# Family Outcomes From a Randomized Control Trial of Relapse Prevention Therapy in First-Episode Psychosis

John F. M. Gleeson, PhD; Sue M. Cotton, PhD; Mario Alvarez-Jimenez, DClinPsy, PhD; Darryl Wade, PhD; Kingsley Crisp, BSW; Belinda Newman, BA (Hons); Daniela Spiliotacopoulos, BA; and Patrick D. McGorry, MD, PhD

***Objective:*** We have previously reported that our combined individual and family cognitive-behavioral therapy (CBT) relapse prevention therapy (RPT) was effective in reducing relapse rates compared to treatment as usual (TAU) within a specialist program for young, first-episode psychosis patients who had reached remission on positive symptoms. Here, we report the outcomes for family participants of *DSM-IV*–diagnosed first-episode psychosis patients recruited between November 2003 and May 2005 over a 2.5-year follow-up period. The primary hypothesis was that, compared to family members receiving TAU, family participants who received RPT would have significantly improved appraisals of stressors related to caregiving. Secondary hypotheses were that RPT would be associated with reduced expressed emotion and improved psychological distress.

***Method:*** Family members were assessed at baseline and at 7-month, 12-month, 18-month, 24-month, and 30-month follow-up on appraisal of caregiving, expressed emotion, and psychological distress using the Experience of Caregiving Inventory, The Family Questionnaire, and the General Health Questionnaire of 28 Items, respectively. The family component of RPT was based on family behavioral therapy for schizophrenia with a specific focus on psychoeducation and CBT for relapse prevention.

***Results:*** Thirty-two families received RPT, and 31 families received TAU. There were significant group effects for aspects of the appraisal of caregiving, including negative symptoms, positive personal experiences, and total positive score on the Experience of Caregiving Inventory. Time effects were evident for emotional overinvolvement and for aspects of the appraisal of caregiving. There were no significant effects for psychological distress.

***Conclusions:*** The relatives of patients who received RPT perceived less stress related to their relative's negative symptoms and an increase in perceived opportunities to make a positive contribution to the care of their relative compared to carers in the TAU condition. Cognitive-behavioral therapy for relapse prevention showed promise in improving the experience of caregiving for family members of first-episode psychosis patients over a 2.5-year follow-up period.

***Trial Registration:*** anzctr.org.au Identifier: ACTRN12605000514606

*J Clin Psychiatry 2010;71(4):475–483*



***Submitted:*** *September 3, 2008; accepted January 2, 2009.*
***Online ahead of print:*** *December 15, 2009 (doi:10.4088/JCP.08m04672yel).*
***Corresponding author:*** *John F. M. Gleeson, PhD, University of Melbourne Psychology Clinic, 14-20 Blackwood Street, The University of Melbourne Victoria, Australia 3010 (jgleeson@unimelb.edu.au).*

The impacts upon family members caring for a relative with schizophrenia are known to be multidimensional, including the stress related to symptoms and behaviors of their relative, grief, stigma associated with severe mental disorder, the increased dependency of their relative upon the family, and dealing with the limitations of mental health services.[1] The transactional model of stress and coping[2] has become a prominent model among researchers in this field. According to this framework, carer stress is defined as a product of the interaction between the carer's appraisal of the constellation of stressors associated with caregiving and the carer's coping resources.[1] This definition has addressed some of the limitations in the operationalization of the construct of carer "burden," which required inferences to be made in relation to the objective impact of the caregiver's role and which did not allow for both positive and negative appraisals of the experience of caregiving to be measured.[1]

Compared to that experienced by carers with a relative diagnosed with schizophrenia, little is known about the stress experienced by families caring for a relative diagnosed with first-episode psychosis (FEP).[3] Available research indicates that, on average, FEP carers experience a moderate level of psychological distress, and that they believe that the illness significantly impacts upon their lives.[4,5] Family members' appraisal of the impact of their FEP relative's disorder has been shown to be a significant predictor of family distress but not objective ratings of their relative's symptoms.[4] Examples of negative carer appraisals in relation to their relative's behavior may include perceptions of recklessness and inconsiderate and embarrassing behavior. Positive appraisals include a perception that the family member has contributed to his or her relative's well-being.[1]

Studies in schizophrenia have shown that family interventions are effective in reducing family stress over 2-year follow-up periods compared to standard care.[6] Studies of the effectiveness of interventions designed specifically for the stress related to caregiving for FEP families are rare.[7] A program evaluation conducted by Addington and

colleagues[3] indicated that a specific FEP family program was acceptable to 80% of families, and that carer psychological well-being significantly improved over a 3-year follow-up period. However, the study was limited by the lack of a comparison group.

Expressed emotion (EE) has been another target of intervention in family research in psychosis. Expressed emotion is an empirically derived construct that entails 3 subtypes of communication patterns within families: hostility, emotional overinvolvement, and critical comments.[8,9] Expressed emotion is well known to be a predictor of relapse in chronic psychosis,[10] although the evidence is less clear-cut in early psychosis.[11–14]

Individual family interventions for high EE in FEP families have been based upon the behavioral family therapy tradition in schizophrenia,[15,16] which has aimed to modify the communication patterns of high-EE relatives toward the patient. The typical components of these interventions have included comprehensive communication skills training and structured learning in the problem-solving model. In one of the few empirical studies in FEP, Zhang and colleagues[17] compared family-based interventions to standard outpatient follow-up, showing positive outcomes in relation to admission rates over an 18-month follow-up period. On the other hand, Linszen and colleagues[18,19] compared their individual-oriented psychosocial program with the addition of a family intervention, which did not demonstrate additional benefits in terms of relapse rates or EE over a 12-month or 5-year follow-up period. Patients whose families received the family intervention, however, spent significantly fewer months in institutions for psychiatric patients compared with those who received the comparison treatment.

