

REVIEW ARTICLE

Psychological treatments in schizophrenia: I. Meta-analysis of family intervention and cognitive behaviour therapy

S. PILLING,¹ P. BEBBINGTON, E. KUIPERS, P. GARETY, J. GEDDES, G. ORBACH
AND C. MORGAN

From the Centre for Outcomes, Research and Effectiveness, Department of Psychology, University College London, Royal Free and University College Medical School, Department of Psychiatry and Behavioural Sciences, UCL, Department of Psychology, Institute of Psychiatry and Department of Psychiatry, St Thomas' Hospital, London; and Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford

ABSTRACT

Background. While there is a growing body of evidence on the efficacy of psychological interventions for schizophrenia, this meta-analysis improves upon previous systematic and meta-analytical reviews by including a wider range of randomized controlled trials and providing comparisons against both standard care and other active interventions.

Method. Literature searches identified randomized controlled trials of four types of psychological interventions: family intervention, cognitive behavioural therapy (CBT), social skills training and cognitive remediation. These were then subjected to meta-analysis on a variety of outcome measures. This paper presents results relating to the first two.

Results. Family therapy, in particular single family therapy, had clear preventative effects on the outcomes of psychotic relapse and readmission, in addition to benefits in medication compliance. CBT produced higher rates of 'important improvement' in mental state and demonstrated positive effects on continuous measures of mental state at follow-up. CBT also seems to be associated with low drop-out rates.

Conclusions. Family intervention should be offered to people with schizophrenia who are in contact with carers. CBT may be useful for those with treatment resistant symptoms. Both treatments, in particular CBT, should be further investigated in large trials across a variety of patients, in various settings. The factors mediating treatment success in these interventions should be researched.

INTRODUCTION

The effectiveness of antipsychotic medication has made it central to the treatment of schizophrenia (Schwartz *et al.* 1993). However, there is an increasing acknowledgement that pharmacological treatment on its own is rarely sufficient for the best outcome in this disabling condition.

There are a number of reasons for this. First, the issue of compliance has made it clear that the social and cognitive context in which pharmacological treatment is delivered has a major effect on its success (Bebbington & Kuipers, 1994). Secondly, the effectiveness of antipsychotic medication has to some extent been called into question. This came about because of the interest in treatment resistance fostered by the introduction of clozapine. Thus, it is now generally held that a significant proportion of patients, perhaps up to 40%, have a poor

¹ Address for correspondence: Mr Stephen Pilling, Centre for Outcomes, Research and Effectiveness (CORE), Department of Psychology, UCL, 1–19 Torrington Place, London WC1E 6BT.

response to antipsychotic medication and continue to show moderate to severe psychotic symptoms (Kane, 1996). The final element in the re-evaluation of the treatment of schizophrenia is that there has been a change in perception of psychological interventions, such that they are now recognized as an important component of a comprehensive therapeutic approach (Department of Health, NHS Executive, 1999).

Antipsychotic drugs have a limited impact on the negative symptoms of schizophrenia, and thus do not contribute to the development of the skills necessary for successful transition back into the community (Lieberman, 1994). A recent meta-analysis has suggested that the benefit even of the new atypical antipsychotics is less than previously thought (Geddes *et al.* 2000). There is thus a clear requirement for the development of new approaches if the wide ranging needs of people with schizophrenia are to be met. This emphasis is new. In comparison to those channelled into pharmacological interventions, relatively few resources have been spent on evaluating and developing other treatments.

The analysis of psychological interventions in schizophrenia presented here is the product of a joint British Psychological Society and Royal College of Psychiatrist's working party on the development of Psychosocial Guidelines for the Treatment of Schizophrenia. It draws largely on the Cochrane methodology (Mulrow & Oxman, 1997), with certain modifications. In identifying areas for review, the working party had two guiding principles. To warrant the inclusion of the type of psychological intervention, we required there should be considerable uncertainty about both the interpretation of the existing research findings and the application of these findings in routine practice. There also had to be a sufficient level of evidence (in the form of randomized controlled trials) to support systematic review and meta-analysis. The current paper describes the methodology used and presents results relating to family interventions (FIs) and cognitive behaviour therapy (CBT). It is the first of a pair intended to assess whether the current enthusiasm for psychological interventions can be justified by the evidence. The second paper (Pilling *et al.* 2001)

covers social skills training and cognitive remediation.

Talking to people with schizophrenia and their relatives

Modern psychological treatments for schizophrenia originate in studies of the impact of the social environment on mental illness. In the United Kingdom there was an interest in the effect of the family environment in the maintenance of major mental disorders, in particular schizophrenia (Brown *et al.* 1962). This led to the development of the concept of expressed emotion (Brown & Rutter, 1966; Brown *et al.* 1972), and the establishment of family interventions for the treatment of schizophrenia (Leff *et al.* 1982). These revolutionized the way that clinicians viewed family members, and had a general effect of improving communication between clinicians and informal carers. The application of CBT for depression (Beck *et al.* 1979) to psychotic disorders has resulted in a complex treatment package with a range of techniques and targets (Fowler *et al.* 1995).

There is considerable variation in the content and application of these psychological interventions. The effectiveness of all psychological interventions for schizophrenia depends on the establishment of a positive therapeutic alliance with the patient (Roth & Fonagy, 1996). Working with people with schizophrenia presents particular difficulties, and the pace and development of the therapeutic alliance demands great flexibility. However, the requirement for such an alliance is clear.

There have been several systematic reviews and meta-analytical studies of psychological interventions in schizophrenia in the past 10 years that cover this area in whole or in part (Mari & Streiner, 1994; Mojtabi *et al.* 1998; Adams, 2000; Dixon *et al.* 2000; Gould *et al.* 2001; Bustillo *et al.* 2001; Pitschel-Walz *et al.* 2001; Rector & Beck, 2001; Cormac *et al.* 2002). These vary considerably in range, depth and focus. In the current paper, we have confined our review to high quality randomized controlled trials (RCTs) providing comparisons either with standard care or with other active interventions. We feel that this is an advance on previous work. We have been able to identify more RCTs than have been reported in previous systematic

reviews. The meta-analyses are based on the examination of original data and not taken from other systematic reviews or meta-analytical studies.

METHOD

Research strategy

Electronic searches for both family interventions and cognitive behavioural interventions were undertaken using *Biological Abstracts* (1980–1999), CINAHL (1982–1999), the Cochrane Library (Issue 2, 1999), the Cochrane Schizophrenia Group's Register of Trials (August, 1999), EMBASE (1980–1999), MEDLINE (1966–1999), PsycLIT (1887–1999), SIGLE (1990–1999), and Sociofile (1980–1999). (More detailed descriptions of both search strategies are available from the authors.) All reference lists of the articles selected were searched for further relevant trials. Review articles were also scanned.

The basis of study selection

Papers were checked for methodological rigour and validity by two reviewers (S.P. and G.O.), who independently inspected all citations, adhering to guidelines for conducting literature reviews (Mulrow & Oxman, 1997). When disputes arose about which category a citation should be allocated to, or its relevance to the report, we attempted to resolve them by discussion. If this failed, a further reviewer (P.B. or P.G.) was asked to review the article and decide. Only RCTs were considered for inclusion in the analysis.

Given the problems in the literature surrounding the definitions of psychosocial interventions and of diagnosis, explicit inclusion criteria were specified.

For an intervention to be classed as 'family intervention' it had to include family sessions with a specific supportive and treatment function, and a minimum of one of the following treatment components: psycho-educational intervention; problem solving/crisis management work; or, intervention with the identified patient. In addition, interventions were required to be for at least 6 weeks.

In order to be classified as 'cognitive behaviour therapy' interventions had to have a

component which involved recipients establishing links between their thoughts, feelings or actions with respect to the target symptoms; and the correction of their misperceptions, irrational beliefs or reasoning biases related to those symptoms. At least one of the following was also required: self-monitoring of the treated person's thoughts, feelings or behaviours with respect to the target symptoms; and the promotion of alternative ways of coping with the target symptoms.

The included studies were based on samples of people with schizophrenia or related disorders, including delusional disorder, schizophreniform disorder and schizoaffective disorder (basically ICD-10 F2; WHO, 1992). Trials where participants were not restricted to people with schizophrenia and from which it was impossible to extract results for this group were not included. Many participants were also reported to have co-morbid mental disorders, such as depression or anxiety disorder.

The individual trials excluded participants for a variety of reasons such as organic brain syndromes, substance misuse and failing to reach a minimum IQ score. Outcomes were death, mental state, relapse, re-admission, burden, expressed emotion, medication compliance and acceptability of treatment. These outcomes were chosen because they were thought to be good indicators of treatment effectiveness, clinically important, and common to most studies.

Analysis of data

Intention-to-treat analysis was performed on all data i.e. on a 'once randomized always analyse' basis. This assumes that those participants who ceased to engage in the study – from whatever group – had an unfavourable outcome (with the exception of the outcome of 'natural death'). While recognizing that most psychosocial therapies focus on those with severe illness and thereby risk high attrition rates, the reviewers felt that attrition of > 50% would call into question the value of the study. Studies losing > 50% of people were therefore excluded, even if they reported relevant outcomes.

