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Okpokoro U, Adams CE, Sampson S

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[Intervention Review]

Family intervention (brief) for schizophrenia

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ABSTRACT

Background

Supportive, positive family environments have been shown to improve outcomes for patients with schizophrenia in contrast with family environments that express high levels of criticism, hostility, or over-involvement, which have poorer outcomes and have more frequent relapses. Forms of psychosocial intervention, designed to promote positive environments and reduce these levels of expressed emotions within families, are now widely used.

Objectives

To assess the effects of brief family interventions for people with schizophrenia or schizophrenia-like conditions.

Search methods

We searched the Cochrane Schizophrenia Group Trials Register (July 2012), which is based on regular searches of CINAHL, EMBASE, MEDLINE and PsycINFO. We inspected references of all identified studies for further trials. We contacted authors of trials for additional information.

Selection criteria

All relevant randomised studies that compared brief family-oriented psychosocial interventions with standard care, focusing on families of people with schizophrenia or schizoaffective disorder were selected.

Data collection and analysis

We reliably selected studies, quality assessed them and extracted data. For binary outcomes, we calculated standard estimates of risk ratio (RR) and their 95% confidence intervals (CI). For continuous outcomes, we estimated a mean difference (MD) between groups and their 95% CIs. We used GRADE to assess quality of evidence for main outcomes of interest and created a 'Summary of findings' table. We assessed risk of bias for included studies.

Main results

Four studies randomising 163 people could be included in the review. It is not clear if brief family intervention reduces the utilisation of health services by patients, as most results are equivocal at long term and only one study reported data for the primary outcomes of interest of hospital admission (n = 30, 1 RCT, RR 0.50, 95% CI 0.22 to 1.11, *very low quality evidence*). Data for relapse are also equivocal by medium term (n = 40, 1 RCT, RR 0.50, 95% CI 0.10 to 2.43, *low quality evidence*). However, data for the family outcome

of understanding of family member significantly favoured brief family intervention (n = 70, 1 RCT, MD 14.90, 95% CI 7.20 to 22.60, *very low quality evidence*). No study reported data for other outcomes of interest including days in hospital; adverse events; medication compliance; quality of life or satisfaction with care; or any economic outcomes.

Authors' conclusions

The findings of this review are not outstanding due to the size and quality of studies providing data; the analysed outcomes were also minimal, with no meta-analysis possible. All outcomes in the 'Summary of findings' table were rated *low or very low quality evidence*. However, the importance of brief family intervention should not be dismissed outright, with the present state of demand and resources available. The designs of such brief interventions could be modified to be more effective with larger studies, which may then have enough power to inform clinical practice.

PLAIN LANGUAGE SUMMARY

Brief family intervention for schizophrenia

Schizophrenia is a serious mental illness that affects a persons thoughts, perceptions and emotions. Research has found that the chance of someone with mental illness having a relapse is greater when their family is over-involved, hostile, critical and dissatisfied - a concept known as 'expressed emotions'. Family interventions have been shown to improve outcomes for people with schizophrenia and are now widely used. They are designed to promote positive family environments and reduce levels of expressed emotions within families as well as providing insight into the signs and symptoms of mental illness, so family members can anticipate and help stop relapse. There have been various psychosocial programmes designed over the years, including: counselling groups for family members; family therapy; educational groups for relatives; group therapy for family members; and educational lectures for family members. These are delivered by skilled, trained mental health professionals, who work with the families every two weeks or so, sometimes across considerable time periods, such as one year.

Brief family intervention is a form of family intervention where a mental health professional educates the person with schizophrenia and their family members about the illness over a limited number of sessions.

This review investigates the effects of brief family intervention for people with schizophrenia, compared to standard or usual care. A search of the Cochrane Schizophrenia Group's trial register was carried out in July 2012. Four randomised studies, with a total of 163 participants were included. Results were limited, so it is not clear if brief family intervention reduces admission to hospital, decreases people using health services and reduces relapse for people with schizophrenia. The review found some evidence that brief family intervention might increase the understanding of family members about mental illness. However, all main findings are not strong and based on low or very low quality evidence. Despite this, the authors of the review suggest that brief family intervention should not be completely dismissed, as it is in a current state of demand and there are usually resources or local services available for people with mental health problems and their families to participate in as a part of recovery. The authors also suggest that brief family intervention could be improved to be more effective but this would depend on larger and better studies of brief family intervention being carried out, which would help guide good practice and lead to better outcomes for people with schizophrenia.

This plain language summary has been written by a consumer, Ben Gray, from RETHINK.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

BRIEF FAMILY INTERVENTION compared to STANDARD CARE for schizophrenia

Patient or population: patients with schizophrenia
Settings: Inpatient, outpatient (India; UK; US)
Intervention: BRIEF FAMILY INTERVENTION
Comparison: STANDARD CARE

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	STANDARD CARE	BRIEF FAMILY INTERVENTION				
Service utilisation - hospital admission - medium to long term hospital admission levels Follow-up: 12 months	**667 per 1000**[1]	**333 per 1000** (147 to 740)	**RR 0.5** (0.22 to 1.11)	30 (1 study)	⊕◯◯◯ **very low**[2,3]	
Service utilisation - days in hospital - medium to long term - not reported	See comment	See comment	Not estimable	-	See comment	No study reported/ measured this outcome.
Global state - relapse - medium to long term relapse rates (clinical judgement) Follow-up: 4 months	**200 per 1000**[1]	**100 per 1000** (20 to 486)	**RR 0.5** (0.1 to 2.43)	40 (1 study)	⊕⊕◯◯ **low**[3,4]	
Global state - compliance with medication - medium to long term - not reported	See comment	See comment	Not estimable	-	See comment	No study reported/ measured this outcome.

Quality of life/satisfaction with care - for recipients or carers - medium to long term - not reported	See comment	See comment	Not estimable	-	See comment	No study reported/measured this outcome.
Family outcome - understanding schizophrenia, average endpoint score Patient Rejection Scale (PRS - high score = greater acceptance). Scale from: 24 to 168. Follow-up: 2 months	The mean family outcome - understanding schizophrenia, average endpoint score in the control groups was **104.2 points**	The mean family outcome - understanding schizophrenia, average endpoint score in the intervention groups was **14.9 higher** (7.2 to 22.6 higher)		70 (1 study)	⊕◯◯◯ **very low**[5,6]	
Economic outcomes - costs of care - long term - not reported	See comment	See comment	Not estimable	-	See comment	No study reported/ measured this outcome.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Mean baseline risk presented for single study.
[2] Risk of bias: 'very serious' - no blinding of participants or study personnel; 29% participant data not accounted; statistical data not reported.
[3] Imprecision: 'serious' - 95% confidence intervals for best estimate of effect include both 'no effect' and appreciable benefit/harm.
[4] Risk of bias: 'serious' - no blinding of participants or study personnel.
[5] Risk of bias: 'very serious' - no mention of allocation concealment/blinding; attrition at 65% - only n = 34 out of N = 200 completed the study and were included in data and analysis.
[6] Indirectness: 'serious' - scale-derived data.

BACKGROUND

Description of the condition

Schizophrenia is a chronic mental health illness. It is described as a neuropsychiatric and mental disorder characterised by abnormalities in the perception or expression of reality. The emotional, social and cost implications for families and people with schizophrenia are highly detrimental, resulting in impairment of social and vocational functioning in the society at large. Approximately 1% of the world's population will suffer from schizophrenia (Barrowclough 1997). The peak age of onset is typically late adolescence and early adulthood, and a combination of both genetic and environmental factors play roles in its development (Van Os 2009). The symptoms of this illness are often described as 'positive' and 'negative'; positive symptoms are hallucinations, delusions, disordered thought and speech; negative symptoms are lack of normal emotional responses, withdrawal, and blunted affect. The course of the illness and management is largely influenced by the predominance of either positive and negative symptoms (Hirsch 2003).

Description of the intervention

The objectives of psychosocial family interventions are varied. They include:

1. improving the capabilities of relatives to anticipate and solve problems;
2. achieving significant change in relatives' behaviour and belief systems;
3. supporting relatives to set and maintain suitable limits and still keep to some degree of separation as appropriate;
4. minimising emotions of anger and guilt felt by the relatives;
5. minimising negative family environment (that is, damping emotional tension in the family by diminishing relatives' burden and psychological stress);
6. building a therapeutic coalition with caregivers of the person with schizophrenia; and
7. encouraging understanding of limitations to patient performance (Pitschel-Walz 2004).

A mental health professional educates the person with schizophrenia and their family members about the illness. They create an alliance in planning treatment and provide mutual support and understanding of the disease. Family intervention furnishes relatives with insight into signs and symptoms that serve as an alert to imminent acute episodes so that strategies may be employed directed towards averting relapse. There have been various psychosocial programmes designed over the years, such as counselling groups for family members, family therapy in single or multiple family settings, psychoeducational groups for relatives, group therapy for family members and educational lectures for family members (Pitschel-Walz 2004). Many of these are delivered by skilled, specifically trained mental health professionals, who work with the families every two weeks or so, across considerable time periods, such as one year.