However, all of the FEP family intervention studies cited here share limitations associated with their comparison control interventions, either because they did not include a control comparison or because the control did not include all of the core components of more contemporary early psychosis programs, such as specialist FEP case management or specific psychosocial interventions tailored to specific phases of the disorder, such as FEP group programs.

The Episode II study[20–22] was the first trial to evaluate the effectiveness of adding cognitive-behavioral therapy (CBT) for relapse prevention to usual treatment provided in accordance with contemporary guidelines for FEP. The Episode II Relapse Prevention Therapy (RPT) included both individual and family CBT components. The decision to include a family therapy component within a relapse prevention intervention was motivated by the aims of reducing family stress and, in relevant cases, reducing high EE.[9,23]

This Episode II trial provided an opportunity to examine the outcomes for families who received family CBT compared to family participants who received treatment as usual (TAU) within a specialist FEP program—The Early Psychosis Prevention and Intervention Centre (EPPIC), Melbourne, Australia, and Barwon Health, Victoria, Australia—which provides psychiatric services to a regional and rural region outside of Melbourne. Furthermore, this study recruited only patients who had reached remission on positive symptoms of psychosis, which provided a unique opportunity to examine the impact of a family intervention upon family stress related to caregiving while controlling for the severity of positive psychotic symptoms.

Previously, we have reported[22] interim findings pertaining to the patient participants in the Episode II study, which indicated that at 7-month follow-up, RPT was associated with a significantly lower rate of relapse when compared to TAU for FEP patients who had reached remission on positive symptoms. However, we have not previously reported on the outcomes for family participants.

The aim of this article was to describe the outcomes for family participants from the Episode II study. Our primary hypothesis was that family members who received RPT would have a significantly improved appraisal of stressors related to caring for their relative at follow-up (7 months, 12 months, 18 months, 24 months, and 30 months) compared to baseline and compared to family members receiving TAU. Our secondary hypotheses were that family members who received RPT would have significantly lower levels of psychological distress and lower levels of EE at follow-up over 2.5 years when compared to family members who had access to TAU alone.

## METHOD

### Design

The Episode II trial comprised a randomized controlled effectiveness trial and compared a combined family and individual CBT for relapse prevention with TAU within 2 specialist FEP services, which included a high-quality service informed by clinical practice guidelines for early psychosis. The study included a total of 6 assessment time points spanning a 2.5-year follow-up period after baseline.

### Participants

We have previously described in detail the sample of FEP patients.[21] Patients from EPPIC and from Barwon Health were recruited between November 2003 and May 2005. Inclusion criteria were a diagnosis of a first episode of a *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*)[24] psychotic disorder; less than 6 months of prior treatment with antipsychotic medications; age 15 to 25 years inclusive; and remission on positive symptoms of psychosis. Remission was defined as 4 weeks or more of scores of 3 (mild) or below on the subscale items hallucinations, unusual thought content, conceptual disorganization, and suspiciousness on the expanded version of the Brief Psychiatric Rating Scale (BPRS).[25,26] Exclusion criteria were ongoing active positive symptoms of psychosis; severe intellectual disability (ie, IQ < 70); inability to converse in or read English; and participation in previous CBT trials.

The study was approved by the Northwestern Mental Health and the Barwon Health Research and Ethics Committees. Eligible patients were invited to participate by the project research assistant (RA) as soon as possible after they reached remission on positive psychotic symptoms. Patients provided additional optional consent for participation of their family members. The participant nominated the family member with whom they had the most frequent contact to complete all of the family assessments. Family participants provided verbal consent. All participants could withdraw consent at any time.

After informed consent was obtained by the RA, baseline measures were completed with the patient and his or her family before the patient participant was randomly assigned to the TAU or RPT group. If the patient was randomly assigned to TAU, his or her family continued to receive the usual available services for families with the programs, which included individual family psychoeducation at both sites. At EPPIC, group psychoeducation and family peer support systems were also routinely offered as part of TAU. If the patient was randomly assigned to RPT, his or her family was allocated to the RPT family therapy with a trained family therapist who was experienced in providing first-episode family therapy (K.C.).

Random allocation was managed by the study statistician (S.M.C.) using computer-generated random numbers. The trial coordinator (D.W.), who was informed of the outcome of randomization via e-mail and telephone, informed the treating team and, in relevant cases, the research therapists of the outcome. The statistician was not involved in any way with either the assessments or the treatments. The RAs (B.N., D.S.) were kept blind to treatment allocation via the following mechanisms: (1) regular and frequent reminders were sent to all clinical staff regarding the importance of the blind; (2) the RA reminded participants of the importance of the blind at the commencement of each research interview; (3) the RA was excluded from all clinical discussions regarding participants; and (4) the RA was forbidden from reading participants' medical records.

### Treatments

Patients randomly assigned to TAU continued with their routine treatment via the EPPIC program or Barwon Health, which was coordinated via an outpatient case manager and outpatient consultant psychiatrist, with access to home-based treatment and a range of psychosocial interventions.[27] These interventions included a group program, family work, accommodation, and vocational services. The model of case management comprised direct provision of monitoring and psychosocial treatment by the appointed case manager, and referral to additional treatment options when indicated. Case managers were provided with orientation and training in guidelines for first-episode psychosis, regular one-to-one supervision from a senior member of the team, and a range of specialist first-episode resources, including psychosocial treatment manuals and audiovisual materials. Case management was provided for a minimum period of 18 months or for a longer period for patients younger than 18 years of age. A case management manual provided detailed guidelines for TAU.[28] Further details of TAU have been provided previously.[21]