Analysis of dichotomous outcomes (e.g. relapse, readmission) was performed using odds ratios. An odds ratio is calculated by dividing the probability of an event in a treatment group

by its odds in the comparison group. Clinical trials typically look for treatments that reduce 'bad event' rates, and therefore aim at an odds ratio of less than one. For example, a treatment that caused a 7% reduction in suicide would have an OR of 0.93. Ninety-five per cent confidence intervals are reported with the odds ratios. The primary analysis employed the fixed effects method of Mantel & Haenzel (1959). This method assumes that a single underlying treatment effect is present across all studies. However, in reality this may not be the case, particularly for psychological treatments. To account for the potential heterogeneity in treatment effects, a random effects analysis was therefore also undertaken (DerSimonian & Laird, 1986). In the random effects analysis, heterogeneity is accounted for both in the width of confidence intervals and the estimate of the treatment effect. With decreasing heterogeneity the random effects approach moves asymptotically towards a fixed effects model.

A similar analysis was undertaken for continuous data, using an effect size (Cohen, 1977). Effect sizes are typically the difference between the mean in the experimental group and the mean in the control group, divided by a pooled standard deviation. Thus, the effect size expresses the difference between means relative to within-group variation. The fixed effects model we used in these analyses was that advocated by Hedges & Olkin (1985), and the reported statistics were either standardized effect sizes or weighted mean differences. Where different measures were used in different trials (e.g. where the Brief Psychiatric Rating Scale (BPRS) (Overall & Gorham, 1962) and the Comprehensive Psychopathological Rating Scale (CPRS) (Åsberg *et al.* 1978) were used to estimate the same underlying effect), or where there was a likelihood of poor inter-rater reliability, standardized effect sizes were calculated, based on the procedures of Glass *et al.* (1981). However, as advocated by Hedges & Olkin (1985), a pooled standard deviation was used instead of the comparison group standard deviation. For the standardized effect size (d), a value of 1.0 indicates that the mean of the treatment group is 1 standard deviation higher than the mean of the comparison group. Each effect size was calculated using StatsDirect (2000), and was corrected for bias using calculations from the gamma distribution. A

DerSimonian/Laird random effect size was also calculated to account for heterogeneity between studies included in the meta-analysis (DerSimonian & Laird, 1986). To avoid applying parametric tests to data that do not meet their requirements, a standard was applied to all continuous data before inclusion. Only papers where standard deviations or standard errors and means were reported were included in the review. When continuous measures started from a finite number (such as 0), data were included only if the standard deviation, multiplied by 2, was less than the mean. Otherwise, the mean was unlikely to be an appropriate measure of the centre of the distribution (Altman & Bland, 1996).

As well as inspecting the graphical presentations, reviewers checked whether the differences between the results of trials were greater than would be expected by chance alone, using tests of heterogeneity. In this case, we used a Q statistic (Hedges & Olkin, 1985). A significance level less than 0.05 on the Q statistic was interpreted as evidence of heterogeneity. When heterogeneity was present, a sensitivity analysis was undertaken. Outlying studies were then removed if they caused a substantive change in the overall findings. Random effects models were also analysed to take into account heterogeneity of treatment.

In addition to the above statistics, the 'number need to treat' (NNT) was calculated. This number is the inverse of the absolute risk reduction i.e. the inverse of the difference in the proportion of events in the control group and in the treatment group. It refers to the number of patients it is necessary to treat in order to prevent one bad outcome (e.g. relapse) that would not have been prevented in the control group. NNTs in this paper are reported rounded up, in accordance with the general consensus (Cook & Sackett, 1995). Confidence intervals for absolute risk reduction and the number needed to treat are based on the iterative method of Miettinen & Nurminen (1985).

Where a sufficient number of trials was available, data were entered into a funnel graph (with trial effect plotted against trial size or 'precision') to assess the presence of publication bias. A formal test of funnel plot asymmetry was undertaken where appropriate (Egger, 1997). Significance levels of $P < 0.05$ were set *a priori*

for accepting the presence of asymmetry. Where only 3–4 studies reported an outcome, or there was little variety in sample size (or precision estimate) between studies, tests of asymmetry were not appropriate.

Family interventions

From this search, a total of 33 trials of family interventions for schizophrenia were identified, although 15 of these were excluded from the meta-analysis for a variety of reasons. The main reasons for exclusion were: the intervention comprised less than six sessions; methods of randomization were inadequate; participants did not exclusively have schizophrenia and related disorders; there was no appropriate control group; or there were no usable data. The 18 remaining studies involved a total of 1467 patients.

Cognitive behavioural interventions

A total of 22 trials concerning cognitive behavioural therapy were identified. However, 14 of these were excluded. The main reasons for exclusion were: methods of randomization were inadequate; the intervention did not meet criteria for 'cognitive behavioural therapy'; or there were no usable data. The eight remaining studies included 528 patients. A full list of all trials identified for both interventions is available from the authors.

Comparisons

Due to the rather diverse nature of the psychosocial treatments and their comparison groups, it was necessary to analyse several different comparisons. However, a global comparison was initially conducted, including all studies that reported outcomes regardless of the comparison group. Then, dependent on the presence of heterogeneity, we analysed studies that compared the intervention only with standard care, or only with other active treatments. Family therapy was also divided into two particular types of intervention, single family and group family interventions. Group family interventions were defined as those where the primary component of the treatment was a regular group session including more than one family. Separate comparisons are reported where appropriate.

RESULTS

Family interventions

The main variables available to form the basis of comparison in family treatment comprised relapse in intervals of various duration dating from the onset of treatment, relapse during intervals commencing from the end of treatment, readmission rates during similar sets of intervals, rates of dropouts, rates of suicide, the effects on burden and expressed emotion, and the level of medication compliance.

Characteristic of participants (Table 1)

A total of 1467 patients were included in the 18 family intervention trials analysed in this review. All studies reported the ages of patients, the mean being 31.2 years. Fourteen studies reported the sex of participants, with 31% female overall. The mean number of prior admissions, as reported in 13 studies, was 2.7. Seven studies report data on mean duration of illness, which was 6.3 years. Various criteria were used to provide a diagnosis of schizophrenia; three studies used DSM-III, seven studies DSM-III-R, one study DSM-IV, one the New Haven index, one the Research Diagnostic Criteria (RDC), and one the Chinese Medical Association's Criteria. Four used the Present State Examination (PSE) to provide an ICD-9 diagnosis.

Outcomes have been grouped into 12-month time periods for convenience and consistency of presentation. However, it should be stressed that measurements were made at some point in that time period, and it may be of greater relevance whether measurements were made during, or after the end of treatment.

Relapse

Of a total of 765 patients for whom relapse rates were reported, 144 out of 381 receiving family interventions and 206 out of 384 receiving other treatments, including standard care, relapsed within a period of 4 years. The results of the relapse analysis are reported in Table 2.

Eleven studies compared relapse with all other treatments over the first 12 months of treatment (Goldstein *et al.* 1978; Falloon *et al.* 1982; Leff *et al.* 1982, 1989; Hogarty *et al.* 1986, 1997a; Tarrier *et al.* 1988; Glynn *et al.* 1992; Xiong *et al.* 1994; McFarlane *et al.* 1995a, b;

Table 1. *Characteristics of family intervention trials*

| Study | N | Intervention | Patient participation | Duration and frequency | Comparison groups | Measures analysed in this report |
|--------------------------------|-----|--|------------------------------|--|---|---|
| Bloch <i>et al.</i> 1995 | 63 | Family counselling education, coping training | Excluded | 6 weekly sessions | Single session: discussion and educational audiotape and booklet | Hospital admission, dropout |
| Buchkremer <i>et al.</i> 1995 | 99 | Therapeutic relative groups: psycho-educational training, problem-solving and relatives self-help groups | Excluded | 1 h per fortnight/2 years | Standard care | Death, relapse, hospital admission, unemployment |
| Falloon <i>et al.</i> 1982 | 39 | Home family therapy, 24 h support, clinic-based crisis intervention and home visits | Included | 1 h per week/3 months, 1 h per 2 weeks/6 months, 1 h per month/15 months | Supportive management: out-patient clinic-based individual supportive psychotherapy | Relapse, hospital admission dropout, drug compliance, unemployment, social impairment |
| Glynn <i>et al.</i> 1992 | 41 | Behavioural family therapy | Included | Mean 21 per sessions per year/1 year | Customary care | Relapse, hospital admission, unemployment, dropout |
| Goldstein <i>et al.</i> 1978 | 104 | Crisis-orientated family therapy | Included | 1 session per week/6 weeks, 6 month follow-up | Standard care | Relapse, dropout |
| Hogarty <i>et al.</i> 1986 | 75 | Family psycho-education and management | Included | 2 h per week/18 months, 1 h per month/6 months | Nursing support and drug treatment | Relapse, drug compliance, EE |
| Hogarty <i>et al.</i> 1997a, b | 77 | Survival skills training and reintegration within the home and community | Included, excluded from some | 1/2 h fortnightly in year 1, 1 per 2-4 weeks for next 2 years | Supportive therapy: active listening, correct empathy, appropriate reassurance | Relapse, dropout |
| Leff <i>et al.</i> 1982 | 24 | Educational sessions: relatives' group, home-based family sessions | Included | Mean 5.6 h over 9 months, 15 month follow-up | Standard care (neuroleptic drugs) | Death, relapse, medication compliance |
| Leff <i>et al.</i> 1989 | 23 | Family therapy in the home with the patient and 2 psycho-education lectures | Included | 1 h per 2 weeks/9 months and then 1 per month for 15 months | Relatives group and 2 psycho-education lectures | Relapse, dropout, EE, social and occupational activities |
| Linszen <i>et al.</i> 1996 | 76 | Behavioural family intervention included individual orientated psychosocial intervention | Included | 1 session per 2 weeks/5 months, 1 per 4 weeks/7 months | Individual orientated psychosocial intervention | Relapse |