How the intervention might work

The probability of the affected member relapsing is greater when the family is over-involved, hostile, critical and dissatisfied - a concept known as 'expressed emotions'. The apparent connection between expressed emotion and relapse was demonstrated some time ago. Brown 1962 and co-workers highlighted the connection between expressed emotions and schizophrenia in families and this has since been corroborated by others (Kuipers 1988; Vaughn 1986). This concept of expressed emotions substantiates the relevance of psychoeducational work with family members who care for people with schizophrenia (Pitschel-Walz 2004).

Designs of interventions focus on diminishing the level of environmental stimuli and expressed emotion through education, training and therapy. Mental health service providers have anticipated knowledgeable family members acting as cohorts in therapy (Böker 1992; Lefley 1990) which, in turn, might positively impact on patients' compliance with medication (Corrigan 1990; Kissling 1994).

Why it is important to do this review

Psychosocial family interventions for people with schizophrenia has been tested in trials and results indicate some positive effects. There is evidence attesting to a diminished rate of relapse in people receiving standard length psychosocial family interventions (Pharoah 2006). There is also some evidence that these particular psychosocial interventions may improve functioning and family well-being.

Short-term psychoeducational programmes that have less content have also been shown to have the potential of imparting basic information and equipping families caring for relatives with schizophrenia with new strategies. These brief educational programmes have been shown to be successful in diminishing distress for these families as a result of better knowledge (Abramowitz 1989; Smith 1987). There is considerable investment in longer forms of family psychosocial interventions as against a shorter approach. Guidelines recommending family intervention do not specify which approach to adopt (NICE 2009). There is potential for considerable savings if the efficacy of shorter and longer approaches are compared.

OBJECTIVES

To assess the effects of brief family interventions for people with schizophrenia or schizophrenia-like conditions.

METHODS

Criteria for considering studies for this review

Types of studies

All relevant randomised controlled trials. If trial was described as 'double-blind' but implied randomisation, we would have included such trials in a sensitivity analysis (see Sensitivity analysis). Where their inclusion did not result in a substantive difference, they would have remained in the analyses. Where their inclusion did result in important clinically significant, but not necessarily statistically significant, differences, we would not have added the data from these lower quality studies to the results of the better trials, but presented such data within a subcategory. We excluded quasi-randomised studies, such as those allocating by alternate days of the week. Where people were given additional treatments, such as standard drug treatment, we included data if the adjunct treatment was evenly distributed between groups.

Types of participants

Adults, however defined, with schizophrenia or related disorders, including schizophreniform disorder, schizoaffective disorder and delusional disorder, by any means of diagnosis, and their families/caregivers/supporters (however defined in each study).
We were interested in making sure that information is as relevant to the current care of people with schizophrenia as possible so proposed to clearly highlight the current clinical state (acute, early post-acute, partial remission, remission), as well as the stage (prodromal, first episode, early illness, persistent) and as to whether the studies primarily focused on people with particular problems (for example, negative symptoms, treatment-resistant illnesses).

Types of interventions

1. Brief family intervention

Any intervention described as 'family intervention' for people with schizophrenia, of brief duration (five sessions or less, or where the number of sessions is not stated but is less than three months duration).
Compared with:

1. Standard care

As defined in each study.

2. Non-brief family intervention

Any intervention described as 'family intervention' for people with schizophrenia of longer duration.

3. Any other non-family psycho-social or educational package

Of brief duration or longer duration.

Types of outcome measures

We divided our outcomes into short term (up to one month), medium term (two to three months) and long term (four months to one year).

Primary outcomes

1. Service utilisation

1.1 Hospital admission

2. Clinical global response

2.1 Relapse

Secondary outcomes

1. Service utilisation

1.1 Days in hospital

2. Clinical global response

2.1 Global state - improved
2.2 Average change or endpoint score in global state
2.3 Leaving the study early
2.4 Compliance with medication

3. Mental state and behaviour

3.1 Positive symptoms (delusions, hallucinations, disordered thinking)
3.2 Negative symptoms (avolition, poor self-care, blunted affect)
3.3 Average change or endpoint score

4. Social functioning

4.1 Average change or endpoint scores
4.2 Social impairment
4.3 Employment status (employed/unemployed)
4.4 Work-related activities
4.5 Unable to live independently
4.6 Imprisonment

5. Family outcomes

5.1 Average score/change in family burden
5.2 Patient and family coping abilities
5.3 Understanding of the family member with schizophrenia
5.4 Family care and maltreatment of the person with schizophrenia
5.5 Expressed emotion
5.6 Quality of life/satisfaction with care for either recipients of care or their carers

6. Adverse events/effects

6.1 Suicide and all causes of mortality
6.2 Other adverse events/effects

7. Economic outcomes

7.1 Cost of care

8. 'Summary of findings' table

We used the GRADE approach to interpret findings (Schünemann 2008) and use GRADEPRO to import data from Review Manager to create 'Summary of findings' tables. These tables provide outcome-specific information concerning the overall quality of evidence from each included study in the comparison, the magnitude of effect of the interventions examined, and the sum of available data on all outcomes that we rate as important to patient-care and decision making. We aimed to select the following main outcomes for inclusion in the Summary of findings for the main comparison,

1. Service utilisation - hospital admission - long term.
2. Service utilisation - days in hospital - long term.
3. Clinical global response - relapse - long term.
4. Clinical global response - compliance with medication - long term.
5. Quality of life/satisfaction with care for either recipients of care or their carers - long term.
6. Economic outcomes - cost of care - long term

No data were available for the outcomes days in hospital, compliance with medication and quality of life/satisfaction with care. We selected an additional outcome of family - understanding schizophrenia which has data presented in the Summary of findings for the main comparison.

Search methods for identification of studies

Electronic searches

Cochrane Schizophrenia Group Trials Register (July 2012)

The register was searched on 3 February 2010 and most recently on 19 July 2012 using the phrase:

[*family* in interventions of STUDY]

This register is compiled by systematic searches of major databases, handsearches and conference proceedings (see Group Module).

Searching other resources

1. Reference searching

We inspected references of all identified studies for further relevant studies.

2. Personal contact

We contacted the first author of each included study for information regarding unpublished trials.

Data collection and analysis

Selection of studies

Review authors OU and SS independently inspected citations from the searches and identified relevant abstracts. A random 20% sample was independently re-inspected by CEA to ensure reliability. Where disputes arose, the full report was acquired for more detailed scrutiny. Full reports of the abstracts meeting the review criteria were obtained and inspected by OU. Again, a random 20% of reports were re-inspected by CEA in order to ensure reliable selection. Where it was not possible to resolve disagreement by discussion, we attempted to contact the authors of the study for clarification.

Data extraction and management

1. Extraction

Review authors OU and SS extracted data from all included studies. In addition, to ensure reliability, CEA independently extracted data from a random sample of these studies, comprising 10% of the total. Again, any disagreement was discussed, decisions documented and, where necessary, we contacted the authors of studies for clarification. With any remaining problems CEA helped to clarify issues and these final decisions were documented. We extracted data presented only in graphs and figures whenever possible, but we included the data only if both review authors independently had the same result. Attempts were made to contact authors through an open-ended request in order to obtain missing information or for clarification whenever necessary. For the purposes of any future version of this review, had we encountered any multi-centre studies, where possible, we would have extracted data relevant to each component centre separately.

2. Management

2.1 Forms

We extracted data onto standard, simple forms.

2.2 Scale-derived data

We included continuous data from rating scales only if:

1. the psychometric properties of the measuring instrument have been described in a peer-reviewed journal (Marshall 2000); and
2. the measuring instrument has not been written or modified by one of the trialists for that particular trial.

Ideally, the measuring instrument should either be i. a self-report or ii. completed by an independent rater or relative (not the therapist). We realise that this is not often reported clearly, we noted whether or not this was the case in Description of studies.

2.3 Endpoint versus change data

There are advantages of both endpoint and change data. Change data can remove a component of between-person variability from the analysis. On the other hand, calculation of change needs two assessments (baseline and endpoint), which can be difficult in unstable and difficult to measure conditions such as schizophrenia. We decided primarily to use endpoint data, and only use change data if the former were not available. We planned to combine endpoint and change data in the analysis as we intended to use mean differences (MD) rather than standardised mean differences (SMD) throughout (Higgins 2011, Chapter 9.4.5.2).

2.4 Skewed data

Continuous data on clinical and social outcomes are often not normally distributed. To avoid the pitfall of applying parametric tests to non-parametric data, we applied the following standards to all data before inclusion:

a) standard deviations (SDs) and means are reported in the paper or obtainable from the authors;

b) when a scale starts from the finite number zero, the SD, when multiplied by two, is less than the mean (as otherwise the mean is unlikely to be an appropriate measure of the centre of the distribution, (Altman 1996);

c) if a scale starts from a positive value (such as the Positive and Negative Syndrome Scale (PANSS, Kay 1986) which can have values from 30 to 210), we modified the calculation described above to take the scale starting point into account. In these cases skew is present if 2 SD > (S-S min), where S is the mean score and S min is the minimum score.