Patients randomly assigned to RPT were introduced to their individual research therapist who additionally adopted the role of outpatient case manager for the duration of their treatment at EPPIC. All patients randomly assigned to RPT continued their follow-up treatment with their outpatient psychiatrist and had access to home-based treatment and group interventions as indicated. The research therapists functioned as fully integrated members of the EPPIC treatment team and as visiting therapists to Barwon Health, which allowed the effectiveness of RPT to be evaluated within existing real-world clinical roles. Key differences between TAU and RPT included the following: (1) the specific focus within individual and family sessions was based on a shared understanding of the risk of relapse; (2) the systematic and phased approach to relapse prevention was established via a range of cognitive-behavioral interventions; (3) the parallel individual and family sessions focused upon relapse prevention; and (4) supervision specifically focused upon relapse prevention. We have previously described the manualized individual therapy.[21]

The family intervention, also manualized and provided by a trained family therapist, was informed by cognitive-behavioral family therapy for schizophrenia[15,16] and family interventions for FEP.[18] The phases of family therapy were (1) assessment and engagement; (2) assessment of family communication; (3) burden and coping; (4) psychoeducation regarding relapse risk; and (5) a review of early warning signs and documentation of a relapse prevention plan. Intensive communication skills training and problem solving were undertaken where indicated. The treatment manual is available by request. The family therapist attended weekly group supervision together with the 2 individual therapists (conducted by clinical supervisors J.G. and D.W.), which provided an opportunity to coordinate the interventions.

Fidelity to family therapy was managed via (1) a treatment manual that detailed the intervention techniques used throughout therapy and (2) feedback provided by the clinical supervisor (J.G.) to the research family therapist (K.C.) in weekly clinical supervision sessions.

### Assessment Procedures

The full range of patient baseline and outcome measures has been outlined elsewhere[21]—here, we detail the relevant family participant measures and provide an overview of the assessment procedures.

Face-to-face interviews were completed with family participants at 6 time points: baseline (T1) and follow-up at 7 (T2), 12 (T3), 18 (T4), 24 (T5), and 30 (T6) months. The Experience of Caregiving Inventory (ECI)[1] was included to

assess appraisals of stressors related to caregiving. It was specifically constructed to assess carers' appraisals of a broad range of aspects related to caring for a relative with psychosis, in accordance with the transactional model of stress. The ECI includes 66 items measuring 8 salient negative areas of caregiving (difficult behaviors, negative symptoms, stigma, problems with services, effects on the family, need to provide back-up, dependency, and loss) together with 2 areas of positive experiences (positive personal experiences and positive aspects of the relationship). For example, items related to the negative areas of caregiving include "I feel unable to leave him home alone" and "He is unreliable about doing things." Items related to the positive aspects of caregiving include "I have contributed to his well-being" and "I have discovered strengths in myself." The negative subscales are combined to generate a total scale.

Additional family measures included a brief self-report estimate of EE via the Family Questionnaire (FQ), which has been shown to have adequate concurrent validity in relation to the Camberwell Family Interview (CFI).[8,29] Specifically, the authors of the FQ have reported that 78% of families with a relative with schizophrenia were categorized correctly in terms of criticism; 71%, in relation to emotional overinvolvement; and 74%, in relation to the overall CFI EE classification.[29] Carer symptoms were assessed using the General Health Questionnaire of 28 Items (GHQ-28).[30] This measure comprises 4 subscales assessing stress, somatic symptoms, depression, and social functioning. A multinational validation study[31] comparing the GHQ-28 with the diagnosis of current mental health disorders using standardized diagnostic interviews have shown that the GHQ is a highly valid screening tool for the presence of psychiatric symptoms in adults presenting in primary care settings, with high validity coefficients and the area under the curve calculated in the range 0.85 to 0.87.

### Statistical Analysis

Data verification was conducted on 22 randomly selected cases from the baseline data, which were re-entered by a research fellow (M.A.-J.). Error rates for each time point were all below the a priori acceptable rate, which was set at 0.50%. Data were screened using a number of techniques, including examination of descriptive statistics, such as measures of central tendency (mean and median), skewness, kurtosis, and the Kolmogorov-Smirnov test for normality of the distribution. Data were transformed when appropriate using logarithmic transformations (plus a constant).[32]

Baseline demographic characteristics of the families in RPT and TAU groups were contrasted using the $\chi^2$ statistic for categorical dependent variables and the independent samples *t* test for dependent variables measured on a continuous scale.

To determine group differences on the family measures (FQ, ECI, GHQ-28), a series of mixed-effects model repeated measures (MMRM) analysis of variance (ANOVA) models were employed. The within-groups factor was time (T1 to T6), and group served as the between-subjects factor. From the model, the main effects for group (Overall, are the RPT and TAU groups different?) and time (How do ratings change over time, regardless of group membership?) can be examined as well as the interaction between these 2 variables. A Toeplitz covariance structure was used to model the relations between observations on different occasions. A series of planned comparisons contrasted change from baseline (T1) to the 4 follow-up time points (T2–T6, or 7 months to 30 months). When the main effect for time was significant, Bonferroni post hoc comparisons were used to determine which time points were significantly different.

Given that there were so many time points (T1–T6) across which group differences were examined in the interaction (12 estimated cell means), the potential for nonsignificant interactions was likely, especially given the sample size. The sensitivity and power of the analysis may be reduced, and there is increased chance of type II errors.[33] Although an interaction *F* statistic may be nonsignificant, there may still be instances where true group differences exist across time points.[33] Therefore, using the MMRM models, a series of planned comparisons contrasted change from baseline (T1) to the 5 follow-up time points (T2–T6, or 7 months to 30 months).

The MMRM differs from traditional repeated measures models, ANOVA and analysis of covariance, in that all existing data comprise the model. Further, MMRM does not require the imputation or substitution of missing data with estimated or hypothetical values.[34] This approach relies on data being missing at random, or the pattern of missing data depends on observed variables.[35] Another advantage of MMRM over traditional repeated measures ANOVA models is that the dispersion and correlation of data at all occasions may be unconstrained or, as in the case of the current study, can be modeled (eg, using Toeplitz covariance). Given the flexibility of MMRM, it can be considered a preferred method of examining the outcomes of clinical trials.[34]

The main effects (time and group) of the MMRM will be reported. Also considered will be the interaction effects; however, more emphasis will be placed on the results from the planned comparisons.

