. Arch Intern Med 2000;160:3278–85.

[9] Iosifescu DV, Nierenberg AA, Alpert JE, et al. The impact of medical comorbidity on acute treatment in major depressive disorder. Am J Psychiatry 2003;160:2122–7.

[10] Evans M, Hammond M, Wilson K, Lye M, Copeland J. Placebo-controlled treatment trial of depression in elderly physically ill patients. Int J Geriatr Psychiatry 1997;12:817–24.

[11] Oslin DW, Datto CJ, Kallan MJ, et al. Association between medical comorbidity and treatment outcomes in late-life depression. J Am Geriatr Soc 2002;50:823–8.

[12] Koike AK, Unutzer J, Wells KB. Improving the care for depression in patients with comorbid medical illness. Am J Psychiatry 2002;159: 1738–45.

[13] Small GW, Birkett M, Meyers BS, et al. Impact of physical illness on quality of life and antidepressant response in geriatric major depression. Fluoxetine collaborative study group. J Am Geriatr Soc 1996;44:1220–5.

[14] Papakostas GI, Petersen T, Iosifescu DV, et al. Axis iii disorders in treatment-resistant major depressive disorder. Psychiatry Res 2003; 118:183–8.

[15] Greenberg PE, Sisitsky T, Kessler RC, et al. The economic burden of anxiety disorders in the 1990s. J Clin Psychiatry 1999;60:427–35.

[16] Walker EA, Katon W, Russo J, et al. Health care costs associated with posttraumatic stress disorder symptoms in women. Arch Gen Psychiatry 2003;60:369–74.

[17] Roy-Byrne P, Craske M, Stein M, et al. A randomized effectiveness trial of cognitive behavior therapy and medication for primary care panic disorder. Arch Gen Psychiatry 2005;62:290–8.

[18] Craske MG, Roy-Byrne PP, Stein MB, et al. Treating panic disorder in primary care: a collaborative care intervention. Gen Hosp Psychiatry 2002;24:148–55.

[19] Roy-Byrne P, Sherbourne CD, Craske MG, et al. Moving treatment research from clinical trials to the real world: the design of a first-generation effectiveness study for panic disorder. Psychiatr Serv 2003; 54:288–300.

[20] Barlow DH, Craske MG. Mastery of your anxiety and panic. 3rd ed. Albany (NY): Graywind Publication; 2000.

[21] Barlow DH, Craske MG. Agoraphobia supplement. 3rd ed. Albany (NY): Graywind Publication; 2000.

[22] Roy-Byrne PP, Stein MS, Bystrisky A, Katon W. Pharmacotherapy of panic disorder: proposed guidelines for the family physician. J Am Board Fam Pract 1998;11:282–90.

[23] Sloan KL, Sales AE, Liu CF, et al. Construction and characteristics of the RxRisk-V: a VA-adapted pharmacy-based case-mix instrument. Med Care 2003;41:761–74.

[24] Wells KB. The design of partners in care: evaluating the cost-effectiveness of improving care for depression in primary care. Soc Psychiatry Psychiatr Epidemiol 1999;34:20–9.

[25] Sales AE, Liu CF, Sloan KL, et al. Predicting costs of care using a pharmacy-based measure risk adjustment in a veteran population. Med Care 2003;41:753–60.

[26] Otto MW, Reilly-Harrington N. The impact of treatment on anxiety sensitivity. In: Taylor S, editor. Anxiety sensitivity: theory, research, and treatment of the fear of anxiety. Mahwah, NJ: Erlbaum, Lawrence; 1999. p. 321–36.

[27] Schmidt NB, Lerew DR, Joiner Jr TE. Prospective evaluation of the etiology of anxiety sensitivity: test of a scar model. Behav Res Ther 2000;38:1083–95.

[28] Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.

[29] Epping-Jordan J, Usten T. The WHODAS II: level the playing field for all disorders. WHO Bull Mental Health 2000;6:5–6.

[30] Stein MB, Sherbourne CD, Craske MG, et al. Quality of care for primary care patients with anxiety disorders. Am J Psychiatry 2004; 161:2230–7.

[31] Steketee G, Perry JC, Goisman RM, et al. The psychosocial treatments interview for anxiety disorders. A method for assessing psychotherapeutic procedures in anxiety disorders. J Psychother Pract Res 1997;6: 194–210.