| | | | | | | |
|--|-----|--|----------------------------|---|--|---|
| MacFarlane <i>et al.</i> 1995 <i>a</i> | 172 | Multiple (six) family group | Excluded for some sessions | Fortnightly for 2 years | Single family treatment | Relapse, readmission, dropout, unemployment |
| MacFarlane <i>et al.</i> 1995 <i>b</i> | 46 | Multiple family treatment | Excluded for some sessions | 1 every 2 weeks (1st 2 years), 1 every month (next 2 years) | Single family treatment | Relapse, dropout |
| Posner <i>et al.</i> 1992 | 55 | Psycho-educational support group programme (patients excluded) | Excluded | 1½ h per week for 8 weeks, follow-up 10 months | Standard care | Death, readmission, dropout |
| Schooler <i>et al.</i> 1997 | 313 | Applied family management and monthly family group | Included | 1½ h per week for 13 weeks, per fortnight for 13 weeks, monthly thereafter | Supportive family management-monthly multi-family group meetings | Readmission, medication compliance, dropout |
| Tarrier <i>et al.</i> 1988 | 83 | Enactive programme: active participation of families in psycho-education and stress management programme | Included | 13 sessions over 9 months, 7 years follow-up | Standard care | Death, relapse, readmission, dropout, EE |
| Vaughan <i>et al.</i> 1992 | 36 | Counselling sessions for family and home exercises | Excluded | 1 h per week for 10 weeks | Standard care | Death, relapse, readmission, medication compliance, dropout |
| Xiong <i>et al.</i> 1994 | 63 | Family educational supportive sessions and monthly family group meetings | Included | 45 min per 2-3 weeks/9 months, 1 per 4 weeks/15 months + 90 min monthly group | Standard care | Death, relapse, readmission, family burden |
| Zhang <i>et al.</i> 1994 | 78 | Educative and family group sessions, additional follow-up as needed | Included | 1 session every 3 months for 18 months | Out-patient department follow-up and medication | Relapse, readmission, medication compliance |

Table 2. *Details of analysis of relapse rates with family interventions*

| Time of data collection | Comparison | Fixed effects odds ratio/effect size (95% CI) | Random effects odds ratio/effect size (95% CI) | Studies <i>N</i> | Patients <i>N</i> | NNT | Q (<i>P</i>) |
|--|---|---|--|---------------------|----------------------|----------------|----------------|
| 1st 12 months | v. All other treatments | 0.63 (0.46 to 0.86) | 0.52 (0.31 to 0.89) | 11 | 729 | 8 (6 to 18) | 23.04 (< 0.01) |
| 1st 12 months | v. Standard care | 0.37 (0.23 to 0.59) | 0.37 (0.23 to 0.60) | 6 | 355 | 6 (4 to 12) | 4.31 (0.51) |
| 1st 12 months | v. Active treatments | 0.89 (0.58 to 1.38) | 1.67 (0.71 to 0.31) | 5 | 357 | -23 (-∞ to -7) | 10.50 (0.03) |
| 1-2 years | v. All other treatments | 0.74 (0.44 to 1.25) | 0.57 (0.18 to 1.82) | 6 | 264 | 13 (6 to ∞) | 17.39 (< 0.01) |
| 1-2 years | Single family treatments v. All other treatments | 0.40 (0.19 to 0.84) | 0.42 (0.11 to 1.64) | 5 | 148 | 6 (3 to 20) | 9.44 (0.06) |
| Follow-up 4-15 months after the end of the treatment | Single family treatments v. Standard care | 0.79 (0.46 to 1.37) | 0.70 (0.27 to 1.76) | 4 | 228 | 19 (6 to ∞) | 7.00 (0.07) |

Q, Heterogeneity statistic ($P < 0.05$ indicates heterogeneity); NNT, number needed to treat (negative number denotes treatment less effective than comparison group, $+/- \infty$ indicates non-significant result).

Table 3. *Details of analysis of readmission rates for family interventions*

| Time of data collection | Comparisons | Fixed effects odds ratio/effect size (95% CI) | Random effects odds ratio/effect size (95% CI) | Studies <i>N</i> | Patients <i>N</i> | NNT | Q (<i>P</i>) |
|-------------------------------|---|---|--|---------------------|----------------------|----------------|----------------|
| 1st 12 months | v. All other treatments | 0.57 (0.33 to 1.0) | 0.38 (0.10 to 1.40) | 4 | 242 | 15 (5 to ∞) | 11.79 (< 0.01) |
| 1st 12 months | v. Standard care | 0.69 (0.37 to 1.27) | 0.43 (0.08 to 2.28) | 3 | 193 | 454 (8 to ∞) | 9.52 (< 0.01) |
| 1st 12 months | Single family treatments v. All other treatments | 0.21 (0.09 to 0.49) | 0.22 (0.09 to 0.51) | 3 | 143 | 3 (2 to 13) | 0.76 (0.68) |
| 1st 2 years | v. All other treatments | 0.60 (0.43 to 0.84) | 0.47 (0.23 to 0.96) | 6 | 638 | 11 (6 to 46) | 15.60 (< 0.01) |
| 1st 2 years | v. Standard care | 0.51 (0.31 to 0.84) | 0.39 (0.11 to 1.34) | 4 | 286 | 9 (5 to 134) | 13.45 (< 0.01) |
| 1st 2 years | Single family interventions v. Standard care | 0.23 (0.11 to 0.46) | 0.24 (0.12 to 0.47) | 3 | 187 | 4 (3 to 7) | 1.18 (0.55) |
| Follow-up up to 2 years after | v. Standard care | 1.08 (0.64 to 1.81) | 1.08 (0.64 to 1.83) | 4 | 253 | -18 (-∞ to -5) | 2.31 (0.51) |

Q, Heterogeneity statistic ($P < 0.05$ indicates heterogeneity); NNT, number needed to treat (negative number denotes treatment less effective than comparison group, $+/- \infty$ indicates non-significant result).

Table 4. Details of analysis of suicide and drop-out rates for family interventions

| Outcome | Analysis | Fixed effects odds ratio/effect size (95% CI) | Random effects odds ratio/effect size (95% CI) | No. of studies | No. of patients | Q (P) |
|--------------------------|---|---|--|----------------|-----------------|--------------|
| Suicide | v. Standard care | 0.86 (0.37 to 2.01) | 0.88 (0.33 to 2.32) | 6 | 1284 | 5.10 (0.27) |
| Treatment non-compliance | v. All other treatments | 1.01 (0.77 to 1.33) | 1.06 (0.76 to 1.48) | 16 | 1284 | 17.60 (0.28) |
| Treatment non-compliance | v. Standard care | 1.28 (0.72 to 2.14) | 1.24 (0.72 to 2.14) | 10 | 643 | 10.52 (0.31) |
| Treatment non-compliance | v. Active treatments | 0.74 (0.53 to 1.04) | 0.64 (0.34 to 1.20) | 6 | 641 | 10.04 (0.07) |
| Treatment non-compliance | Single family treatments v. active treatments | 0.69 (0.46 to 1.04) | 0.62 (0.30 to 1.31) | 4 | 423 | 4.36 (0.22) |
| Treatment non-compliance | Group family treatments v. active treatments | 0.85 (0.47 to 1.55) | 0.53 (0.08 to 3.46) | 2 | 218 | 1.48 (0.23) |

Q, Heterogeneity statistic ($P < 0.05$ indicates heterogeneity). Number needed to treat not reported as inappropriate to the outcomes.

Linszen *et al.* 1996). Family interventions showed a consistent and significant benefit, with a number needed to treat of eight, and an absolute difference in risk of relapsing of 12.8%. This benefit was greater and more homogeneous when family therapy was compared only with standard care. When family interventions were compared only with other active interventions, there was no significant benefit over this time period. Relapse rates for between 1 and 2 years into treatment were also presented in six studies (Falloon *et al.* 1982; Hogarty *et al.* 1986, 1997*a, b*; Leff *et al.* 1989; Xiong *et al.* 1994; McFarlane *et al.* 1995*a*). Single family treatments showed some evidence of a positive effect on relapse at this stage over and above all other treatments. However, this effect was vitiated when interventions involving multiple family groups were included.

Four studies (Goldstein *et al.* 1978; Leff *et al.* 1982; Tarrier *et al.* 1988; Vaughan *et al.* 1992) provided data on relapses recorded up to 15 months after the end of treatment. There was no evidence for any beneficial effects of single family interventions on the likelihood of relapsing at the follow-up stage.