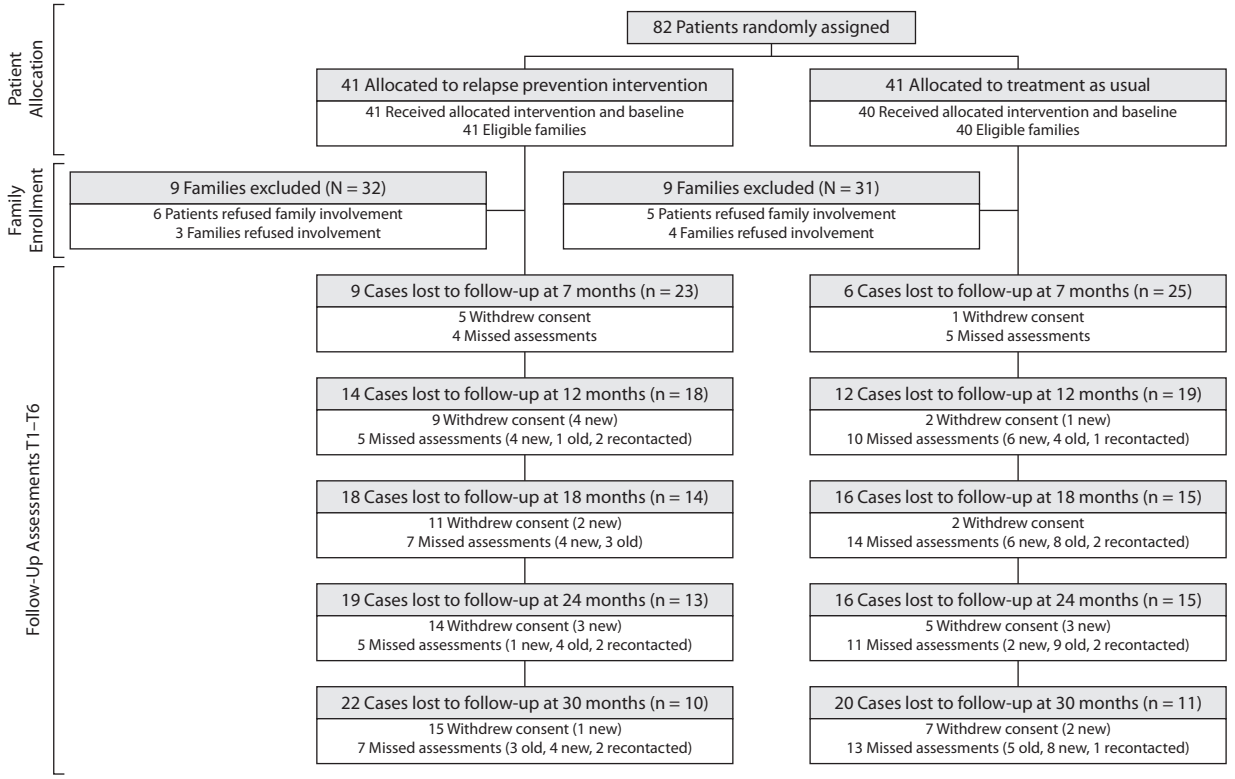
## RESULTS

### Patient and Family Attrition

Recruitment to the study occurred at both patient and family levels (Figure 1), and allocation of families was dependent upon patient randomization. At baseline, 1 participant dropped out after randomization to the TAU group, and no data were available for this patient (thus, 41 in RPT

  
© Copyright 2010 Physicians Postgraduate Press, Inc.

Figure 1. Family Participation Through Various Stages of the Study




and 40 in TAU). Further details on the patient flow can be found elsewhere.[22]

Family member attrition and participation through the Episode II study is depicted in Figure 1. Forty-one families in the RPT group and 40 in the TAU group were eligible for recruitment into the study. Data were not available for 9 families in the RPT group due to patients refusing to consent to their family being involved (n = 6) or families not consenting (n = 3). Similarly, data were not available for 9 families from the TAU group (patients refused family involvement, n = 5; families refused involvement, n = 4).

In Figure 1, lost to follow-up was defined in terms of cases that formally withdrew consent or cases that missed assessment time points. Missed assessments could be sporadic (occurred at 1 assessment time point) or of a monotone pattern (data missed at 1 time point and the remainder of time points). There were some instances in which participants missed 1 assessment time point but were recontacted at the proceeding time point. These cases are also highlighted in Figure 1. There were no significant differences in the rates of those lost to follow-up between the 2 groups at the 5 follow-up time points.

Participants who were and were not lost to follow-up at T6 (30 months) were compared on a range of demographic variables. There were no significant differences between completers and those lost to follow-up at T6 with respect to caregivers' age or any of the baseline family measures.

### Demographic and Baseline Group Comparisons

Relatives of patients in the RPT group were significantly more likely to be employed in part-time and casual employment than families in the TAU group ($\chi^2_1 = 4.24$, $P = .039$ [Table 1]). The reverse was noted for the "other" employment status category, with families in the TAU group more likely to fall into this category ($\chi^2_1 = 8.95$, $P = .003$). The "other" category included home duties, studying, unemployment benefits, and volunteer work.

Relatives of patients in the RPT group were significantly more likely to be residing with the patient at the time of the study ($\chi^2_1 = 5.38$, $P = .020$). Relatives in the 2 groups did not differ on any of the baseline ECI total or subscale scores, the GHQ-28 total or subscale scores, or the FQ (see Tables 1 and 2). They also did not differ significantly in terms of levels of distress as measured by a cut-off value ≥ 5 on the GHQ-28 (RPT = 38.7%, n = 12; TAU = 41.9%, n = 13).

