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Does Improvement in Symptoms and Quality of Life in Chronic Schizophrenia Reduce Family Caregiver Burden?

Taeho Greg Rhee, PhD, MSW[a,b] and **Robert A. Rosenheck**[c,d,e]

[a]Department of Internal Medicine, School of Medicine, Yale University, New Haven, CT, USA

[b]Yale Center for Outcomes Research and Evaluation (CORE), Yale-New Haven Health System, New Haven, CT, USA

[c]Department of Psychiatry, School of Medicine, Yale University, New Haven, CT, USA

[d]Veterans Affairs (VA) New England Mental Illness Research, Education and Clinical Centers (MIRECC), West Haven, CT, USA

[e]Veterans Affairs (VA) Connecticut Healthcare System, West Haven, CT, USA

Abstract

The longitudinal association of changes in clinical status among adults with schizophrenia and changes in family caregiver burden has not been demonstrated. Using data from the NIMH-funded CATIE schizophrenia trial (n=446 family caregivers), we examined the association of changes in patient symptoms and quality of life with changes in measures of family caregiver burden. Clinical changes in patient symptoms and quality of life were not significantly associated with changes in family caregiver burden. The weak association likely reflects that small clinical changes in chronically ill adults are insufficient to affect long established experiences of burden.

Keywords

Schizophrenia; caregiver; burden; quality of life; symptoms

1. INTRODUCTION

Living with schizophrenia often results in extensive caregiving by both family members and non-kin (Awad and Voruganti, 2008; Chan, 2011). Past studies have demonstrated that many caregivers experience significant cognitive, psychological, social, and financial burden, including anxiety, depression, social stigmatization, and economic constraints (Chan, 2011; Gutierrez-Maldonado et al., 2005; Hayes et al., 2015; Kate et al., 2013; Perlick et al., 2006;

Corresponding Author: Greg Rhee PhD, MSW, School of Medicine, Yale University, 333 Cedar Street, PO Box #208025, New Haven, CT, 06520, USA (Phone: +1-773-398-9564; taeho.rhee@yale.edu).

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Stanley et al., 2017). However, most of these studies relied on cross-sectional research designs (Caqueo-Urizar and Gutierrez-Maldonado, 2006; Gutierrez-Maldonado et al., 2005; Lerner et al., 2018), had relative small sample sizes (<200) (Caqueo-Urizar and Gutierrez-Maldonado, 2006; Gutierrez-Maldonado et al., 2005; Parabiaghi et al., 2007; Roick et al., 2006), or were conducted outside the U.S. (Caqueo-Urizar and Gutierrez-Maldonado, 2006; Gutierrez-Maldonado et al., 2005; Hayes et al., 2015; Parabiaghi et al., 2007; Roick et al., 2006; Stanley et al., 2017), limiting their generalizability to the U.S. context. Furthermore, none of these studies, to our knowledge, has investigated the longitudinal relationship between reduction in patient symptoms and alleviation of family caregiver burden.

This study used data from the NIMH-funded Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial (Stroup et al., 2003; Swartz et al., 2003). Previous studies of CATIE identified a four-factor structure of the family caregiver burden measure (Perlick et al., 2006); reported that symptoms and quality of life were significantly associated with burden at baseline (Perlick et al., 2006); and showed no differences between pharmacologic treatments (i.e., four second generation antipsychotics or perphenazine, a first generation antipsychotic) in longitudinally measured family burden (Perlick et al., 2010; Rosenheck et al., 2000). We sought to determine whether and to what extent caregiver burden for relatives of patients with chronic schizophrenia is reduced as patients' symptoms decline and/or quality of life improves following the initiation of a change in antipsychotic medication.

2. METHODS

2.1 Data source and study sample

The CATIE schizophrenia trial (Stroup et al., 2003; Swartz et al., 2003), was conducted from January 2001 to December 2004 across 57 different sites in the U.S, with 1,460 patients diagnosed with schizophrenia. Details of the trial design and protocol development have been published previously (Stroup et al., 2003; Swartz et al., 2003). Of the 1,460 participants, 623 (42.7%) identified a principal family caregiver who was the one most involved in their care and who agreed to be interviewed for assessment of their experience as a caregiver during the trial. We further limited our final analytic sample by caregivers who completed both baseline and at least one follow-up interview (n=446).

2.2 Measures

Family burden.—Family burden was assessed using a revised version of the Family Experience Interview Schedule (FEIS), which contains 44 variables (Perlick et al., 2006). A previously published factor analysis of the CATIE baseline data, identified four factors (Perlick et al., 2006): caregiver perceived patient problem behavior (Factor 1), resource demands and routine disruption experienced by the caregiver (Factor 2), impairments in caregiver activities of daily living (Factor 3), and perceived patient helpfulness to the caregiver (Factor 4).