Endpoint scores on scales often have a finite start and end point and these rules above can be applied. Skewed data from studies of less than 200 participants were presented as other data within the Data and analyses section rather than into a statistical analysis. Skewed data pose less of a problem when looking at means if the sample size is large and skewed data from studies with over 200 participants would have been entered into statistical analysis.

When continuous data are presented on a scale that includes a possibility of negative values (such as change data), it is difficult to tell whether data are skewed or not and we did not apply the above rules to change data.

2.5 Common measure

To facilitate comparison between trials, we converted variables that can be reported in different metrics, such as days in hospital (mean days per year, per week or per month) to a common metric (e.g. mean days per month).

2.6 Conversion of continuous to binary

Where possible, efforts were made to convert outcome measures to dichotomous data. This can be done by identifying cut-off points on rating scales and dividing participants accordingly into 'clinically improved' or 'not clinically improved'. It is generally assumed that if there is a 50% reduction in a scale-derived score such as the Brief Psychiatric Rating Scale (BPRS, Overall 1962) or the PANSS (Kay 1986), this could be considered as a clinically significant response (Leucht 2005; Leucht 2005a). However, no such reductions in score were reported in any of the included studies.

2.7 Direction of graphs

Where possible, we entered data in such a way that the area to the left of the line of no effect indicates a favourable outcome for brief family therapy. Where keeping to made would have made it impossible to avoid outcome titles with clumsy double-negatives (e.g. 'Not improved') we would have reported data where the left of the line indicates an unfavourable outcome had we encountered such data.

Assessment of risk of bias in included studies

Again, review authors OU and SS worked independently to assess risk of bias by using criteria described in the *Cochrane Handbook for Systemic reviews of Interventions* (Higgins 2011) to assess trial quality. This set of criteria is based on evidence of associations between overestimate of effect and high risk of bias of the article such as sequence generation, allocation concealment, blinding, incomplete outcome data and selective reporting.

Where the raters disagreed, the final rating was made by consensus, with the involvement of another member of the review group. Where inadequate details of randomisation and other characteristics of trials were provided, we contacted the authors of the studies in order to obtain further information. Non-concurrence in quality assessment were reported, but where disputes arose as to which

category a trial was to be allocated, again, resolution was made by discussion.

We noted the level of risk of bias in both the text of the review (Figure 1; Figure 2) and in the Summary of findings for the main comparison.

Figure 1. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

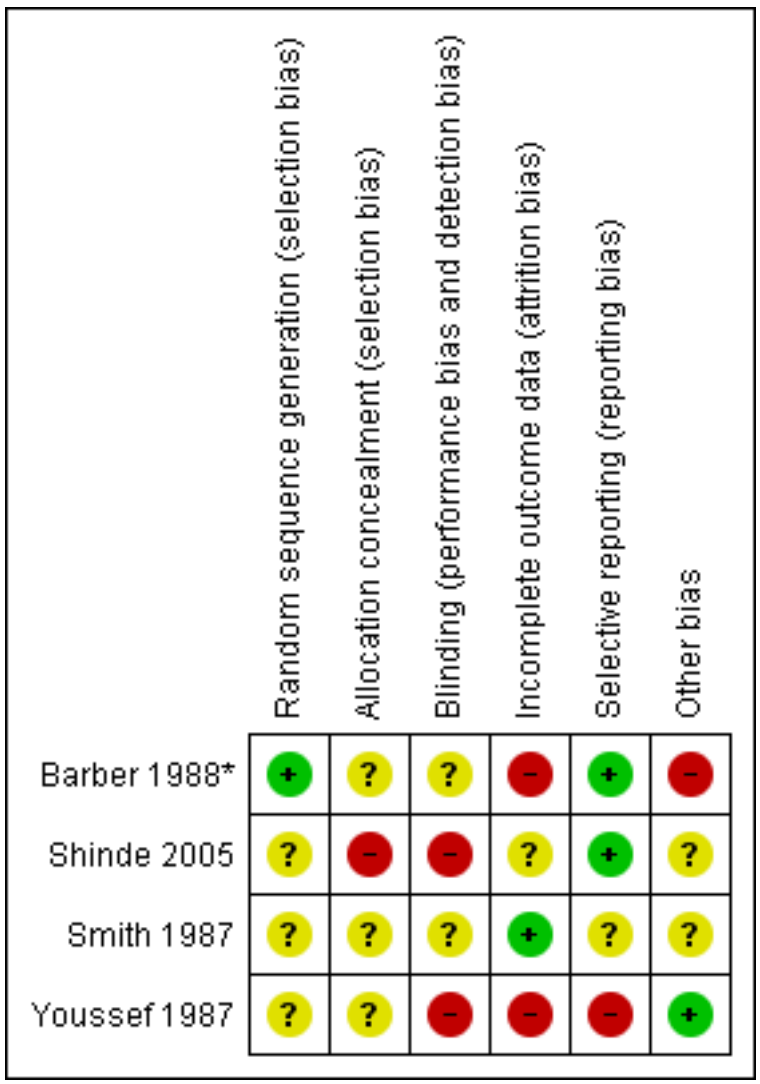
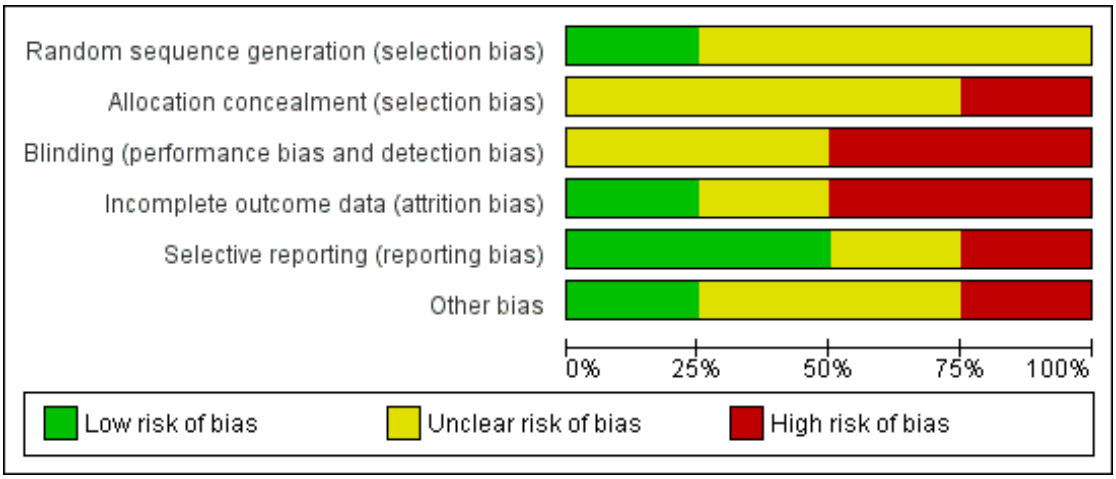


Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Measures of treatment effect

1. Binary data

For binary outcomes we calculated a standard estimation of the risk ratio (RR) and its 95% confidence interval (CI). It has been shown that RR is more intuitive (Boissel 1999) than odds ratios and that odds ratios tend to be interpreted as RR by clinicians (Deeks 2000). The Number Needed to Treat/Harm (NNT/H) statistic with its confidence intervals is intuitively attractive to clinicians but is problematic both in its accurate calculation in meta-analyses and interpretation (Hutton 2009). For binary data presented in the 'Summary of findings' table, where possible, we calculated illustrative comparative risks.

2. Continuous data

For continuous outcomes, we estimated the mean difference (MD) between groups. We prefer not to calculate effect size measures (standardised mean difference SMD). However, if scales of very considerable similarity had been used, we would have presumed there was a small difference in measurement, and we would have calculated the effect size and transformed the effect back to the units of one or more of the specific instruments.

Unit of analysis issues

1. Cluster trials

Studies increasingly employ 'cluster randomisation' (such as randomisation by clinician or practice) but analysis and pooling of clustered data poses problems. Firstly, authors often fail to account for intra-class correlation in clustered studies, leading to a 'unit of analysis' error (Divine 1992) whereby P values are spuriously low, confidence intervals unduly narrow and statistical significance overestimated. This causes type I errors (Bland 1997; Gulliford 1999).

Had we encountered any cluster randomised studies, and where clustering was not accounted for in primary studies, we would have presented data in a table, with a (*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review we will seek to contact the first authors of studies to obtain intra-class correlation coefficients (ICCs) for their clustered data and to adjust for this by using accepted methods (Gulliford 1999). Where clustering could be incorporated into the analysis of primary studies, we would have presented these data as if from a non-cluster randomised study, but adjusted for the clustering effect.

We have sought statistical advice and have been advised that the binary data as presented in a report should be divided by a 'design effect'. This is calculated using the mean number of participants per cluster (m) and the ICC [Design effect = 1+(m-1)*ICC] (Donner 2002). In subsequent versions of this review, if any cluster randomised studies are found, if the ICC is not reported it will be assumed to be 0.1 (Ukoumunne 1999).