Readmission

Readmission rates for up to one year into treatment were reported in four studies (Falloon *et al.* 1982; Glynn *et al.* 1992; Xiong *et al.* 1994; Buchkremer *et al.* 1995). There is a considerable benefit of single family interventions over all other treatment conditions (Table 3), with an NNT of 3, and a 48.8% absolute difference in the risk of being readmitted. However, when interventions involving group family approaches were included, comparisons of family treat-

ments, both with standard care and with all other treatments, no longer showed a positive effect on readmission rates.

From six studies, information was available on readmission rates for up to 2 years into treatment (Falloon *et al.* 1982; Glynn *et al.* 1992; Xiong *et al.* 1994; Zhang *et al.* 1994; Buchkremer *et al.* 1995; Schooler *et al.* 1997). Family interventions showed consistent benefits over all other treatments in the number of patients readmitted to hospital, even over this prolonged period. The NNT for this comparison was 11, and the absolute difference in readmission between the trials was 9.7% in favour of family intervention.

If family treatments were compared with standard care alone (by removing the Falloon *et al.* (1982) and Schooler *et al.* (1997) studies), the size of effect was less, but still pointed to a reduction in readmission. The difference between the random effects and fixed effects analyses and their confidence intervals pointed to some heterogeneity. A separate comparison of single family interventions and standard care was made. This greatly reduced the heterogeneity and demonstrated a far greater benefit of single family treatments over standard care than when group family treatments were included. The pooled odds ratios were 0.23 for the fixed effects model and 0.24 for the random effects model. Conversely, when the group family treatments alone were compared with standard care, there was no demonstrable benefit over treatment as usual.

Four studies (Posner *et al.* 1992; Vaughan *et al.* 1992; Bloch *et al.* 1995; Buchkremer *et al.* 1995) provided follow-up information on readmission rates up to 2 years after the end of

Table 5. Details of analysis of 'burden', expressed emotion and medication compliance for family interventions

| Outcome | Comparison | Fixed effects odds ratio/effect size (95% CI) | Random effects odds ratio/effect size (95% CI) | Studies N | Patients N | NNT | Q (P) |
|----------------------------|-----------------------------------|---|--|--------------|---------------|--------------|-------------|
| Burden | v. Standard care | WMD -0.19 (-0.52 to -0.13) | WMD -0.14 (-0.76 to 0.47) | 3 | 146 | N/A | 6.88 (0.03) |
| Burden | Single family v. Standard care | WMD -0.43 (-0.82 to -0.05) | WMD -0.42 (-0.88 to -0.03) | 2 | 105 | N/A | 1.41 (0.24) |
| Expressed emotion | Single family treatments | 0.90 (0.48 to 1.67) | 0.90 (0.48 to 1.72) | 4 | 114 | 27 (6 to ∞) | 3.08 (0.38) |
| Compliance with medication | v. All other treatments | 0.63 (0.40 to 1.01) | 0.63 (0.40 to 1.01) | 5 | 393 | 10 (6 to 90) | 2.48 (0.65) |

Q, Heterogeneity statistic ($P < 0.05$ indicates heterogeneity); NNT, number needed to treat (negative number denotes treatment less effective than comparison group, $+/- \infty$ indicates non-significant result); WMD, weighted mean difference.

treatment, but they showed no advantage for family interventions.

Suicide

There have been suggestions that family interventions lead to increases in suicide rates so this is an important measure to examine. Six studies recorded suicide rates (Leff *et al.* 1982; TARRIER *et al.* 1988; Posner *et al.* 1992; Vaughan *et al.* 1992; Xiong *et al.* 1994; Buchkremer *et al.* 1995). However, the rates were low and there was consequently considerable imprecision in the analysis. There was, however, no evidence for an increase in suicide rates in family interventions (Table 4).

Treatment non-compliance (see Table 4)

Treatment non-compliance or 'drop-out' can be considered as an estimate of tolerability of family interventions among patients and their relations. Sixteen trials provided data on treatment non-compliance in family interventions compared to all other treatments, including standard care (Goldstein *et al.* 1978; Falloon *et al.* 1982; Leff *et al.* 1982, 1989; Hogarty *et al.* 1986, 1997a, b; TARRIER *et al.* 1988; Glynn *et al.* 1992; Posner *et al.* 1992; Vaughan *et al.* 1992; Zhang *et al.* 1994; Bloch *et al.* 1995; Buchkremer *et al.* 1995; McFarlane *et al.* 1995a, b; Schooler *et al.* 1997).

When studies comparing family interventions with other active treatments were examined, no evidence for a reduction in drop-out rates in the family intervention condition was found. In these six studies, the comparators were: individual supportive psychotherapy (Falloon *et*

al. 1982; Hogarty *et al.* 1997a, b); a relative's group and psycho-education sessions (Leff *et al.* 1989); individualized family treatment with a focus on education (MacFarlane *et al.* 1995a, b); and supportive family management and monthly relatives' group meetings (Schooler *et al.* 1997). No comparisons found any difference in treatment non-compliance between the comparison treatment and group or single family interventions. However, group family treatments were associated with a significantly greater non-compliance than single family treatments (1.46 (1.02 to 2.09) $P = 0.05$) on a fixed effects analysis.

Family outcomes (see Table 5)

Several family outcome measures were reported, but only two were adopted by a sufficient number of studies to render them suitable for analysis. These were measures of burden and of expressed emotion. Three studies involving 146 patients compared the effect of family interventions on feelings of burden experienced by the family with that of standard care only (Posner *et al.* 1992; Xiong *et al.* 1994; Bloch *et al.* 1995). Family interventions conferred no advantage in this respect.

However, the heterogeneity in the first comparison ($Q = 6.88, 0.03$) was thought sufficient for us to remove the group family treatment study (Posner *et al.* 1992) and reanalyse the data. The two single family intervention studies do, in fact, provide some evidence of a beneficial effect of family interventions on the level of burden experienced by families. The standardized weighted mean difference using the fixed effects model was -0.43, and -0.42 using

Table 6. *Characteristics of cognitive behaviour therapy trials*

| Study | <i>N</i> | Intervention and method | Duration and frequency | Comparison group | Measures analysed in this study |
|--------------------------------|----------|--|---|--|---|
| Bradshaw, 1996 | 16 | Coping skills treatment | 1½ h per week for 24 weeks, | Problem solving group | Relapse |
| Carpenter <i>et al.</i> 1987 | 42 | Developing shared view of illness, identify environmental stressors and minimizing their impact, 6 sessions with family | 45 min per week for 2 years | Maintenance medication | Readmission Treatment non-compliance |
| Drury <i>et al.</i> 1996 | 62 | Individual challenging and testing key-beliefs, group cognitive therapy and coping strategy enhancement | 8 h per week for 9 months (3 h CT, 5 h structured activities) | Recreation and support: leisure and social activities away from ward and standard care | Treatment non-compliance Mental state – important improvement |
| Kuipers <i>et al.</i> 1997 | 60 | Coping strategies enhancement, modifying dysfunctional beliefs, managing social disability | 1 h per week/fortnight for 9 months, 9 months follow-up | Standard care: routine care, case management and medication | Death Mental state – important improvement Mental state – BPRS Relapse Treatment non-compliance |
| Hogarty <i>et al.</i> 1997a, b | 101 | Focus on ‘modifying model of person’, environmental and emotional monitoring and internal coping strategies | 1 session per week with less contact in year 3 with those who had achieved treatment objectives | Supportive therapy | Mental state (BPRS) Global assessment of function Medication compliance |
| Kemp <i>et al.</i> 1996 | 74 | Compliance therapy, reviewing history of illness, discussing the benefits and drawbacks of drug treatment, the stigma of drugs, the discrepancy between the patient’s action and beliefs | 20–60 min twice a week for 2–3 weeks, 18 month follow-up | Supportive counselling | CPRS – no important improvement |
| Sensky <i>et al.</i> 2000 | 86 | Collaborative understanding of symptoms. Pattern of engagement, normalizing rational. Analysis of beliefs, guided discovery and graded homework. Use of inference chaining | 9 months total, 45 min per week for up to 2 months, less than monthly for next 7 months | Befriending intervention | Treatment non-compliance, mental state – no important improvement (BPRS), relapse |
| Tarrier <i>et al.</i> 1998 | 87 | Coping strategy enhancement, training in problem solving, strategies to reduce relapse | 1 h twice a week for 10 weeks | 1 Supportive counselling 2 Standard care | |

Table 7. Details of analysis for relapse/readmission with CBT

| Time of data collection | Analysis | Fixed effects odds ratios | Random effects odds ratios | Studies <i>N</i> | Patients <i>N</i> | NNT (95% CI) | Q (<i>P</i>) |
|-------------------------|-------------------------|---------------------------|----------------------------|------------------|-------------------|--------------|----------------|
| During treatment | v. All other treatments | 0.69 (0.44 to 1.10) | 0.69 (0.44 to 1.10) | 6 | 363 | 17 (7 to ∞) | 3.16 (0.68) |
| During treatment | v. Active treatments | 0.74 (0.43 to 1.28) | 0.74 (0.42 to 1.28) | 4 | 238 | 12 (5 to ∞) | 2.27 (0.51) |
| During treatment | v. Standard care | 0.73 (0.37 to 1.47) | 0.73 (0.36 to 1.47) | 3 | 163 | 16 (5 to ∞) | 1.76 (0.41) |
| Follow-up | v. All other treatment | 0.86 (0.46 to 1.60) | 0.83 (0.16 to 4.24) | 2 | 161 | 17 (5 to ∞) | 5.69 (0.02) |

Q, Heterogeneity statistic ($P < 0.05$ indicates heterogeneity); NNT, number needed to treat (negative number denotes treatment less effective than comparison group, +/− ∞ indicates non-significant result).

the random effects model. Four studies report levels of overall expressed emotion, and demonstrate no advantage of family interventions over all other treatments (Leff *et al.* 1982; Hogarty *et al.* 1986; Tarrier *et al.* 1988; Leff *et al.* 1989) (see Table 5).