Patient symptoms and quality of life measures.—We used five different measures for evaluating change in patient symptoms and quality of life. Symptoms of schizophrenia were assessed with the summed average score of the 30-item, rater-evaluated, Positive and Negative Syndrome Scale (PANSS) (Swartz et al., 2003). Depression was assessed with the Calgary Depression Rating Scale. Mental health related quality of life was assessed with the self-reported SF-12 mental health summary score (Perlick et al., 2006, 2010; Swartz et al., 2003). Additional quality of life measures included the rater-assessed Heinrichs-Carpenter Quality of Life scale and self-reported Lehman Quality of Life Interview (Perlick et al., 2006, 2010; Swartz et al., 2003). For patient symptoms, higher scores indicate severer symptoms, while higher scores on the quality of life measures indicate better quality of life. Detailed information about variable descriptions and constructions can be found in earlier CATIE studies (Perlick et al., 2006, 2010; Swartz et al., 2003).

Other variables.—Based on earlier CATIE studies (Perlick et al., 2006, 2010; Stroup et al., 2003; Swartz et al., 2003), we included both patient and caregiver covariates, including age, race/ethnicity, gender, education, marital status, and income in both patients and caregivers (Perlick et al., 2006, 2010), and currently living with the patient (yes/no) as reported by caregivers.

Analytical plan

For key variables representing the four family burden factors as reported by the primary family caregiver, as well as patient symptoms and quality of life, we constructed standardized measures of change by subtracting the baseline score from the follow-up score and dividing the result by the standard deviation of the average baseline value across all subjects. This generated a standardized (Z-score) measure of changes in both patient symptoms and quality of life, and of the four family burden factors. These variables thus represent the Cohen's *d*, the effect size of change over time, calculated as the mean of change in each measure divided by the standard deviation of the baseline mean (Fritz et al., 2012).

Second, we performed standardized linear mixed bivariate analyses to investigate the associations of each measure of change in patient symptom and quality of life with change in each of the four family burden factors during post-baseline follow-up assessments. All of analyses were conducted using SAS 9.4 (Cary, NC) and Stata 15.1 6-Core/MP (College Station, TX).

3. RESULTS

Of 446 caregivers, the mean age was 52.8 (SD±13.9) years; 73.1% of them were female; 59.0% were married; and 59.6% reported that they live with the patient at baseline. Altogether 49.6% were the parents of the patient, 16.1% were spouses, 15.9% were siblings, 4.5% were adult children of the patients, and 11.2% were other relatives of the patients. Among patients diagnosed with schizophrenia, mean age was 39.3 (SD±11.5), 75.6% were male, and they reported that, on average, 13.1 years (SD±11.0) had passed since they first experienced symptoms of their current illness.

Baseline family burden factors, as well as patient symptoms and quality of life have been reported previously(Perlick et al., 2006). For family burden factor 1, effect size of change was −0.28 (Table 1, bottom row), indicating that on average, the follow-up mean is 0.28 standard deviations lower than that of the baseline mean in Factor 1. For family burden Factors 2 to 4, the effect sizes for change were −0.26, −0.08, and −0.02, respectively, magnitudes that are conventionally considered small (Fritz et al., 2012).

The effect sizes of changes in patient symptoms and quality of life measures ranged from −0.39 to 0.14 (see Table 1, first column). The Calgary depression scale and PANSS measures had effect sizes of −0.15 and −0.39, respectively, indicating small to moderate symptom reductions. QOL measures had effect sizes of 0.14 (Heinrichs-Carpenter), 0.11 (Lehman), and 0.14 (SF-12), representing small magnitudes of improvement.

Bivariate linear mixed model analysis of correlates of change in family burden showed no significant association between changes in the PANSS, Heinrichs-Carpenter's QOL, Calgary's depression and SF-12 mental health summary and changes in any of the four family burden factors. Change in the Lehman QOL summary score was positively associated with change in Factor 1 with a small magnitude of association (B=0.08; 95% CI=0.01, 0.16). Among other covariates, time (in months) and living with the patient were significantly associated with three family burden factors (Factors 2–4). For each month of trial participation burden decreased as measured by Factors 1 to 3 ($p<0.001$ for Factors 1 and 2, and $p=0.034$ for Factor 3). Living with the patient was associated with increased burden in Factors 2 to 4.

4. DISCUSSION

This study presents standardized data on the magnitude of changes in patient symptoms and quality of life following a medication change, and their association with changes in family caregiver burden. First, the effect sizes for patient changes are mostly small, as might be expected in a sample suffering from schizophrenia for 13 years on average. Due in part to a long waxing and waning course of their illness, even when a new medication change was made, it appears that recovery from modest exacerbations were of modest magnitude over the subsequent 18 months (Jobe and Harrow, 2005; Newman et al., 2012; Rosenheck et al., 2000). It is still possible that if effect sizes of patient symptoms were big enough, caregiver burdens might have significantly reduced. Future research will need to assess this hypothesis.