Family work was available to all families. The Mann-Whitney *U* test was used to determine differences between the two groups with respect to use of family therapy. There were no significant differences between RPT and TAU in terms of contacts with family therapy across the treatment


© Copyright 2010 Physicians Postgraduate Press, Inc.

**Table 1. Baseline Demographic Characteristics of Families in the Relapse Prevention and Treatment as Usual Groups[a]**

| Characteristic | Total Sample (N = 63) | Relapse Prevention (n = 32) | Treatment as Usual (n = 31) |
|---|---|---|---|
| Caregiver's age, mean (SD), y | 45.5 (9.5) | 44.2 (10.4) | 46.8 (8.4) |
| Country of birth, Australia | 57.1 (36) | 50.0 (16) | 64.5 (20) |
| English speaking | 95.2 (60) | 96.9 (31) | 93.5 (29) |
| Marital status, married | 47.6 (30) | 43.8 (14) | 51.6 (16) |
| Employment status[b] | | | |
| Unemployed | 24.2 (15) | 19.4 (6) | 29.0 (9) |
| Full-time paid work | 27.4 (17) | 25.8 (8) | 29.0 (9) |
| Part-time or casual paid work | 41.9 (26) | 54.8 (17) | 29.0 (9) |
| Other | 17.5 (11) | 3.2 (1) | 32.3 (10) |
| Relationship to patient | | | |
| Parent | 87.3 (55) | 84.4 (27) | 90.3 (28) |
| Spouse | 7.9 (5) | 12.5 (4) | 3.2 (1) |
| Sibling | 3.2 (2) | 3.1 (1) | 3.2 (1) |
| Grandparent | 1.6 (1) | 0.0 (0) | 3.2 (1) |
| Living with client, yes | 87.3 (55) | 96.9 (31) | 77.4 (24) |

[a]Characteristics are measured as % (n) unless otherwise noted.
[b]Multiple response categories.

phase (ie, T1–T2, $z = -0.80$, $P = .424$) or throughout the study period ($z = -0.76$, $P = .45$).

## Burden of Care and Carer Symptoms

The descriptive statistics for the ECI subscales and total scores are depicted in Table 2. Overall, regardless of time, the RPT group had significantly higher mean scores on the positive personal experiences subscale ($F_{1,62.17} = 4.19$, $P = .045$) and total positive score ($F_{1,63.58} = 4.39$, $P = .040$) as compared to the TAU group (viz, group main effect).

Significant main effects for time were noted for need to back up ($F_{5,75.43} = 3.80$, $P = .004$), dependency ($F_{5,97.61} = 6.62$, $P < .001$), and loss ($F_{5,89.80} = 3.19$, $P = .011$) subscales. For need to back up, the mean score at T6 was significantly lower than for baseline ($P = .006$) and T2 ($P = .035$). For dependency, the mean score at baseline was significantly lower than at all other time points ($P$ values range from < .001 to .028). Finally, for loss, there was a significant reduction for the entire sample in scores from baseline to T5 ($P = .003$).

Although there were no significant interactions for all ECI components, planned comparisons indicated that the RPT group demonstrated significantly greater reductions in negative symptoms than the TAU group from T1–T4 ($P = .012$) and T1–T5 ($P = .040$).

There were no significant group or time differences found on the GHQ-28 total score (see Table 2) or for any of its subscales (results for subscales are not reported). Planned comparisons also supported nonsignificant findings.

## Expressed Emotion

No significant group differences (viz, main effect for group) were found on the critical comments or emotional overinvolvement subscales of the FQ (see Table 2). However, there was a significant difference over time (viz, main

**Table 2. Mean (SE) Scores for Expressed Emotion, Carer Burden, and Carer Symptoms in the Relapse Prevention and Treatment as Usual Groups[a]**