Compliance with medication

Compliance with medication was reported in five trials containing 393 patients (Falloon *et al.* 1982; Leff *et al.* 1982; Hogarty *et al.* 1986; Zhang *et al.* 1994; McFarlane *et al.* 1995). Meta-analysis consistently showed a benefit of all types of family interventions over all other treatments, with an odds ratio of 0.63. Full details of the analysis are given in Table 5.

Summary

All family interventions (i.e. both single and group family therapies) were more effective at reducing relapse in the first 12 months of treatment than all other treatments. As would be expected, the largest effect was obtained in trials comparing family interventions with standard care. At 1–2 years after beginning treatment, only single family interventions were effective at reducing relapse in comparison to all other treatments. Only single family interventions reduced readmission in the first year compared with all other treatments. Up to 2 years into treatment however, all family treatments are effective at reducing readmission, with the greatest effect being apparent for single family treatments in trials comparing them to standard care. There were no differences in suicide rates between family interventions and other treatments, and likewise no reduction in the relative's sense of burden. All family interventions had lower rates of treatment non-compliance than comparison active treatments,

and all increased compliance with medication in comparison to all other treatments. It was not possible to identify any particular family characteristics (e.g. levels of expressed emotion) or patient characteristics (e.g. severity of disorder or age of onset) associated with different outcomes. Neither did clear evidence emerge of an impact of the frequency or duration of treatment on outcomes.

Cognitive behaviour therapy

The characteristics of participants

The main characteristics of the CBT trials are reported in Table 6. A total of 393 patients took part in the trials included in these analyses. The mean age for participants was reported in six studies and was 33.9 years overall, with a range of 18 to 65. The sex of participants was not reported for 22 participants in one study, but of the rest, 60.4% were male. The mean duration of illness was reported in four studies: on average patients had been first diagnosed 11 years before induction. Thus, the participants were older and had a longer duration of illness than those in family interventions. This may be because CBT was often deliberately used where existing treatment was ineffective, that is in groups that were persistently resistant to medication.

Relapse/readmission

Six trials containing 368 patients reported relapse or symptom deterioration rates for CBT compared with all other treatments (Carpenter *et al.* 1987; Bradshaw, 1996; Drury *et al.* 1996; Hogarty *et al.* 1997*a, b*; Kuipers *et al.* 1997; Tarrier *et al.* 1998). The criteria used to define relapse varied between studies. For example, Tarrier *et al.* (1998) defined it as readmission to

hospital for an exacerbation of clinical symptoms resulting in functional impairment and admission for at least five days. Kuipers *et al.* (1997) in contrast used a deterioration equivalent to five or more points on the BPRS as their definition of relapse. Tarrrier *et al.* (1998) compared CBT both with standard care and with supportive counselling. For clarity, we have therefore divided this study into Tarrrier I (for the comparison with standard care) and Tarrrier II (for the comparison with supportive psychotherapy). Where our analysis was of CBT compared to all other interventions, patients from both comparison treatments in this study were included. There was no clear evidence that CBT prevented relapse or readmission during treatment, when compared to all other treatments (see Table 7).

Two studies provided information on relapse rates at follow-up after the end of treatment, and again CBT failed to reduce relapse rates (which were in any case already low in these patients) (Kemp *et al.* 1996; Tarrrier *et al.* 1998).

Mental state

Two measures of mental state are reported in the studies with sufficient frequency for it to be possible to use them. These are continuous ratings from the BPRS and the CPRS, and 'important improvement in mental state'.

Endpoint data are provided by two studies involving 126 patients (Kemp *et al.* 1996; Kuipers *et al.* 1997). There was no benefit for CBT over other treatments, as reported in Table 8. However, follow-up data, collected up to 9 months after treatment, were also presented in the same studies, and they did demonstrate a clear positive effect of CBT in reducing scores on the BPRS. The weighted mean difference was -2.99 for both the fixed and random effects models. Thus, it looks as though the benefits of CBT are maintained while those of the comparison treatments are not.

'Important improvement' in mental state was rated in four suitable trials, containing 273 patients, during the medium to long term into treatment (Drury *et al.* 1996; Kuipers *et al.* 1997; Tarrrier *et al.* 1998; Sensky *et al.* 2000). The outcome was defined slightly differently in each of the studies. Drury *et al.* (1996) defined 'important improvement' as a stabilization of positive symptoms, insight and dysphoria.

Kuipers *et al.* (1997) defined it as a reduction in 40% or more of an individual's scores on the BPRS. Tarrrier *et al.* (1998) and Sensky *et al.* (2000) define it as a 50% or greater reduction in symptom scores on the BPRS and on the CPRS, respectively.

CBT showed consistent benefits in terms of mental state, compared to all other treatments. The pooled fixed effects odds ratio was 0.27, the pooled random effects odds ratio, 0.28. The studies appear homogenous, and the finding can therefore be taken as relatively robust. Overall, CBT patients had a 22.1% greater chance of improving their mental state by the above criteria. Full details of the analysis are reported in Table 8.

At follow-up, up to 9 months after the end of treatment, two studies provided information on improvement in mental state, compared with standard care (Kuipers *et al.* 1998; Tarrrier *et al.* I, 1998). There was a strong effect of CBT on mental state, even up to 9 months after the treatment had been completed. However, the random effects analysis casts uncertainty due to the heterogeneity, and makes it possible to say only that there is some evidence of a benefit of CBT over other treatments at follow-up (see Table 8).

Treatment non-compliance (Table 9)

Five studies recorded 'drop-out' rates for comparisons between CBT and all other treatments (Carpenter *et al.* 1987; Bradshaw, 1996; Drury *et al.* 1996; Kuipers *et al.* 1997; Tarrrier *et al.* 1998). They included 240 patients. No evidence was found to suggest that CBT increased the likelihood of dropping out compared with all other treatments. The analysis comparing CBT with standard care (without the Tarrrier I study, as this seemed responsible for heterogeneity) provided evidence of reduced dropout in CBT. The pooled odds ratio was 0.38.

Improvement in functioning

Two studies provided data on global functioning at the end of treatment, measured on the Global Assessment of Functioning scale (Kemp *et al.* 1996; Bradshaw, 1996). CBT was compared with other active treatments, supportive counselling and a problem solving group, respectively.

Table 8. *Details of analysis for continuous and 'no important improvement' mental state data in CBT trials*

| Outcome | Time of data collection | Analysis | Fixed effects odds ratios | Random effects odds ratios | No. of studies | No. of patients | NNT (95% CI) | Q(P) |
|--------------------------------|------------------------------------|-------------------------|------------------------------------|------------------------------------|----------------|-----------------|--------------|-------------|
| Mental state (NII) | Medium to long term into treatment | v. All other treatments | 0.27 (0.15 to 0.49) | 0.28 (0.15 to 0.51) | 4 | 273 | 5 (4 to 9) | 1.23 (0.73) |
| Mental state (NII) | Follow-up (9–18 months after) | v. Standard care | 0.25 (0.10 to 0.64) | 0.27 (0.05 to 1.43) | 2 | 119 | 6 (3 to 27) | 2.76 (0.10) |
| Mental state – continuous BPRS | At end of treatment | v. All other treatments | Effect size –1.25 (–4.29 to –1.80) | Effect size –1.25 (–4.29 to –1.80) | 2 | 126 | N/A | 1.00 (0.32) |
| Mental state – continuous BPRS | Follow-up (9–18 months after) | v. All other treatments | Effect size –0.52 (–0.94 to –0.11) | Effect size –0.52 (–0.94 to –0.11) | 2 | 126 | N/A | 0.11 (0.74) |

Q, Heterogeneity statistic ($P < 0.05$ indicates heterogeneity); NNT, number needed to treat (negative number denotes treatment less effective than comparison group, $+/- \infty$ indicates non-significant result); NII, no important improvement.