Furthermore, where cluster studies are appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies will be possible using the generic inverse variance technique.

2. Cross-over trials

A major concern of cross-over trials is the carry-over effect. It occurs if an effect (e.g. pharmacological, physiological or psychological) of the treatment in the first phase is carried over to the second phase. As a consequence, on entry to the second phase the participants can differ systematically from their initial state, despite a wash-out phase. For the same reason cross-over trials are not appropriate if the condition of interest is unstable (Elbourne 2002). Had we encountered any cross-over trials, as both effects are very likely in severe mental illness, we would only have used data from the first phase of cross-over studies.

3. Studies with multiple treatment groups

In future updates of this review, where a study involves more than two treatment arms, if relevant, the additional treatment arms will be presented in comparisons. If data presented are binary, these will simply be added and combined within the two-by-two table. If data are continuous, we will combine the data following the formula in section 7.7.3.8 (Combining groups) of the *Cochrane Handbook for Systemic reviews of Interventions*. Where the additional treatment arms may not be relevant, these data will not be reproduced. For this current review, no such studies were identified.

Dealing with missing data

1. Overall loss of credibility

At some degree of loss of follow-up, data must lose credibility (Xia 2009). We chose that, for any particular outcome, where more than 50% of data were unaccounted for, we did not reproduce these data or use them within analyses. If, however, more than 50% of those in one arm of a study were lost, but the total loss was less than 50%, we marked such data with (*) to indicate that such a result may well be prone to bias. This was the case with Barber 1988*.

2. Binary

In the case where attrition for a binary outcome was between 0% and 50% and where these data were not clearly described, we presented data on a 'once-randomised-always-analyse' basis (an intention-to-treat analysis). Those leaving the study early were all assumed to have the same rates of negative outcome as those who completed, with the exception of the outcomes of death and adverse effects. For these outcomes, the rate of those who stay in the study - in that particular arm of the trial - were used for those who did not. We undertook a sensitivity analysis to test how prone the primary outcomes were to change when data only from people who completed the study to that point were compared to the intention-to-treat analysis using the above assumptions.

3. Continuous

3.1 Attrition

In the case where attrition for a continuous outcome was between 0% and 50%, and data only from people who completed the study to that point were reported, we presented and used such data.

3.2 Standard deviations

If standard deviations (SDs) were not reported, we first tried to obtain the missing values from the authors. If not available, where there are missing measures of variance for continuous data, but an exact standard error (SE) and confidence intervals available for group means, and either a 'P' value or 't' value available for differences in mean, we can calculate them according to the rules described in the *Cochrane Handbook for Systemic reviews of Interventions* (Higgins 2011). When only the SE is reported, SDs are calculated by the formula SD = SE * square root (n). Chapters 7.7.3 and 16.1.3 of the *Cochrane Handbook for Systemic reviews of Interventions* (Higgins 2011) present detailed formulae for estimating SDs from P values, t or F values, confidence intervals, ranges or other statistics. If these formulae do not apply, we can calculate the SDs according to a validated imputation method, which is based on the SDs of the other included studies (Furukawa 2006). Although some of these imputation strategies can introduce error, the alternative would be to exclude a given study's outcome and thus to lose information. However, we did not impute any of these values for this current version of the review.

3.3 Last observation carried forward

We anticipated that in some studies the method of last observation carried forward (LOCF) would be employed within the study report. As with all methods of imputation to deal with missing data, LOCF introduces uncertainty about the reliability of the results (Leucht 2007). Therefore, if LOCF data ha been used in the trial, where less than 50% of the data were assumed, we would have presented these data but indicated that they were the product of LOCF assumptions.

Assessment of heterogeneity

1. Clinical heterogeneity

We considered all included studies initially, without seeing comparison data, to judge clinical heterogeneity. We simply inspected all studies for clearly outlying people or situations which we had not predicted would arise. When such situations or participant groups arose, these were fully discussed.

2. Methodological heterogeneity

We considered all included studies initially, without seeing comparison data, to judge methodological heterogeneity. We simply inspected all studies for clearly outlying methods which we had not predicted would arise. When such methodological outliers arose, these were fully discussed.

3. Statistical heterogeneity

3.1 Visual inspection

If sufficient studies had been included, we plannedto visually inspect graphs to investigate the possibility of statistical heterogeneity.

3.2 Employing the I^2 statistic

We planned to investigate heterogeneity between studies by considering the I^2 method alongside the Chi^2 'P' value. The I^2 provides an estimate of the percentage of inconsistency thought to be due to chance (Higgins 2003). The importance of the observed value of I^2 depends on i. magnitude and direction of effects and ii. strength of evidence for heterogeneity (e.g. 'P' value from Chi ^{2} test, or a confidence interval for I^2). An I^2 estimate greater than or equal to around 50% accompanied by a statistically significant Chi^2 statistic, would have been interpreted as evidence of substantial levels of heterogeneity (Section 9.5.2 - Higgins 2011). If substantial levels of heterogeneity had been found in the primary outcome, we planned to explore the reasons for heterogeneity (Subgroup analysis and investigation of heterogeneity).

Assessment of reporting biases

1. Protocol versus full study

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results. These are described in section 10.1 of the *Cochrane Handbook for Systemic reviews of Interventions* (Higgins 2011). We attempted to locate protocols of included randomised trials. If the protocol was available, we compared outcomes in the protocol and in the published report. If the protocol was not available, we compared outcomes listed in the methods section of the trial report with actual reported results.

2. Funnel plot

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). These are again described in Section 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We are aware that funnel plots may be useful in investigating reporting biases but are of limited power to detect small-study effects. We intended not to use funnel plots for outcomes where there were 10 or fewer studies, or where all studies were of similar sizes. Because meta-analysis was not possible in this review, no funnel plots were used.

Data synthesis

We understand that there is no closed argument for preference for use of fixed-effect or random-effects models. The random-effects method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. This often seems to be true to us and the random-effects model takes into account differences between studies even if there is no statistically significant heterogeneity. There is, however, a disadvantage to the random-effects model. It puts added weight onto small studies which often are the most biased ones. Depending on the direction of effect, these studies can either inflate or deflate the effect size. We chose random-effects model for all analyses.

Subgroup analysis and investigation of heterogeneity

1. Subgroup analyses - only primary outcomes

1.1 Clinical state, stage or problem

We proposed to undertake this review and provide an overview of the effects of brief family interventions for people with schizophrenia in general. In addition, however, we planned to report data on subgroups of people in the same clinical state, stage and with similar problems.

2. Investigation of heterogeneity

If inconsistency was high, this would have been reported. First we would have investigated whether data have been entered correctly. Second, if data were correct, we would have visually inspected the graph and removed studies outside of the company of the rest to see if homogeneity was restored. For this review, we decided that, had we encountered any heterogeneity, should this occur with data contributing to the summary finding of no more than around 10% of the total weighting, data would be presented. If not, data would not have been pooled and issues would be discussed. We know of no supporting research for this 10% cut-off but are investigating the use of prediction intervals as an alternative to this unsatisfactory state.

Again, had we encountered such heterogeneity, when unanticipated clinical or methodological heterogeneity were obvious we

simply would have stated hypotheses regarding these for future reviews or versions of this review.

Sensitivity analysis

1. Implication of randomisation

We aimed to include trials in a sensitivity analysis if they were described in some way as to imply randomisation. For the primary outcomes, we planned to include these studies and if there was no substantive difference when the implied randomised studies were added to those with better description of randomisation, then we would have used all data from these studies. However, due to a lack of studies and results for our primary outcomes, we did not perform any meta-analyses. Therefore, we could not perform a sensitivity analysis for implication of randomisation.

2. Assumptions for lost binary data

Where assumptions have to be made regarding people lost to follow-up (see Dealing with missing data), we compared the findings of the primary outcomes when we used our assumption/s and when we used data only from people who completed the study to that point. If there was a substantial difference, we reported the results and discussed them but continued to employ our assumption/s.

Where assumptions were made regarding missing SDs data (see Dealing with missing data), we compared the findings of the primary outcomes when we used our assumption/s and when we used data only from people who completed the study to that point. A sensitivity analysis was undertaken to test how prone results were to change when completer-only data only were compared to the imputed data using the above assumption/s. If there was a substantial difference, we reported these results and discussed them but continued to employ our assumption/s.

3. Risk of bias

If we were able to perfom meta-analyses we would have analysed the effects of excluding trials that were judged to be at high risk of bias across one or more of the domains of randomisation (implied as randomised with no further details available), allocation concealment, blinding and outcome reporting for the meta-analysis of the primary outcome. If the exclusion of trials at high risk of bias did not substantially alter the direction of effect or the precision of the effect estimates, then data from these trials were included in the analysis.

4. Imputed values

Had we encountered any cluster randomised trials, we also would have undertaken a sensitivity analysis to assess the effects of including data from trials where we used imputed values for ICC in calculating the design effect.

In subsequent versions of the review where cluster randomised trials may be identified, if substantial differences are noted in the direction or precision of effect estimates in any of the sensitivity analyses listed above, we will not pool data from the excluded trials with the other trials contributing to the outcome, but present them separately.