| | Time 1 (Baseline) | | Time 2 (7 mo) | | Time 3 (12 mo) | | Time 4 (18 mo) | | Time 5 (24 mo) | | Time 6 (30 mo) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | RP | TAU | RP | TAU | RP | TAU | RP | TAU | RP | TAU | RP | TAU |
| ECI | | | | | | | | | | | | |
| Difficult behaviors | 11.6 (1.4) | 10.4 (1.4) | 10.9 (1.5) | 10.3 (1.5) | 12.6 (1.6) | 10.7 (1.6) | 9.3 (1.8) | 7.6 (1.7) | 10.3 (1.8) | 8.8 (1.7) | 9.0 (2.0) | 9.4 (2.1) |
| Negative symptoms | 11.2 (1.2) | 8.9 (1.2) | 11.5 (1.3) | 10.6 (1.3) | 11.1 (1.4) | 10.0 (1.4) | 6.7 (1.5) | 9.2 (1.4) | 6.9 (1.5) | 8.8 (1.5) | 8.8 (1.7) | 7.5 (1.8) |
| Stigma | 5.3 (0.7) | 4.7 (0.8) | 5.0 (0.8) | 5.6 (0.8) | 4.1 (0.9) | 5.3 (0.9) | 4.2 (1.0) | 5.0 (0.9) | 3.2 (1.0) | 4.7 (1.0) | 2.8 (1.1) | 4.7 (1.1) |
| Problems with services | 6.5 (1.1) | 7.4 (1.1) | 6.9 (1.2) | 9.1 (1.2) | 8.2 (1.3) | 7.8 (1.3) | 7.0 (1.5) | 9.2 (1.4) | 5.9 (1.5) | 8.7 (1.4) | 5.2 (1.7) | 7.8 (1.7) |
| Need to back up | 10.9 (1.0) | 9.9 (1.0) | 10.4 (1.1) | 9.7 (1.0) | 9.5 (1.1) | 9.5 (1.1) | 10.1 (1.3) | 8.2 (1.2) | 8.5 (1.3) | 9.4 (1.2) | 8.1 (1.3) | 6.2 (1.3) |
| Dependency | 11.0 (0.8) | 9.7 (0.8) | 8.8 (0.9) | 8.7 (0.9) | 8.9 (0.9) | 7.9 (0.9) | 7.9 (1.0) | 8.3 (1.0) | 7.2 (1.1) | 7.8 (1.0) | 7.2 (1.1) | 7.0 (1.1) |
| Loss | 11.6 (1.0) | 10.5 (1.0) | 10.3 (1.1) | 9.2 (1.1) | 10.3 (1.2) | 9.0 (1.2) | 10.1 (1.3) | 8.6 (1.3) | 6.9 (1.4) | 7.8 (1.3) | 7.9 (1.5) | 8.3 (1.5) |
| Total negative score | 76.9 (6.6) | 70.4 (6.7) | 72.9 (7.1) | 72.3 (7.0) | 74.9 (7.6) | 70.1 (7.5) | 64.6 (8.3) | 65.6 (8.0) | 58.7 (8.5) | 65.0 (8.1) | 60.4 (9.5) | 59.7 (9.6) |
| Positive personal experience | 16.3 (1.2) | 14.5 (1.2) | 18.0 (1.3) | 15.5 (1.3) | 18.7 (1.4) | 13.6 (1.4) | 16.8 (1.6) | 14.9 (1.5) | 17.0 (1.6) | 14.4 (1.5) | 16.4 (1.7) | 12.2 (1.7) |
| Good aspects of relationships | 14.4 (0.8) | 13.7 (0.8) | 14.0 (0.9) | 13.1 (0.8) | 13.9 (0.9) | 13.4 (0.9) | 14.7 (1.0) | 13.6 (1.0) | 14.4 (1.1) | 12.9 (1.0) | 16.1 (1.2) | 13.1 (1.2) |
| Total positive score | 30.7 (1.6) | 28.2 (1.7) | 32.2 (1.8) | 28.6 (1.8) | 32.7 (2.0) | 26.5 (1.9) | 31.2 (2.2) | 28.0 (2.1) | 31.5 (2.3) | 27.5 (2.2) | 32.5 (2.5) | 25.5 (2.5) |
| Family questionnaire | | | | | | | | | | | | |
| Critical comments | 22.7 (1.3) | 20.4 (1.3) | 21.1 (1.4) | 20.7 (1.4) | 21.3 (1.5) | 21.0 (1.5) | 18.8 (1.7) | 18.0 (1.7) | 17.7 (1.7) | 20.2 (1.6) | 18.6 (1.8) | 20.4 (1.8) |
| Emotional overinvolvement | 24.9 (1.1) | 25.3 (1.2) | 22.0 (1.2) | 25.0 (1.2) | 21.2 (1.3) | 23.8 (1.3) | 21.4 (1.4) | 22.8 (1.4) | 19.9 (1.4) | 22.5 (1.3) | 20.2 (1.5) | 22.2 (1.5) |
| GHQ-28 total score | 5.7 (1.1) | 5.7 (1.1) | 4.0 (1.2) | 4.7 (1.2) | 5.7 (1.3) | 4.7 (1.3) | 3.8 (1.5) | 4.1 (1.4) | 3.5 (1.6) | 3.4 (1.5) | 4.9 (1.8) | 2.8 (1.7) |

[a]Mean (SE) estimated from mixed-effects model repeated-measures analyses.
Abbreviations: ECI = Experience of Caregiving Inventory, GHQ-28 = General Health Questionnaire of 28 Items, RP = relapse prevention, TAU = treatment as usual.

effect for time) for the emotional overinvolvement subscale, $F_{5,104.6} = 7.80$, $P < .001$. The mean for emotional overinvolvement at baseline was significantly higher than the means obtained for all other time points ($P$ values ranging from < .001 to .022). There were no significant interactions for time by group on any of the family outcome measures. Planned comparisons were also not significant.

## DISCUSSION

These results provide partial support for our hypothesis that family members with relatives with FEP who had reached remission on positive symptoms would gain significant and sustained benefit in terms of appraisals related to caregiving if their relative was randomly assigned to a specific relapse prevention intervention that combined both individual and family RPT compared with TAU within a specialist FEP program. This is the first randomized controlled study to demonstrate this benefit for family members caring for a relative with FEP. Results in randomized trials designed to evaluate the effectiveness of family-based psychoeducation interventions in relation to caregiver burden in family members with a relative with chronic psychosis have been mixed.[36,37]

Our results show a specific advantage in caregiver appraisals in relation to negative symptoms and greater positive personal experiences of caring and greater overall positive scores, which additionally includes good aspects of the relationship. There were no significant group effects for other subscales of the experience of caregiving. Addington and colleagues[3] did not previously find significant changes in their family members in the positive aspects of caregiving. Our pattern of findings in relation to the experience of caregiving may be a result of an increased preparedness among the families for intervening early to prevent possible relapses. This early intervention may have increased the families' recognition of their potential to contribute to the care and well-being of their relative, thereby increasing their appraisals of the positive aspects of caregiving. This finding could also be interpreted with reference to the paradigm of positive psychology—enhanced recognition of personal strengths related to caregiving may have mediated changes in appraisals.[38]

In relation to our secondary hypotheses, there was no significant group effect for any of the EE scales, and there were no significant effects for psychological distress as measured by the GHQ-28. The EE result was perhaps not surprising given that communications skills training was only employed in select cases throughout RPT to avoid the known potential for paradoxical effects in low EE FEP families.[18] This finding highlights that reducing EE is not a necessary condition in FEP in order to prevent relapse and that selectively focusing on EE is feasible and safe. Notwithstanding our present finding, we believe that caution in the selective targeting of EE in FEP remains the most prudent course of action until there is further understanding of its role in FEP.