Table 9. *Details of analysis for drop-out and improvement in functioning in CBT trials*

| Outcome | Period of measurement | Analysis | Fixed effects odds ratios | Random effects odds ratios | No. of studies | No. of patients | NNT (95% CI) | Q (P) |
|----------------------------|-----------------------|------------------------------------|----------------------------------|----------------------------------|----------------|-----------------|------------------------|-------------|
| Treatment non-compliance | N/A | v. All other treatments | 0.82 (0.45 to 1.50) | 0.79 (0.28 to 2.16) | 5 | 267 | –50 (– ∞ to –8) | 7.81 (0.10) |
| Treatment non-compliance | N/A | v. Standard care | 0.86 (0.40 to 1.84) | 0.90 (0.14 to 5.81) | 3 | 220 | 16 (6 to ∞) | 7.84 (0.02) |
| Treatment non-compliance | N/A | v. Standard care without Tarrier I | 0.38 (0.14 to 1.02) | 0.38 (0.14 to 1.04) | 2 | 149 | 5 (4 to 15) | 0.92 (0.34) |
| Treatment non-compliance | N/A | v. Other active treatments | 0.77 (0.29 to 2.01) | 0.77 (0.29 to 2.01) | 3 | 137 | 162 (7 to ∞) | 0.03 (0.85) |
| Improvement in functioning | At end of treatment | v. Active treatments | Effect size 0.36 (–0.06 to 0.79) | Effect size 0.84 (–0.69 to 2.38) | 2 | 90 | N/A | 6.29 (0.01) |

Q, Heterogeneity statistic ($P < 0.05$ indicates heterogeneity); NNT, number needed to treat (negative number denotes treatment less effective than comparison group, $+/- \infty$ indicates non-significant result).

Some evidence was found for an improvement in global functioning at the end of treatment: the standardized weighted mean difference was 0.36 for the fixed effects model, and 0.84 for the random effects. The large amount of heterogeneity and the reliance on only two very small studies indicates caution when interpreting this finding.

Summary

On continuous measures of mental state, there is no evidence for increased effectiveness of CBT during treatment, but a clear, positive effect at follow-up. CBT had a clear advantage over all other treatments on the measure 'important improvement' in mental state during treatment, and this effect persisted for up to 18 months after treatment. In the trials included in this analysis, CBT had lower drop-out rates than standard care.

CBT offered no other advantage in the treatment of schizophrenia. As with family interventions it was not possible to identify any patient characteristics (e.g. severity of disorder or age of onset) associated with different outcomes. Nor was there any clear evidence about the frequency or duration of treatment associated with better outcome.

DISCUSSION

Family intervention

Our analysis demonstrates that the early promise of family intervention in schizophrenia has been maintained. However, there are caveats. Mari & Streiner (1994) have pointed out that there has been some decline in effect over time (see Fig. 2). They tentatively attributed this to the charisma and enthusiasm of the early proponents of family intervention. This certainly points to the requirement for robust implementation of these interventions, if they are to be used.

The diminishing effect of family intervention over time (see Fig. 2) may in part be explained by the increased use of family group approaches (Posner *et al.* 1992; Buchkremer *et al.* 1995; MacFarlane *et al.* 1995a; Schooler *et al.* 1997). Our analyses suggest that, on an intention to treat basis, there is no general benefit to these group approaches over single family approaches. In contrast, evidence for the positive effect of single family treatment over group family ap-

proaches does emerge from our analyses. For example, the 'number needed to treat' to prevent relapse during the first year of treatment for single family treatments was 11, while for group family treatments it was -34. (A negative NNT indicates a detrimental treatment.) In general, we found that in terms of patient outcomes such as the re-emergence of psychotic symptoms, or readmission to hospital, single family interventions were more effective.

However, some caution in interpreting these results is required; most importantly, the group family treatments covered in this review are very variable in content (ranging from eight sessions over a short time period (Posner *et al.* 1992) to fortnightly for the first 2 years and then monthly sessions over a 4-year period (McFarlane *et al.* 1995b). Although on an intention to treat analysis, no group family intervention demonstrated any benefit over single family interventions on the measures reported, such group approaches may be especially beneficial on measures that were not often reported, for example family burden (see below). It is also possible that group family approaches are of particular benefit to sub-populations, but again this was not reported in any way that allowed for a subgroup analysis in the studies under review.

There are a number of other possible reasons for reduced effectiveness in later studies. Thus, an increasing number use an active treatment component as the comparison group. This will tend to reduce the effect size of any experimental treatment. Other potential explanations include the possibility that techniques fail to generalize to more diverse and challenging patient groups and that the standard services with which these interventions are compared are generally improving. The use of intensive case management, individualized programme planning and the development of more integrated health and social service provision for mentally ill people over the past 20 years have contributed to a significant improvement in the overall quality of mental health care. It is harder for new treatments, both psychological and pharmacological, to demonstrate an advantage over existing treatments in the context of generally improving services.

Despite the importance of the study of the family environment in generating interest

in family interventions, the potential benefit for family members themselves has received little attention in the trials reviewed here. Where it has been identified as a focus for intervention or a measure of outcome (e.g. Posner *et al.* 1992; Xiong *et al.* 1994; Bloch *et al.* 1995), the results are rarely reported in the consistent way required for effective meta-analysis. Although initial evaluations of the impact of family interventions on family burden are not encouraging (e.g. Okawa *et al.* 2000), there should be further research, using not only direct and indirect measures of burden but also assessment of family members' satisfaction and well-being. It is here that group (and in particular multiple family group) approaches to treatment might show more demonstrable effects. Bringing families together in groups might have specific and beneficial effects on isolation and stigma. These aspects of outcomes should be considered in further research into group approaches. The burden of care in schizophrenia is an issue that requires recognition, and attempts to ameliorate it, rather than to provide support, may be misplaced.

We were unable to draw conclusions about whether particular groups of patients (for example, those presenting for the first time to services) or types of family (for example, families rated high or low on EE) benefit differentially from family interventions. Some studies grouped families on the basis of these variables, e.g. Leff *et al.* (1989), but there were too few for meta-analysis. It therefore seems important that research should address the characteristics of individual patients or families associated with positive outcomes. This might lead to a better understanding of the relatively high attrition rate associated with family interventions in clinical practice (Magliano *et al.* 1999).

In addition, there would probably be benefit in identifying the essential components of family intervention. It is possible that psycho-education by itself is not of benefit (Cozolino *et al.* 1988), but it remains unclear how much the direct involvement of the identified patient in the provision of treatment is associated with positive outcomes. The relatively good outcome of single family groups, which usually involves the presence of the index patient, suggests this might be so. This should be clarified through further research. Perhaps of greater importance is the

frequency and duration of treatment required for positive outcomes. The interventions covered in this report vary from only 6 weeks (Goldstein *et al.* 1978; Bloch *et al.* 1995) to 2 years (Hogarty *et al.* 1986). Likewise, the spacing of treatments ranges from weekly (e.g. Falloon *et al.* 1982; Vaughan *et al.* 1992) to sessions every month (or even 2–3 months – Xiong *et al.* 1994). Bustillo *et al.* (2001) suggest that infrequent non-intrusive family meetings may also be useful, as families have a range of problems, and may not all need intensive input. Research should therefore also focus on the optimal duration and frequency of effective treatments. The value of booster sessions following a regular intervention should also be investigated.

We also need to understand the factors, organizational and clinical, that promote the effective implementation of family interventions in routine clinical practice. There is a considerable if largely descriptive body of literature (e.g. Fadden, 1997) describing some of these factors, but the absence of formal research limits the conclusions that can be drawn about possible strategies and thereby the recommendations that can be made for overcoming these difficulties.

Finally, through a careful monitoring of the process of change in the course of research interventions, the techniques of family intervention can be refined. Future trials should therefore address not only clinical outcomes but also process measures likely to lead to the sustained development of more focused and successful treatment for those who most need it.

Cognitive behaviour therapy

Cognitive behavioural treatments are at a relatively early stage of development. There are few trials, and patient numbers in the trials tend to be small. This inevitably restricts the conclusions that can be drawn. However, despite the limited number of trials, the treatments have been implemented in a wide range of settings.

Our analyses demonstrated that cognitive behaviour therapy was effective in improving mental state on measures of 'important improvement', both during treatment and at follow-up. On continuous measures, this effect is only visible at follow-up. The finding of a positive impact of CBT on mental state is not surprising, as CBT tackles the underlying cog-

nitions hypothesized to be inextricably linked to mental state. However, why positive effects on continuous measures of mental state are only apparent at follow-up is less clear. The finding may arise from the inclusion of the Kemp *et al.* (1996) study, which was of very short duration (3 weeks) and was included in the continuous measures analysis but not the dichotomous one. This demonstrated virtually no positive effect of CBT on mental state during treatment. The treatment in this study was essentially compliance therapy, and it is possible that increased compliance after the cessation of treatment mediated these results. In addition, CBT led to fewer dropouts than standard care. As standard care is less intrusive and thus probably more tolerable, this could be seen as favourable for CBT. However, the lack of difference between CBT and other active treatments is perhaps less positive, as there is likely to be increased pressure for patients to remain in the experimental treatment group (Jones *et al.* 2001).

Our analyses do suggest that cognitive behavioural interventions for schizophrenia offer a potentially effective treatment. The results from the early trials are promising despite their small numbers. Nevertheless, in comparison, for example with most trials of anti-psychotic medication, they provide reasonably good follow-up data over extended periods. The positive results of the meta-analysis can therefore be taken as confirming the promise of cognitive behavioural treatment in schizophrenia.

Much work is needed to refine the treatment in terms of identifying the most effective components and the best methods for delivering it. However, given that many people continue to suffer from symptoms and difficulties despite extensive pharmacological and service-based interventions, it is important that efforts are made to develop CBT. If its promise is confirmed it should be made more generally available in secondary care mental health services, thereby offering a greater choice of psychosocial interventions for sufferers and their carers.