5. Fixed-effect and random-effects

All data were synthesised using a random-effects model, however, we also synthesised data for the primary outcome using a fixed-effect model to evaluate whether the greater weights assigned to larger trials with greater event rates, altered the significance of the results compared to the more evenly distributed weights in the random-effects model.

RESULTS

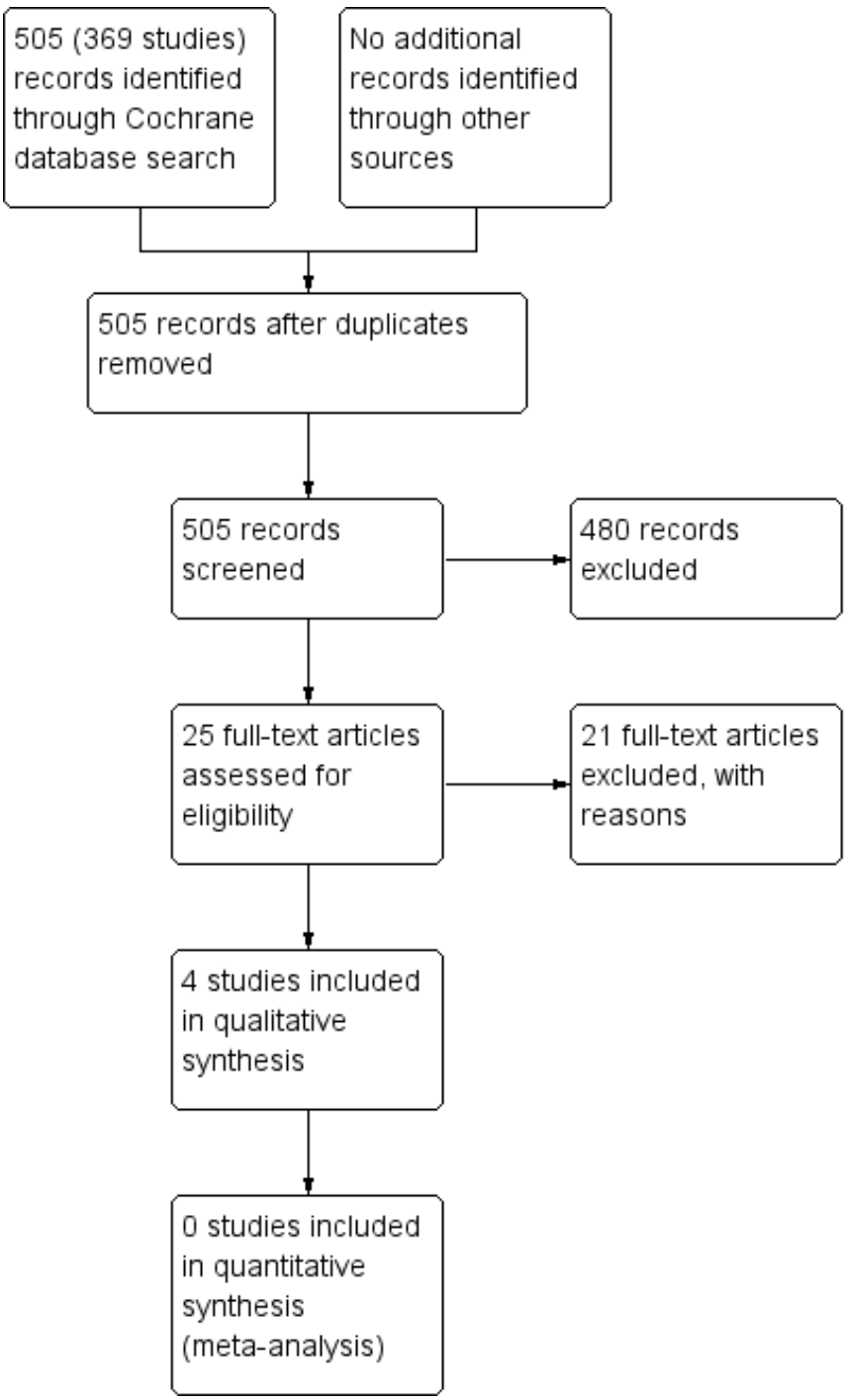
Description of studies

For a detailed description, see Characteristics of included studies and Characteristics of excluded studies.

Results of the search

The trial search found 505 references (369 studies) from the July 2012 search; after first excluding studies based on title and abstract, 25 full-text articles were assessed for eligibility. Twenty-one of these were excluded, leaving four studies left for inclusion in this review (see Figure 3).

Figure 3. Study flow diagram.



Included studies

See Characteristics of included studies for detailed descriptions of each study. Four studies were included in this review (Barber 1988*; Shinde 2005; Smith 1987; Youssef 1987).

1. Methods

All trials were described as 'randomised', however two studies did not describe the method used to randomly allocate participants to treatment (Smith 1987; Youssef 1987). Barber 1988* provided details as to randomisation methods; this was described as 'simple random sampling', where participant code numbers were "randomly selected and divided into 2 groups of 100 each, and random assignment of subjects to control and experimental group[s] were determined by a flip of a coin" (p66). Shinde 2005 described the use of a random number table "to assort the 40 participants and their caregivers", however precise details were not provided. None of the included studies described concealment of allocation and doubt remains as to how impervious all methods of allocation were to the introduction of bias.

2. Setting

Two studies were conducted in the United States (Barber 1988*; Youssef 1987); one in India (Shinde 2005); and another in the UK (Smith 1987). Two studies used a mix of inpatient and outpatient participants (Shinde 2005; Smith 1987), while the other studies included either only inpatient (Youssef 1987) or outpatient (Barber 1988*). Studies ranged from one month (Shinde 2005, with a three-month follow-up); two months (Barber 1988*); six months (Smith 1987); to a follow-up period of 12 months (Youssef 1987).

3. Participants

All people with schizophrenia/schizoaffective disorder and their families/relatives (however defined in each study) participated in the brief family intervention program (however defined in each study). When reporting results, however, there was a mix amongst studies, with some investigating the effects of brief family intervention and reporting outcomes for: people with schizophrenia alone (Youssef 1987); family members/relatives alone (Barber 1988*; Smith 1987); or a combination of people with schizophrenia and their family members/relatives (Shinde 2005).

3.1 People with schizophrenia

In total, N = 163 people with schizophrenia were randomised to receive either brief family intervention or 'standard care'. Overall, the age of people with schizophrenia/schizoaffective disorder ranged from 20 to 60 years old. All studies reported the sex of the people with schizophrenia/schizoaffective disorder, with n = 104 males and n = 59 females. People with schizophrenia/schizoaffective disorder had varied histories, and most studies involved families whose relatives had multiple admissions. Most of the studies enrolled only family members who had significant contact with the relatives with schizophrenia.

Participants in most included trials had a diagnosis of schizophrenia - the included studies that used a qualitative diagnostic tools included Barber 1988* (DSM III); Shinde 2005 (ICD-10). In the remaining studies, diagnosis was determined by the presence of one or more first rank symptoms (Smith 1987) (Schneider 1959)), while participants in Youssef 1987 had schizoaffective disorder, and no diagnostic tools were specified.

Only in Smith 1987 was it specified that participants were required to be stabilised on depot or oral antipsychotic medication; no other study made reference to whether or not people with schizophrenia/schizoaffective disorder were receiving medication at the time of the brief family intervention.

3.2 Family members/relatives

The included studies reporting family outcome data provided details of the family/relative/primary caregiver (Barber 1988*; Shinde 2005). In the three studies that provided information relating to family/relatives (Barber 1988*; Shinde 2005; Smith 1987), there were n = 110 family members (with n = 41 males, and n = 69 females), between the ages of 23-67 years old.

'Family members/relatives' were defined differently between studies; Barber 1988* used the term 'primary family caregivers' but provided no definition, however this included predominantly parents, then spouses, siblings, children and 'other'. 'Primary caregivers' were described in Shinde 2005 as a "family member who lives in the same household as the index patient, who spends time with him/her, and/or is directly and actively involved in the care of the patient (supervising medication, bringing him/her to hospital for follow-up) for at least one month" (p31-2). Smith 1987 included 'family members' such as parents, spouses and 'other' relatives. Youssef 1987 did not measure family/caregiver outcomes, and no information was provided in the report.

4. Interventions

1. Intervention group

All participants received a family intervention with educational component; however, the structure of each intervention was different between studies. These included 'family workshops', which involved education of families as to the diagnosis, treatment, symptoms, problems and other issues related to schizophrenia, in a six-hour, one-day workshop (Barber 1988*).

In Shinde 2005, family members were required to attend three (weekly) one-hour sessions within four weeks; the sessions were divided into education about schizophrenia; assessing and handling difficult problems' and handling communication and emotions.

Participants in Smith 1987 (relatives) were required to attend four weekly sessions, in which a semi-structured seminar was delivered to family members, with a question and answer session encouraged for participation. Family members also received a work booklet corresponding to the material covered in the brief education session, with an invitation to complete relevant homework. A patient-family teaching programme was employed in Youssef 1987, in which participants attended three consecutive one-hour sessions (led by the investigator and co-led by the unit nurse) of a discussion-based question and answer group, in order to explain the meaning of the illness, causes and treatments.