The nonsignificant GHQ-28 results suggest that either a longer course of family intervention may be warranted for family members experiencing symptoms indicative of mood or anxiety disorders or more interventions specifically targeted at those symptoms may be required. We note, for example, that Addington and colleagues,[3] who reported a significant improvement in family well-being over a 3-year follow-up period, reported that the number of family sessions ranged from 2–21. It is also possible that the baseline level of distress may have been lower in the current sample, making it more difficult to detect change over time.

In addition to the benefits of RPT for specific aspects of caregiver stress, the main effects over time for loss, dependency, need for back-up, and emotional overinvolvement indicate that family stress and family communication styles should not be considered to be static in first-episode families. This result is consistent with previous findings regarding the course of EE[11,13,39] and with previous findings from a specialist FEP program, which reported significant improvements in the levels of negative aspects of the burden of caregiving in FEP families (not restricted to relatives of patients who had reached remission) over the first 3 years after the commencement of treatment.[3] One advantage of our study is that we have controlled for the potential confounding effect of the severity of baseline positive psychotic symptoms in the patient participants.

It is possible that families are continually reappraising and shifting their attributions of the changes in their relatives' recovery and adjusting their perception of their role accordingly.[40] The changes on the ECI and FQ scales over time indicated that, as a group, families were developing or regaining hope for their relative and reducing the intensity of their caregiving role in line with perceived improvements in their relative. These changes in the experience of caregiving and emotional overinvolvement may also reflect the time course for families in integrating new understandings about psychosis as their relative moves through remission into fuller recovery (or relapse).

In light of these results, once remission is achieved on positive symptoms of psychosis after FEP, consideration should be given to offering the patient and his or her family a specific relapse prevention intervention in order to reduce the risk of relapse and in order to improve the family's experience of caregiving. The main effects for time indicate that FEP services should monitor initial changes over time in EE in response to psychoeducation and supportive interventions in high-EE families, as opposed to streaming families during the initial stages of treatment into interventions that specifically target high emotional overinvolvement.

The strengths of our study included (1) the innovative focus upon a specific subgroup of FEP patients and their families; (2) the successful integration of a family intervention together with an individual intervention; (3) the

duration of the follow-up period, which enabled us to indicate a sustained benefit of our family intervention; (4) the control intervention, which included access to family interventions that are typically available within FEP programs; and (5) the randomized design with raters blind to treatment condition. The limitations included the use of a self-report measure of EE, the rate of attrition from the study, and the patient-based and not family-based randomization procedure.

We plan to undertake a detailed analysis of the components of the family intervention. Further research is needed into the longer term course of family distress and appraisals of caregiving after FEP. Future trials of family interventions should further investigate the potential benefits for the positive aspects of caregiving-related preventive family interventions.

***Author affiliations:*** Marqués de Valdecilla Public Foundation–Research Institute (FMV-IFIMAV), Santander, Spain (Dr Alvarez-Jimenez); Department of Psychology (Dr Gleeson) and Department of Psychiatry (Drs Cotton, Wade, and McGorry and Mss Newman and Spiliotacopoulos), The University of Melbourne, Australia; and Australian Centre for Posttraumatic Mental Health (Dr Wade); NorthWestern Mental Health Program (Dr Gleeson); and Orygen Youth Health and Research Centre (Drs Cotton, Alvarez-Jimenez, and McGorry; Mr Crisp; and Mss Newman and Spiliotacopoulos), Victoria, Australia.

***Potential conflicts of interest:*** **Dr McGorry** is a consultant for, has received grant/research support from, and has received honoraria from Eli Lilly, Janssen, Pfizer, and AstraZeneca. **Drs Gleeson, Cotton, Alvarez-Jimenez,** and **Wade; Mr Crisp;** and **Mss Newman** and **Spiliotacopoulos** have no personal affiliations or financial relationships with any commercial interest to disclose relative to the article.

***Funding/support:*** This study was funded by an unrestricted grant from Eli Lilly via the Lilly Melbourne Academic Psychiatry Consortium. In addition, the study was supported by the Colonial Foundation and a Program Grant from the National Health and Medical Research Council of Australia, grant ID 350241. The salary for Dr Alvarez-Jimenez was funded by Marqués de Valdecilla Public Foundation–Research Institute (FMV-IFIMAV).