While the interventions all met the criteria for CBT and would be recognizable to those trained in the technique, there was considerable variation in the nature and duration of treatment provided. Many treatments involved a large investment of time and effort on the part of both the therapist and participant. For example,

Kuipers *et al.* (1997) provided up to nine months of individual CBT on a weekly or fortnightly basis. Although the evidence available from the current trials is limited, there is some suggestion that longer-term treatments are associated with a better outcome. This is evident from the increased effect over time of CBT on mental state (for example, Sensky *et al.* 2000). The majority of the studies also concentrate on outpatients with chronic disorders, with the most notable exception being Drury *et al.* (1996), which looked at a population of in-patients with a relatively recent onset of the disorder. The current Socrates trial (Lewis *et al.* 2002), which focuses on treatment of recent onset patients, may well provide further information on the value of CBT for such patients.

At this stage in the development of CBT, there is a need for further research that address several issues. The first area for consideration is the range of outcomes. As stated above, there is a need for a robust measure of relapse, applied with consistency across studies. In addition the impact of CBT should be measured not only on the target symptoms (usually hallucinations and delusions) but also on mental state generally and affective state in particular.

As with family interventions, the impact of duration and frequency of treatment should be the focus of further research. The results are likely to have considerable implications for the future availability of CBT, in particular whether it remains a treatment for relatively few patients provided by highly trained specialists or becomes more widely available.

Little is known about the patient populations that might benefit most from CBT. The majority of interventions have focused on chronic or treatment resistant schizophrenia. The lack of effect on relapse rates can be understood in this context: the patients are chronically symptomatic, so improvement is an appropriate measure, while relapse generally is not. It is clear, however, that more needs to be understood of the effect of CBT at different stages of the illness and on different presenting symptoms. In patients prone to relapse and recovery, the use of CBT to reduce relapse should be investigated. In part, the answers to these questions will lie in a better understanding of the process of change in treatment. If it turns out that the skills required to deliver the treatment are considerable, it may

be necessary to restrict it to groups particularly likely to benefit or in which symptoms are distressingly resistant to other treatments.

General research implications

Given limitations on resources and the fact that the psychological interventions produced similar outcomes, there are significant research and clinical issues concerning the relative efficacy of different treatments and their ease of implementation in routine clinical practice. This argues, in the first instance, for large pragmatic trials comparing the effectiveness of cognitive behavioural and family interventions. Further work may consider not only the outcomes obtained but also the refinement and feasibility of treatments. For certain populations, for example those at risk of relapse, the relative merits of CBT and FIs should be carefully evaluated.

The trials reviewed were characterized by a limited range of outcome measures. There were very few, if any, measures of patient satisfaction, and few measures of quality of life, together with a lack of consistency in the definition and specification of the primary outcome measures. There is a considerable appeal in simple dichotomous outcomes measures such as admission to hospital, but as the improvement of community-based mental health services and the introduction of Crisis Resolution Teams (Department of Health, NHS Executive, 2000) influences the process of admission, the value of these measures must be questioned. A more pragmatic and robust measure of relapse needs to be applied consistently across trials. Continuous measures are appropriate for treatments in community-based services. They are also more informative statistically. Again, consistent usage would assist systematic review. Finally, health economic data have seldom been collected in these trials and the requirement for this to be part of any large trial cannot be over-emphasized.

The authors would like to thank Clive Adams and the Cochrane Schizophrenia Group for their assistance in the preparation of this paper.

REFERENCES

Adams, C. E. (2000). *Psychosocial Interventions for Schizophrenia*. Effective Health Care Bulletin. NHS Centre for Reviews and Dissemination, University of York: York.

- Altman, D. G. & Bland, J. M. (1996). Detecting skewness from summary information. *British Medical Journal* **313**, 200.
- Åsberg, M., Perris, C., Schalling, D. & Sedvall, G. (1978). CPRS: development and applications of a psychiatric rating scale. *Acta Psychiatrica Scandinavica* **69** (suppl. 271), 5–27.
- Bebbington, P. E. & Kuipers, E. (1994). The predictive utility of expressed emotion in schizophrenia. *Psychological Medicine* **24**, 707–718.
- Beck, A. T., Rush, A. J., Shaw, B. F. & Emery, G. (1979). *Cognitive Therapy for Depression*. Guilford Press: New York.
- Bloch, S., Szmukler, G. I., Herrman, H., Benson, A. & Colussa, S. (1995). Counselling caregivers of relatives with schizophrenia: themes, interventions, and caveats. *Family Process* **34**, 413–425.
- Bradshaw, W. (1966). Structured group work for individuals with schizophrenia: a coping skills approach. *Research on Social Work Practice* **6**, 139–154.
- Brown, G. W. & Rutter, M. (1966). The measurement of family activities and relationships: a methodological study. *Human Relations* **19**, 241–263.
- Brown, G. W., Monck, E. M., Carstairs, G. M. & Wing, J. K. (1962). Influence of family life on the course of schizophrenic illness. *British Journal of Preventative and Social Medicine* **16**, 55–68.
- Brown, G. W., Birley, J. L. & Wing, J. K. (1972). Influence of family life on the course of schizophrenic disorders: a replication. *British Journal of Psychiatry* **121**, 241–258.
- Buchkremer, G., Holle, R., Schulze Mönking, H. & Hornung, W. P. S. (1995). The impact of therapeutic relatives groups on the course of illness in schizophrenic patients. *European Psychiatry* **10**, 17–27.
- Bustillo, J. R., Lauriello, J., Horan, P. & Keith, S. J. (2001). The psychosocial treatment of schizophrenia: an update. *American Journal of Psychiatry* **158**, 163–175.
- Carpenter, W., Heinrichs, D. & Hanlon, T. (1987). A comparative trial of pharmacologic strategies in schizophrenia. *American Journal of Psychiatry* **144**, 1466–1470.
- Cohen, J. (1977). *Statistical Power Analysis for the Behavioural Sciences*. Academic Press: New York.
- Cook, R. J. & Sackett, S. L. (1995). The number needed to treat: a clinically useful measure of treatment effect. *British Medical Journal* **310**, 452–454.
- Cormac, I., Jones, C. & Campbell, C. (2002). Cognitive behaviour therapy for schizophrenia (Cochrane Review). In *Cochrane Library*, 1. Update Software: Oxford.
- Cozolino, L. J., Goldstein, M. J. & Nuechterlein, K. H. (1988). The impact of education about schizophrenia on relatives varying in expressed emotion. *Schizophrenia Bulletin* **14**, 675–687.
- Department of Health, NHS Executive (1999). *National Service Framework For Mental Health*. Department of Health: Wetherby.
- Department of Health, NHS Executive (2000). *The NHS Plan: A Plan for Investment, a Plan for Reform*. Department of Health: Wetherby.
- DerSimonian, R. & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials* **7**, 177–188.
- Dixon, L., Adams, C. & Lucksted, A. (2000). Update on family psychoeducation for schizophrenia. *Schizophrenia Bulletin* **26**, 5–20.
- Drury, V., Birchwood, M., Cochrane, R. & Macmillan, F. (1996). Cognitive therapy and recovery from acute psychosis: a controlled trial. I. Impact on psychotic symptoms. *British Journal of Psychiatry* **169**, 593–601.
- Egger, M. (1997). Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal* **315**, 629–634.
- Fadden, G. (1997). Implementation of family interventions in routine clinical practice following staff training programs: a major cause for concern. *Journal of Mental Health* **6**, 599–612.
- Falloon, I. R. H., Boyd, J. L., McGill, C. W., Razani, J., Moss, H. B. & Gilderman, A. M. (1982). Family management in the prevention of the exacerbation of schizophrenia: clinical outcome of a two-year longitudinal study. *New England Journal of Medicine* **306**, 1437–1440.