2. Comparison group

This included 'standard inpatient/outpatient treatment', where participants were informed that they were on a waiting list to receive the intervention at the end of three months (Shinde 2005); 'routine clinical information' without the educational workshop component (Barber 1988*); specification that participants did not receive the patient-family teaching program, with no further information (Youssef 1987); and 'brief family intervention by post', which involved the delivery of a postal information booklet, with homework, delivered on a weekly basis over a four-week period (Smith 1987).

4. Outcome scales

Some data were possible to extract from a variety of scales that were used to assess outcomes of service utilisation, measures of family functioning and knowledge acquisition from some or all of the included studies. We were however, unable to use some of the scale-derived data due to poor reporting. Scales that provided usable data for the review are explained below.

4.1. Clinical global state

4.1.1. Global Assessment Scale - GAS (Endicott 1976)
A clinician-rated scale by which an individual is rated on a scale from zero to 100, which represents a continuum from psychological or psychiatric sickness to health (1= 'extremely unwell' to 100= 'extremely well'). This scale was used in Youssef 1987 to measure levels of improvement, but no continuous data were reported.

4.2. Mental state

4.2.1. Positive and Negative Syndrome Scale - PANSS (Kay 1986)
PANSS was developed from the BPRS and the Psychopathology Rating Scale. It is used to evaluate positive, negative and other symptom dimensions in schizophrenia. The scale has 30 items, each measured on a seven-point scoring system varying from 1 = absent to 7 = extreme. Shinde 2005 was the only study to report data using this scale.
4.2.2 Symptom Rating Test - SRT (Kellner 1973)
The SRT was initially designed as a method of measuring psychological distress in a way to be able to detect changes in the clinical state of the patient. The 30-item measure, with four subscales, derives separate scores for anxiety (eight items); depression (eight items); somatic disturbances (seven items) and inadequacy (seven items). Each item is scored so as a high score indicates a greater level of psychological distress, on a scale of zero to two (0 = 'never', 1 = 'sometimes', 2 = 'often'). This scale was used only by Smith 1987.

4.3. Family outcome

4.3.1. Burden Assessment Schedule - BAS (Thara 1998)
The BAS was developed by the Schizophrenia Research Foundation (India) to assess the burden of the primary caregiver. The scale aims to assess both objective and subjective burden; objective burden characterised as the physical challenges posed to the caregiver that are a consequence of the behavioural changes in the receiver of care - for example, changes in family relations, health and employment. The subjective burden is the emotional level of burden that is experienced by the primary caregiver, including levels of anxiety, levels of morale, depression or perception of strain. This is a 40-item instrument, rated on a one to three rating scale (with 1 = 'not at all', 2 = 'to some extent', and 3 = 'very much'); scores range from 40 to 120, with a greater score indicating greater burden on the primary caregiver. Shinde 2005 was the only study to report data using this scale.
4.3.2. Family Crisis Oriented Personal Evaluation Scales - FCOPES (McCubbin 1981)
This scale was constructed to identify problem-solving and behavioural strategies used by families when faced with problems or crises. This is a self-administered 29-item survey, which assesses (a) the individual to family network, or how willing the person is to share difficulties with relatives and how they internally handle these problems between its members; and (b) the family to social environment, or whether they seek encouragement and support from social circles outside of the family unit. There are five subscales to the FCOPES, including, acquiring social support (nine items); re-framing (eight items); seeking spiritual support (four

items); mobilising to acquire and accept help (four items); and passive appraisal (four items); these are each rated on a scale of one to five (1 = 'strongly disagree' and 5 = 'strongly agree'). Due to the mixture of positive and negative items in the scale, and that each family member may view problems differently, the meaning of the scores and their applicability are uncertain. For this reason, results from this scale have been presented in a separate table; Shinde 2005 was the only study to report data using this scale.

4.3.3. Family Emotional Involvement and Criticism Scale - FEICS (Shields 1992)

The FEICS is a self-report scale, developed to measure - from the perspective of the recipient - the two major variables of expressed emotion; emotional involvement (EI) and perceived criticism (PC). The scale consists of 14 items; rated between one to five (1 = 'almost never', 2 = 'once in a while', 3 = 'sometimes', 4 = 'often', 5 = 'almost always'). Each variable has a subscale, each consisting of seven items; the PC score is obtained from the total of even numbered items of the FEICS, and the EI subscale score is obtained from the odd numbered items. The higher the score, the greater the presence of EE, indicating a negative outcome. Shinde 2005 was the only study to report data using this scale.

4.3.4. Family Distress Scale - FDS (Pasamanick 1967)

This is a 22-item scale that measures the impact of having a relative with schizophrenia in the family in terms of the extent of disruption on family life, embarrassment and the concern of self and others. This scale was used in Smith 1987.

4.3.5. Patient Rejection Scale - PRS (Kreisman 1979)

The PRS is a questionnaire developed to measure level of acceptance or rejection that families have towards the relative with schizophrenia. This is a 24-item tool with half being positive items and half negative items; the responses to the questionnaire are measured on a scale of one to seven; since some of those items are negative, the scoring for those items are reversed; a neutral response gives a score of four and unanswered items are scored four, with possible scores varying from 168 to 24 - a neutral score is 196. The higher the score, the greater level of acceptance. This scale was used in Barber 1988*.

5. Redundant data

A large number of scales were used in the studies. Many measures, even those within included studies, were either non-peer reviewed (as in Barber 1988* and Smith 1987) or reported in such a way as to render the results unusable (Shinde 2005). Data were either not reported at all or did not distinguish treatment groups. Youssef 1987 measured global state using the GAS (Endicott 1976) but no data were reported on the outcome. Where data were presented, it was common not to have means or variances reported or inaccurate 'P' values presented. Of the scales that did provide useful data, these were all dichotomised. This made it possible to display the data but the redundancy of effort within each study was considerable.

6. Follow-up

Participants were followed up for between three months (Barber 1988*) and one year (Youssef 1987).

7. Missing outcomes

The outcomes with usable data from the included studies were minimal, which reduces the applicability the studies on the course of the illness; missing outcomes in this review include: causes of mortality, adverse events, clinical global response, relapse, behaviour, social functioning and economic outcomes. One study measured global assessment using the GAS but did not report any data (Youssef 1987).

8. Awaiting assessment

No studies await assessment.

9. Ongoing studies

We are not aware of any ongoing studies.

Excluded studies

We excluded 21 studies in total, 10 of which did not specify the number of sessions used in the intervention. Three studies were not randomised and two other trials did not present outcome numerical data in a form that made it possible to re-report in this review. Five studies were not brief family intervention (with more than five sessions); and a final excluded study was not specific to schizophrenia.

Risk of bias in included studies

Overall the quality of trials was not good (Figure 1 and Figure 2) and all results must be considered as being at risk of, at the very least, a moderate risk of bias (Summary of findings for the main comparison).

Allocation

Only Barber 1988* described how randomisation was undertaken. None of the other three trials give description. No study reassured the reader that the randomisation sequence was adequately concealed.

Blinding

Trialists were all aware of the possibility of the introduction of observer bias by not blinding raters to the group to which people or families were allocated. Barber 1988* and Smith 1987 did not describe blinding methods, and both Shinde 2005 and Youssef 1987 were rated as a 'high' risk of bias under this category, as both

mentioned that blinding was not employed - i.e. that participants were informed of the purpose of the study. It is likely that many people rating outcomes were not blind to group of allocation.

Incomplete outcome data

Overall, reasons for withdrawal from studies are well-reported, although there was no follow-up for those who left the treatment early in order to acquire data for a full intention-to-treat analysis. Only one study reported full follow-up, with no drop-outs during the intervention period (Smith 1987), with the remaining studies reporting less than 50% attrition. However, attrition was at 65% in Barber 1988*, and so this study was 'starred' and subject to a sensitivity analysis to determine whether the omission of the results change the estimate of effect.

Selective reporting

Most included studies reported all specified outcomes; however, Youssef 1987 did not report statistical data for pre-specified outcomes. Original protocols to these trials were unobtainable, and it may be that under-reporting did occur but this was not obvious to the reader of the final report.

Other potential sources of bias

We not aware that the trialists had any vested interest in the result. Often those undertaking a package of care or an approach to care have considerable track record of research in the area and it could be difficult for them to find outcomes that are incompatible with previous work. There was no obvious bias in how the papers were written, and no study provided funding information.