Second, changes in each of the family caregiver burden factors also showed small effect sizes. Further, we investigated the association by caregiver type (i.e., spouse, parent, or sibling), but no difference was found (data not shown). Following the reasoning presented above, it is likely that levels of family burden had largely been stabilized after an average of 13 years of caregiving and did not change substantially with the small observed changes in the clinical status of their relatives. These findings are also consistent with previous findings (Perlick et al., 2010; Rosenheck et al., 2000) that differences in randomly assigned medications did not lead to significant differences in patient symptom or quality of life outcomes or in family burden.

Our findings thus suggest that changes in pharmacological intervention in patients with long-term schizophrenia, as was the case in the CATIE trial (Perlick et al., 2010), have little differential impact on levels of family caregiver burden. Non-pharmacological, psycho-social interventions to alleviate family burden may be more effective early in the illness or need to be specifically directed at the situation of the family and not just at the patient. It was notable that living with the patient was positively associated with three of four family caregiver burden factors. This is not surprising as families that live together are likely to have much more frequent and intensive contact and resultant stress.

Several limitations in this study deserve comment. First, due to the requirements for voluntary informed consent for the CATIE trial, sicker patients who pose greater challenges for their families may not have been included (Stroup et al., 2003). The generalizability of our findings to more severely ill patients is thus unknown. Second, while the duration of illness is 13 years on average, we do not know whether these patients had their medication therapy continuously or not. Third, the CATIE-Schizophrenia trial does not capture the period of non-adherence, and thus, we could not assess the association between non-adherence of medication and burden of caregivers. Fourth, while the disability level of patients may have a more meaningful association with caregiver burden, the current data do not capture disability level explicitly. Lastly, while we found no statistically significant associations in linear mixed bivariate analyses, small, non-significant findings beyond the sensitivity of our measures may still be clinically meaningful. Methodologically, it is often difficult to translate statistical significance into clinical meaningfulness in psychiatric effectiveness research (Rosenheck et al., 2000). Further refinement of the measures may be warranted.

Despite these limitations, this study has several strengths, including a relatively large sample and multiple well-known clinical measures. The negative findings suggest that additional research is needed to develop family-specific interventions (Dixon et al., 2011; Lucksted et al., 2012) to better alleviate family caregiver burden as improving clinical outcomes in patients may not be sufficient to the task.

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Highlights

- Patient symptoms improved slightly over 18 months in chronic schizophrenia.
- Patient symptoms were not significantly associated with family caregiver burden.
- Improved quality of life in patients was not associated with reduced family caregiver burden.
- Family-specific interventions are needed to reduce family caregiver burden.

Table 1.

Effect size of patient clinical change and family burden, and linear mixed bivariate analysis of changes in family burden, 2001–2004 Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE).

	Cohen's *d* effect size of patient clinical change	**Change in factor 1**		**Change in factor 2**		**Change in factor 3**		**Change in factor 4**	
		B	***P*- Value**	**B**	***P*- value**	**B**	***P*- value**	**B**	***P*- value**
Model 1:									
Change in PANSS (total)	−0.39	−0.04	0.287	0.01	0.814	−0.05	0.133	0.03	0.377
Model 2:									
Change in QOL (Heinrichs-Carpenter)	0.14	0.05	0.209	0.07	0.099	−0.00	0.903	−0.06	0.156
Model 3:									
Change in QOL (Lehman)	0.11	0.08	0.027	0.07	0.072	−0.03	0.465	−0.06	0.134
Model 4:									
Change in Depression (Calgary)	−0.15	−0.01	0.792	0.06	0.105	0.02	0.531	0.03	0.341
Model 5:									
Change in SF-12 mental health summary	0.14	−0.07	0.081	−0.02	0.736	0.01	0.717	−0.01	0.775
Model 6:									
Time		−0.02	<0.001	−0.02	<0.001	−0.01	0.034	0.01	0.242
Model 7:									
Living with the patient		0.12	0.074	0.39	<0.001	0.14	0.049	0.66	<0.001
Cohen's *d* effect size of family burden change		−0.28	-	−0.26	-	−0.08	-	−0.02	-

Note: Factor 1 denotes caregiver perceived patient problem behavior, factor 2 denotes resource demands and routine disruption for the caregiver, factor 3 denotes impairments in caregiver activities of daily living, and factor 4 denotes perceived patient helpfulness to the caregiver. B stands for a standardized coefficient from a standardized linear mixed bivariate analysis.