- Fowler, D., Garety, P. A. & Kuipers, L. (1995). *Cognitive Behaviour Therapy for Psychosis*. Wiley: Chichester.
- Geddes, J., Freemantle, N., Harrison, P. & Bebbington, P. (2000). Atypical antipsychotics in the treatment of schizophrenia: systematic overview and meta-regression analysis. *British Medical Journal* **321**, 1371–1376.
- Glass, G. V., McGaw, B. & Smith, M. L. (1981). *Meta-analysis in Social Research*. Sage: Beverly Hills, CA.
- Glynn, S. M., Randolph, E. T., Eth, S., Paz, G. G., Leong, G. B., Shaner, A. L. & Van Vort, W. (1992). Schizophrenic symptoms, work adjustment, and behavioural family therapy. *Rehabilitation Psychology* **37**, 323–338.
- Goldstein, M. J., Rodnick, E. H., Evans, J. R., May, P. R. A. & Steinberg, M. R. (1978). Drug and family therapy in the aftercare of acute schizophrenics. *Archives of General Psychiatry* **35**, 1169–1177.
- Gould, R. A., Mueser, K. T., Bolton, E., Mays, V. & Goff, D. (2001). Cognitive therapy for psychosis in schizophrenia: an effect size analysis. *Schizophrenia Research* **48**, 335–342.
- Hedges, L. V. & Olkin, I. (1985). *Statistical Methods for Meta-analysis*. Academic Press: London.
- Hogarty, G. E., Anderson, C. M., Reiss, D. J., Kornblith, S. J., Greenwald, P., Javna, C. D. & Madonia, M. J. (1986). Family psychoeducation, social skills training and maintenance chemotherapy in the aftercare treatment of schizophrenia: I. One-year effects of a controlled study on relapse and expressed emotion. *Archives of General Psychiatry* **43**, 633–642.
- Hogarty, G. E., Kornblith, S. J., Greenwald, P., DiBarry, A. L., Cooley, S., Ulrich, R. F., Carter, M. & Flesher, S. (1997a). Three years trials of personal therapy with schizophrenics living with or independent of family I: description of study and effects on relapse rates. *American Journal of Psychiatry* **154**, 1504–1513.
- Hogarty, G. E., Greenwald, P., Ulrich, R. F., Kornblith, S. J., DiBarry, A. L., Cooley, S., Carter, M. & Flesher, S. (1997b). Three years trials of personal therapy with schizophrenics living with or independent of family II: effects on adjustment of patients. *American Journal of Psychiatry* **154**, 1514–1524.
- Kane, J. M. (1996). Treatment resistant schizophrenic patients. *Journal of Clinical Psychiatry* **57** (suppl. 9), 35–40.
- Kemp, R., Hayward, P., Applewhaite, G., Everitt, B. & David, A. (1996). Compliance therapy in psychotic patients: randomised controlled trial. *British Medical Journal* **312**, 345–349.
- Kuipers, E., Garety, P., Fowler, D., Dunn, G., Bebbington, P., Freeman, D. & Hadley, C. (1997). London East-Anglia randomised controlled trial of cognitive behavioural therapy for psychosis I: effects of the treatment phase. *British Journal of Psychiatry* **171**, 319–327.
- Kuipers, E., Fowler, D., Garety, P., Chisholm, D., Freeman, D., Dunn, G., Bebbington, P. & Hadley, C. (1998). London East-Anglia randomised controlled trial of cognitive behavioural therapy for psychosis III: follow-up and economic evaluation at 18 months. *British Journal of Psychiatry* **173**, 61–68.
- Leff, J., Kuipers, L., Berkowitz, R., Eberlein-Fries, R. & Sturgeon, D. (1982). A controlled trial of social interventions in the families of schizophrenic patients. *British Journal of Psychiatry* **141**, 121–134.
- Leff, J., Berkowitz, R., Shavit, N., Strachan, A., Glass, I. & Vaughn, C. (1989). A trial of family therapy versus a relative's group for schizophrenia. *British Journal of Psychiatry* **154**, 58–66.
- Lewis, S., Tarrier, N., Haddock, G., Bentall, R., Kinderman, P., Kingdon, D., Siddle, R., Drake, R., Everitt, J., Leadley, K., Benn, A., Grazebrook, K., Haley, C., Akhtar, S., Davies, L., Palmer, S., Faragher, B. & Dunn, D. (2002). Randomised controlled trial of cognitive-behaviour therapy in early schizophrenia: acute phase outcomes. *British Journal of Psychiatry* (in the press).
- Lieberman, R. P. (1994). Psychosocial treatments for schizophrenia. *Psychiatry* **57**, 104–114.
- Linszen, D., Dingemans, P., Van der Does, J. W., Nugter, A., Scholte, P., Lenoir, R. & Goldstein, M. J. (1996). Treatment, expressed emotion and relapse in recent onset schizophrenic disorders. *Psychological Medicine* **26**, 333–342.
- McFarlane, W. R., Link, B., Dushay, R., Marchal, J. & Crilly, J. (1995a). Psychoeducational multiple family groups: four-year relapse outcome in schizophrenia. *Family Processes* **34**, 127–144.
- McFarlane, W. R., Lukens, E., Link, B., Dushay, R., Deakins, S. A., Newmark, M., Dunne, E. J., Horen, B. & Toran, J. (1995b). Multiple-family groups and psychoeducation in the treatment of schizophrenia. *Archives of General Psychiatry* **52**, 679–687.
- Magliano, L., Fadden, G., Fiorillo, A., Malangone, C., Sorrentino, D., Robinson, A. & Maj, M. (1999). Family burden and coping strategies in schizophrenia: are key relatives really different to other relatives. *Acta Psychiatrica Scandinavica* **99**, 10–15.
- Mantel, N. & Haenszel, W. (1959). Statistical aspects of the analysis of data from retrospective studies. *Journal of National Cancer Institute* **22**, 719–748.
- Mari, J. J. & Streiner, D. (1994). An overview of family interventions and relapse on schizophrenia: meta-analysis of research findings. *Psychological Medicine* **24**, 565–578.
- Miettinen, O. S. & Nurminen, M. (1985). Comparative analysis of two rates. *Statistics in Medicine* **4**, 213–226.
- Mojtabai, R., Nicholson, R. A. & Carpenter, B. N. (1998). Role of psychosocial treatments in the management of schizophrenia: a meta-analytic review of controlled outcome studies. *Schizophrenia Bulletin* **24**, 569–587.
- Mulrow, C. D. & Oxman, A. D. (eds.) (1997). *Cochrane Collaboration Handbook*. In *The Cochrane Library* (database on disk and CDROM). The Cochrane Collaboration. Update Software, 1997: Oxford.
- Okawa, N., Oshima, I. & Goto, M. (2000). The effects of family interventions for the patients with mental illness in health centers focusing on the relatives' own life. *Nippon Koshu Eisei Zasshi* **47**, 580–588.
- Overall, J. E. & Gorham, D. R. (1962). The Brief Psychiatric Rating Scale. *Psychological Reports* **10**, 799–812.
- Pilling, S., Bebbington, P., Kuipers, E., Garety, P., Geddes, J., Martindale, B., Orbach, G. & Morgan, C. (2002). Psychological treatments in schizophrenia: II. Meta-analyses of social skills training and cognitive remediation. *Psychological Medicine* **32**, 783–791.
- Pitschel-Walz, G., Leucht, S., Bauml, J., Kissling, W. & Engel, R. R. (2001). The effect of family interventions on relapse and re-hospitalization in schizophrenia: a meta-analysis. *Schizophrenia Bulletin* **27**, 73–92.
- Posner, C. M., Wilson, K. G., Krai, M. J., Lander, S. & McIlwraith, R. D. (1992). Family psychoeducational support groups in schizophrenia. *American Journal of Orthopsychiatry* **62**, 206–218.
- Rector, N. A. & Beck, A. T. (2001). Cognitive behavioral therapy for schizophrenia: an empirical review. *Journal of Nervous and Mental Disease* **189**, 278–287.
- Roth, A. & Fonagy, P. (1996). *What Works for Whom? A Critical Review of Psychotherapy Research*. Guilford: New York.
- Schooler, N. R., Keith, S. J., Severe, J. B., Matthews, S. M., Bellack, A. S., Glick, I. D., Hargreaves, W. A., Kane, J. M., Ninan, P. T., Frances, A., Jacobs, M., Liberman, J. A., Mance, R., Simpson, G. M. & Woerner, M. G. (1997). Relapse and rehospitalisation during maintenance treatment of schizophrenia. *Archives of General Psychiatry* **54**, 453–463.
- Schwartz, B. J., Cecil, A. & Iqbal, N. (1993). Psychosocial treatments of schizophrenia. *Psychiatric Annals* **23**, 216–221.
- Sensky, T., Turkington, D., Kingdon, D., Scott, J., Scott, J., Siddle, R., O'Carroll, M. & Barnes, T. (2000). A randomized controlled trial of cognitive behavioural therapy for persistent symptoms in schizophrenia resistant to medication. *Archives of General Psychiatry* **57**, 165–172.
- Smith, J. & Birchwood, M. (1993). The needs of high and low expressed emotion families: a normative approach. *Social Psychiatry and Psychiatric Medicine* **28**, 11–16.
- StatsDirect (2000). *Statistical Software Package*. Tidestone Technologies Inc., Ashwell, Herts.
- Tarrier, N., Barrowclough, C., Vaughn, C., Bamrah, J. S., Porceddu, K., Watts, S. & Freeman, H. (1988). Community management of

- schizophrenia: a controlled trial of behavioural interventions with families to reduce relapse. *British Journal of Psychiatry* **153**, 532–542.
- Tarrier, N., Yusupoff, L., Kinney, C., McCarthy, E., Gledhill, A., Haddock, G. & Morris, J. (1998). Randomised controlled trial of intensive cognitive behaviour therapy for patients with chronic schizophrenia. *British Medical Journal* **317**, 303–307.
- Vaughan, K., Doyle, M., McConaghy, N., Blaszczyński, A., Fox, A. & Tarrier, N. (1992). The Sydney Intervention trial: a controlled trial of relatives' counselling to reduce schizophrenic relapse. *Social Psychiatry Psychiatric Epidemiology* **27**, 16–21.
- World Health Organization (1992). *The Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10)*. WHO: Geneva.
- Xiong, W., Phillips, M. R., Hu, X., Wang, R., Dai, Q., Kleinman, J. & Kleinman, A. (1994). Family based intervention for schizophrenic patients in China: a randomised controlled trial. *British Journal of Psychiatry* **165**, 239–247.
- Zhang, M., Wang, M., Li, J. & Phillips, M. R. (1994). Randomised-control trial of family intervention for 78 first-episode male schizophrenic patients: an 18-month study in Suzhou, Jiangsu. *British Journal of Psychiatry* **165** (suppl. 24), 96–102.