Effects of interventions

See: **Summary of findings for the main comparison** BRIEF FAMILY INTERVENTION compared with STANDARD CARE for schizophrenia

COMPARISON 1: BRIEF FAMILY INTERVENTIONS versus STANDARD CARE

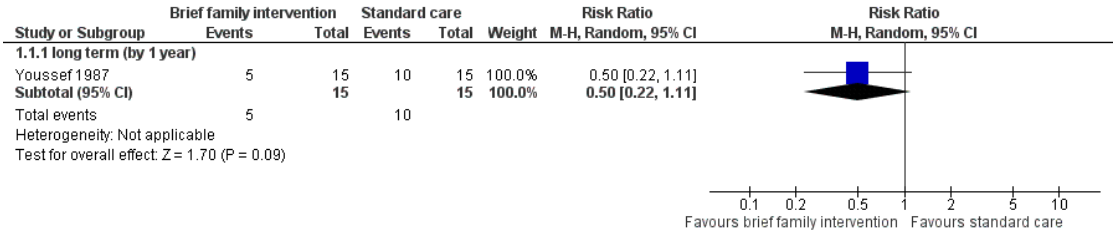
Three of the included studies provided data for this (Barber 1988*; Shinde 2005; Youssef 1987). Only one study provided data per outcome - therefore, a meta-analysis was not possible using these results.

1. Service utilisation

1.1 Hospital admission

By 12 months, one study showed that less people receiving brief family intervention were admitted to hospital (Figure 4) - this was not significant (P = 0.09) (n = 30, 1 RCT, risk ratio (RR) 0.50, 95% confidence interval (CI) 0.22 to 1.11, Analysis 1.1).

Figure 4. Forest plot of comparison: 1 BRIEF FAMILY INTERVENTION vs STANDARD CARE, outcome: 1.1 Service utilisation: 1. hospital admission.



2. Global State

Brief family intervention was favoured only slightly by medium term over standard care, with slightly fewer relapses; however, the results were not significant (n = 40 , 1 RCT, RR 0.50, 95% CI 0.10 to 2.43, Analysis 1.2).

2.1 Relapse

2.2 Improved (GAS)

Again, by long term, there was non-significant favour of brief family intervention for numbers of people improved (n = 30, 1 RCT, RR 1.27, 95% CI 0.91 to 1.78, Analysis 1.3).

2.3 Antipsychotic dose increased

By medium term, only slightly more people receiving standard care needed an increase in antipsychotic medication (n = 40, 1 RCT, RR 0.67, 95% CI 0.29 to 1.52, Analysis 1.4).

3. Mental state

3.1 Positive symptoms (PANSS, high score = worse)

There was only slight favour of brief family intervention by medium term for lower scores on the PANSS positive symptoms subscale (n = 35, 1 RCT, mean difference (MD) -0.89, 95% CI -2.84 to 1.06, Analysis 1.5).

3.2 Negative symptoms (PANSS, high score = worse)

Again, there was only slight favour of brief family intervention by medium term for lower scores on the PANSS negative symptoms subscale (n = 35, 1 RCT, MD -0.62; 95% CI -3.35 to 2.11, Analysis 1.6).

3.3 Total average score (PANSS, high score = worse)

Similar results were seen in the accumulative score on the PANSS by medium term, with a slight, non-significant favour of brief family intervention (n = 35, 1 RCT, MD -2.72, 95% CI -9.79 to 4.35, Analysis 1.7).

4. Family outcome

4.1 Average score for understanding of family member with schizophrenia (PRS, high score = greater acceptance)

One study rated level of acceptance and showed a significant increase in understanding by family members through a greater level of acceptance (n = 70,1 RCT, RR 14.90, 95% CI 7.20 to 22.60, Analysis 1.8).

4.2 Burden/stress - average score (BAS, high score = greater burden)

One study reported the level of burden/stress on caregivers with a slight favour of brief family intervention by medium term (n = 35, 1 RCT, MD -2.52, 95% CI -10.43 to 5.39, Analysis 1.9).

4.3 Family coping - average score (FCOPES)

One study reported family coping using the FCOPES; due to the mixture of positive and negative items within the scale and the largely subjective nature of the scale, the results have been presented in an additional table, as the true meaning of the scores and their applicability are uncertain. The results are best inspected by viewing Analysis 1.10.

4.4 Expressed emotions (EE) - average score (FEICS, high score = greater EE)

Results by medium term demonstrated slight favour of brief family intervention for less levels of expressed emotion, however results are not significant (n = 35, 1 RCT, MD -1.88, 95% CI -5.61 to 1.85, Analysis 1.11).

5. Leaving the study early

Medium-term data were equivocal for numbers of participants leaving the study early (n = 40, 1 RCT, RR 0.67, 95% CI 0.12 to 3.57, Analysis 1.12).

COMPARISON 2: BRIEF FAMILY INTERVENTION BY FACE-TO-FACE versus BRIEF FAMILY INTERVENTION BY POST

Only one study provided data for this outcome (Smith 1987); again, meta-analysis was not possible.

1 Family outcome

1.1. Stress - average score (SRT, high score = worse, skewed)

Results were skewed and are presented in a separate table. By short term, it is suggested that people who received brief family intervention face-to-face were more likely to demonstrate lower levels of stress. However, by medium term, there was no difference in results. These results need to be interpreted with caution, and are best inspected by viewing Analysis 2.1.

1.2 Burden - average score (FDS, high score = worse, skewed)

By short and medium term, the results suggest a lesser level of burden experienced by family members when receiving brief family intervention face-to-face. Again, results are skewed and should be interpreted with caution (Analysis 2.2).

SENSITIVITY ANALYSIS

Due to lack of studies and results for our primary outcomes (only one study reported data), no meta-analyses were performed. Therefore, we could not perform a sensitivity analysis for;

1. implication of randomisation
2. risk of bias;
3. imputed values.

This was because there was only one study per primary outcome, and the effect of excluding this study would leave us with no data to compare. There was no difference in the estimate of the effect when using fixed-effect or random-effect models on this basis.

DISCUSSION

There were no studies found with comparisons of brief family intervention versus non-brief family intervention; moreover, the variety of outcome measures in this brief family intervention review is not at a par with the outcome measures of the larger non-brief family intervention review (Pharoah 2010).

Summary of main results

COMPARISON 1: BRIEF FAMILY INTERVENTIONS versus STANDARD CARE

Unfortunately, no meta-analyses were possible between studies; owing to a lack of standardised outcomes and scarcity of data; the data we found are largely equivocal.

1. Service utilisation

It is not clear that the brief approach to family intervention has any advantage over standard care in terms of hospital admission as only one trial (n = 30) measured this outcome(Youssef 1987). Non-brief family intervention showed significant advantage over standard care with less people receiving brief family intervention admitted into hospital at one year but this was not statistically significant; once again, the few trials in the review reduces the validity of study reports, more trials and larger studies will produce more definite conclusions. We have reproduced the relevant findings of the larger family intervention review (Pharoah 2010) for ease of comparison (Table 1). A cross-section of all selected studies from the initial search revealed there was no standardised design for brief family interventions which may compromise the quality of the interventions in the studies and hence narrow the effectiveness over well-established standard care services, however findings from this review can form basis for hypothesis for further research with standardised designs for brief family intervention.

2. Global state

Shinde 2005 was only study in the review that reported global state relapse as an outcome, it did not state relapse criteria; although the data favoured brief family intervention over standard care in preventing relapse, it was not statistically significant. This was the case for the remaining global state outcomes of improvement (using the GAS scale) and increase in antipsychotic dose, where results were equivocal. More data on global state (particularly relapse and improvement rates) would have been greatly welcomed, and the authors suggest that future research into this area puts greater focus on patient-oriented outcomes.

3. Mental state

The same, small study (n = 35) provided outcome data for each mental state outcome (using PANSS), however, it is not recommended or even possible to draw any meaningful conclusions from the data. Again, there is slight, non-significant favour of brief family intervention over standard care, but the extent of any potential benefit cannot be stated with any confidence. The larger, non-brief family intervention had mixed an equivocal results in effects of mental state (Pharoah 2010).

4. Family outcome

Several studies have emphasised the role of the family environment on the overall prognosis of patients with schizophrenia and therefore numerous measures are being utilised by various trialists. The only two trials measuring family outcomes in this review were small studies using different measures of outcome (Barber 1988*; Shinde 2005). Barber 1988* showed that brief family intervention significantly increases the understanding of caregivers and family members which is reflected in the level of acceptance of patients compared to standard care. Shinde 2005 suggested that brief family intervention reduced burden and stress on family members and they are more likely to cope with and manage problematic situations. A similar trend was noted in reducing levels of expressed emotions in families receiving brief family intervention compared to standard care. The diathesis-stress model of schizophrenia has implications on the course of illness; this model suggests that reduction of stressful environmental stimuli can reduce the stress on persons with schizophrenia and improve their outcome.

Overall, the findings suggest that the brief approach to family intervention may improve the family atmosphere by creating better understanding of relatives to patients behaviour which reduces conflicts in the relationship when compared to standard care; better family atmosphere is also achieved by reduction in burden and stress on the relatives (Levene 1996). The small number of studies and the small sample size of the studies (n = 105) coupled with several measures of outcome compromises the power of the report. However, these findings are similar to results from the larger review of non-brief family intervention (Table 1).