***Role of sponsor:*** None of the sponsors had any involvement in any aspect of the study or manuscript.

## REFERENCES

1. Szmukler GI, Burgess P, Herrman H, et al. Caring for relatives with serious mental illness: the development of Experience of Caregiving Inventory. *Soc Psychiatry Psychiatr Epidemiol.* 1996;31(3-4):137–148.
2. Lazarus RS, Folkman S. *Stress, Appraisal, and Coping*. New York, NY: Springer; 1984.
3. Addington J, McCleery A, Addington D. Three-year outcome of family work in an early psychosis program. *Schizophr Res.* 2005; 79(1):107–116.
4. Addington J, Coldham EL, Jones B, et al. The first episode of psychosis: the experience of relatives. *Acta Psychiatr Scand.* 2003;108(4):285–289.
5. Tennakoon L, Fannon D, Doku V, et al. Experience of caregiving: relatives of people experiencing a first episode of psychosis. *Br J Psychiatry.* 2000;177:529–533.
6. Falloon IR, Montero I, Sungur M, et al. Implementation of evidence-based treatment for schizophrenic disorders: two-year outcome of an international field trial of optimal treatment. *World Psychiatry* 2004;3(2):104–109.
7. Addington J, Burnett P. Working with families in the early stages of psychosis. In: Gleeson JF, McGorry P, eds. *The First Psychotic Relapse: Understanding the Risks and the Opportunities for Prevention*. Chichester, United Kingdom: Wiley; 2004.
8. Vaughn C, Leff J. Measurement of expressed emotion in families of psychiatric patients. *Br J Soc Clin Psychol.* 1976;15(2):157–165.
9. Kavanagh DJ. Recent developments in expressed emotion and schizophrenia. *Br J Psychiatry.* 1992;160:601–620.
10. Marom S, Munitz H, Jones PB, et al. Expressed emotion: relevance to rehospitalization in schizophrenia over 7 years. *Schizophr Bull.* 2005;31(3):751–758.
11. Leff J, Wig NN, Bedi H, et al. Relatives' expressed emotion and the course of schizophrenia in Chandigarh: a two-year follow-up of a first-contact sample. *Br J Psychiatry.* 1990;156:351–356.
12. Huguelet P, Favre S, Binyet S, et al. The use of the Expressed Emotion Index as a predictor of outcome in first admitted schizophrenic patients in a French speaking area of Switzerland. *Acta Psychiatr Scand.* 1995;92(6):447–452.
13. Lenior ME, Dingemans PMAJ, Schene AH, et al. The course of parental expressed emotion and psychotic episodes after family intervention in recent-onset schizophrenia: a longitudinal study. *Schizophr Res.* 2002;57(2–3):183–190.
14. King S, Dixon MJ. Expressed emotion and relapse in young schizophrenia outpatients. *Schizophr Bull.* 1999;25(2):377–386.
15. Falloon IRH. *Handbook of Behavioral Family Therapy*. New York, NY: The Guilford Press; 1988.
16. Mueser KT, Glynn S. *M. Behavioral Family Therapy for Psychiatric Disorders*. 2nd ed. Oakland, CA: New Harbinger; 1999.
17. Zhang M, Wang M, Li J, et al. Randomised-control trial of family intervention for 78 first-episode male schizophrenic patients: an 18-month study in Suzhou, Jiangsu. *Br J Psychiatry Suppl.* 1994;165(24):96–102.
18. Linszen D, Dingemans P, Van Der Does JW, et al. Treatment, expressed emotion and relapse in recent onset schizophrenic disorders. *Psychol Med.* 1996;26(2):333–342.
19. Lenior ME, Dingemans P, Linszen DH, et al. Social functioning and the course of early-onset schizophrenia: five-year follow-up of a psychosocial intervention. *Br J Psychiatry.* 2001;179:53–58.
20. Gleeson J. Preventing Episode II: relapse prevention in first-episode psychosis. *Australas Psychiatry.* 2005;13(4):384–387.
21. Gleeson J, Wade D, Castle D, et al. The Episode II trial of cognitive and family therapy for relapse prevention in early psychosis: rationale and sample characteristics. *J Ment Health.* 2008;17(1):19–32.
22. Gleeson JFM, Cotton SM, Alvarez-Jimenez M, et al. A randomized control trial of relapse prevention therapy for first-episode psychosis patients. *J Clin Psychiatry.* 2009;70(4):477–486.
23. Nuechterlein KH, Snyder KS, Mintz J. Paths to relapse: possible transactional processes connecting patient illness onset, expressed emotion, and psychotic relapse. *Br J Psychiatry.* 1992;161(suppl 18):88–96.
24. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Washington, DC: American Psychiatric Association; 1994.
25. Lukoff D, Liberman RP, Nuechterlein KH. Symptom monitoring in the rehabilitation of schizophrenic patients. *Schizophr Bull.* 1986; 12:578–593.
26. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep.* 1962;10:799–812.
27. McGorry PD, Edwards J, Mihalopoulos C, et al. EPPIC: an evolving system of early detection and optimal management. *Schizophr Bull.* 1996;22(2):305–326.
28. Early psychosis prevention and intervention centre. *Case Management in Early Psychosis: A Handbook*. Victoria, Australia: Parkville; 2001.
29. Wiedemann G, Rayki O, Feinstein E, et al. The Family Questionnaire: development and validation of a new self-report scale for assessing expressed emotion. *Psychiatry Res.* 2002;109(3):265–280.
30. Goldberg DP. *The Detection of Psychiatric Illness by Questionnaire: A Technique for the Identification and Assessment of Non-Psychotic Psychiatric Illness*. London, England: Oxford University Press; 1972.
31. Goldberg DP, Gater R, Sartorius N, et al. The validity of two versions of the GHQ in the WHO Study of Mental Illness in General Health Care. *Psychol Med.* 1997;27(1):191–197.
32. Tabachnick BG, Fidell LS. *Using Multivariate Statistics (5th ed.)*: Boston, MA: Allyn & Bacon/Pearson Education; 2007.
33. Lindmann HR. *Analysis of Variance in Complex Experimental Designs*. San Francisco, CA: W.H. Freeman and Company; 1974.
34. Gueorguieva R, Krystal JH. Move over ANOVA: progress in analyzing repeated-measures data and its reflection in papers published in the *Archives of General Psychiatry*. *Arch Gen Psychiatry.* 2004;61(3): 310–317.

35. Mallinckrodt CH, Clark WS, Carroll RJ, et al. Assessing response profiles from incomplete longitudinal clinical trial data under regulatory considerations. *J Biopharm Stat.* 2003;13(2):179–190.
36. Szmukler G, Kuipers E, Joyce J, et al. An exploratory randomised controlled trial of a support programme for carers of patients with a psychosis. *Soc Psychiatry Psychiatr Epidemiol.* 2003;38(8):411–418.
37. Gutierrez-Maldonado J, Caqueo-Urizar A. Effectiveness of a psychoeducational intervention for reducing burden in Latin American families of patients with schizophrenia. *Qual Life Res.* 2007;16(5):739–747.
38. Seligman MEP, Steen TA, Park N, et al. Positive psychology progress: empirical validation of interventions. *Am Psychol.* 2005;60(5):410–421.
39. Patterson P, Birchwood M, Cochrane R. Preventing the entrenchment of high expressed emotion in first episode psychosis: early developmental attachment pathways. *Aust N Z J Psychiatry.* 2000;34(suppl):S191–S197.
40. McNab C, Haslam N, Burnett P. Expressed emotion, attributions, utility beliefs, and distress in parents of young people with first episode psychosis. *Psychiatry Res.* 2007;151(1–2):97–106.