5. Leaving the study early

Again, with only one study (Shinde 2005) providing any data for this outcomes, it is difficult to draw any meaningful conclusions. More detailed data regarding reasons for leaving the study early would have provided us with a better idea of how the intervention, or lack of intervention, impacts on participants' willingness to participate in the study, or indeed any adverse events that may lead to early drop-outs.

COMPARISON 2: BRIEF FAMILY INTERVENTION BY FACE-TO-FACE versus BRIEF FAMILY INTERVENTION BY POST

1. Family outcome

The only trial that compared face-to-face intervention and intervention by post showed no clear superiority of face-to-face intervention over that by post in terms of stress and burden on the relatives but trialists had recorded significant results using parametric tests (Smith 1987).

Overall completeness and applicability of evidence

1. Completeness

The outcomes in the included studies of this review did not report many of our outcomes, which were chosen in order to be comparable to outcomes of other interventions for schizophrenia for ease of assessment. The reporting of unusable data and incomplete reporting of data further reduces the variety of outcomes for analysis, the quality and size of the studies reduces the power of the results and also reduces the chances of coming across studies with varied outcomes. The most elaborate outcomes in this review were family-oriented, which were not even exhaustive, outcomes such as compliance, relapse, mental state, social functions, global assessment. These varied outcomes make it easy for assessment by all the stake holders involved, which includes policy makers, clinicians, relatives of patients and the patients

2. Applicability

Most of the included studies were carried out in university teaching hospitals and research institutes, which provide higher quality of standard care compared to community-based treatment in which the majority of patients with schizophrenia are managed.

Participants were largely diagnosed with schizophrenia, with the exception of Youssef 1987, in which participants were diagnosed with schizoaffective disorder; however different diagnostic tools were employed in each of the three remaining studies (DSM-III, ICD-10, and Schneider 1959 criteria). Furthermore, each study was undertaken in largely different environments; two studies undertaken in the US (one in a university-affiliated, state-supported community outpatient clinic in a large cosmopolitan area; the other an inpatient psychiatric unit of a general hospital), one in the UK and another in India (both inpatient and outpatient). Therefore, this raises issues regarding applicability of these results to the general population on a national and global scale, particularly because the method of brief family intervention differed between studies, with varying length of sessions and depth as to course or workshop sessions and accompanying materials used by participants. Furthermore, the expectation of what would be considered 'standard care' would differ on this international basis.

Quality of the evidence

Overall, the quality of reporting was poor (Figure 1). Most included studies did not describe how the randomisation was conducted. With the nature of the intervention, blinding is difficult to account for; two studies out of the included four reported that no blinding was used, with the remaining two studies not making any reference to use of blinding. Therefore there is, at the very least, a moderate risk of overestimating the effect of the intervention.

Potential biases in the review process

The process of searching for studies was thorough. We strictly followed the review protocol in the process of study selection, data extraction and analysis. Only published reports were considered in this review, which may perpetuate a publishing bias; all the Chinese studies were excluded due to unspecified number of sessions, with the assumption that no information was omitted during translation, which was not detailed.

Agreements and disagreements with other studies or reviews

There are no other known reviews for brief family intervention in schizophrenia. Similar reviews are those of larger non-brief family interventions, which excluded studies with family intervention of less than five sessions; the limited outcomes reported with this review were similar and supported by the larger non-brief family interventions review (Pharoah 2010).

AUTHORS' CONCLUSIONS

Implications for practice

1. For people with schizophrenia

One outstanding reward of brief family intervention is that it makes the family atmosphere more conducive for patients with schizophrenia with less time commitment to the programme; family members' burden and stress are much reduced, which in turn may improve their quality of life despite having a relative with schizophrenia to care for. These benefits help people with schizophrenia and their families take advantage of such programs provided by their service providers. The results of this systematic review draws together the existing best available evidence; unfortunately, due to poor outcome reporting and lack of patient-centred outcomes, we cannot state with confidence the overall benefit a person may expect to achieve after receiving brief family intervention. All data reported for global state and mental state outcomes display only a slight, non-significant favour for brief family intervention over standard care. Findings were only significant for the family outcome of understanding the patient with schizophrenia, however, this was from data of one study with a small sample size. Although family and carer-centred outcomes are important, more research is needed into more patient-centred outcomes including social functioning, quality of life, mental state and any adverse events or effects.

2. For clinicians

Patient and relative engagement rates for psychosocial intervention programs are low despite their proven effectiveness; this might be due to the long commitment associated with such interventions. Brief interventions are less time-consuming, with minimal resources involved. The beneficial effect of brief family intervention on the well-being of a caregiver also reflects on the patient, which could make the intervention worth prescribing. What this review has found, however, is that the current research has not placed enough focus on patient-centred outcomes, which makes it difficult to judge the effect and actual benefit this intervention may have on people with schizophrenia. Until more conclusive evidence is found, this therapy should be employed with caution, on an individual patient basis.

3. For policy makers

Service managers and funders always have limited resources, and are challenged to achieve the best outcomes using such resources. Brief family intervention aims to help to achieve benefits with limited resources, and managers may want to consider such interventions in order to help to meet the demands of a larger number of patients over a short period of time. The results of this systematic review, however, are largely equivocal and - due to a lack of standardised outcomes allowing for meta-analyses - results are not pooled, which gives us less power in the results and little confidence in the estimate of the effects reported. More research is needed into a more standardised approach of brief family intervention before any concrete conclusions can be drawn as to any real or cost benefit of this intervention.

Implications for research

1. General

We excluded 21 trials (please refer to Characteristics of excluded studies for details), due to the poor quality of data reporting, diminishing the already limited evidence-base and also Chinese studies that were non-specific in terms of number of sessions. Following CONSORT for good reporting of clinical trials more closely would have helped to considerably increase the amount of data available in this review. Any clinical trials that are undertaken in the future should conform with the AllTrials initiative of transparency in past, present and future research, namely: registration of the study protocol; summary results reporting as well as *full* results reported (unredacted); and the availability of individual participant data.

2. Specific

There is a need for more well-designed, conducted and reported randomised studies investigating the efficacy of brief family intervention Table 2. The outcome measures were not varied, the few were focused mainly on effects on the relatives with no direct effects on the patient with schizophrenia as regards course of illness. Future trials should explore a wider variety of standardised outcomes measures centred on the patients. The design and content of brief family interventions should be clearly reported so as to encourage the use of data reported in evidence-based reports and systematic reviews. A wide variety of outcomes will make reports from such trials more attractive to policy makers and managers. Continuous data should be reported with mean, standard deviations and number of participants. Endpoint score should always be used when reporting data derived from scales (Table 3).

Benefits of a brief form of family intervention may potentially encapsulate more than any associated cost-saving; by equipping family members with the basic information relating to care and new strategies, a stronger culture of support could emerge, allowing both families and patients greater empowerment over their situation. Any potential harms of this type of intervention need researching in future randomised controlled trials, but could include the risk of delivering fundamental, supportive information in this brief, condensed manner; longer follow-up periods will be useful in assessing whether educational information is retained amongst both families and patients after completion of studies. As previously stated, the lack of patient-centred outcomes makes it difficult to identify explicit benefits or harms of brief family intervention, something that future research can shed light on. Two out of the four included studies provided useable data for levels of burden or stress on the family (Shinde 2005; Smith 1987); however, no study investigated/reported results for potential adverse events associated with the intervention. Further studies should address this

paucity of data to take this important outcome into consideration for both patient and family.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barber 1988*

Methods	Allocation: random. Blindness: not stated. Duration: 2 months. Setting: outpatient - university-affiliated, state supported, community outpatient psychiatric clinic for adults and children situated in a cosmopolitan area comprising approximately 2 million people (US)
Participants	N = 200*. People with schizophrenia: Diagnosis: schizophrenia (DSM III). Age: mean 32.7 years (SD + 1.19), range 20 - 60 years. Sex: 18F, 52M. Ethnicity: not stated. History: all receiving prescribed medication; mean age of onset 24.70 years (SD + 5.68) ; range 16 - 42 years Included: living with primary care giver or at least had weekly contact (face-to-face or telephone) with the relative Excluded: patients with a secondary diagnosis of mental retardation [sic] or organic brain syndrome were not included in the study Participants - 'primary family caregivers': n = 70 (n = 44 parents; n = 8 spouse; n = 9 sibling; n = 4 child; n = 5 other). Age: mean 49 years (SD + 12.5), range 23 - 67 years. Sex: 53F, 17M. Ethnicity: White (n = 34); Black (n = 26); Hispanic (n = 6); Oriental (n = 4). History: living with participant or at least had weekly contact (face to face or telephone) with the participant Included: those not currently attending a family educational group or had attended in past 6 months Excluded: primary family caregivers of patients with a secondary diagnosis of mental retardation [sic] or organic brain syndrome were included in the study
Interventions	1. Brief family intervention: 'family workshop' - conducted by three registered psychiatric nurses, a social worker and a psychiatrist. Semi-structured family workshop in which families are instructed regarding the diagnosis of schizophrenia, treatment, symptoms, problems, medications, course of illness, early sings of relapse and coping strategies - six-hour, one-day workshop lasting 5 sessions, n = 100. 2. Standard care: 'routine clinical information' without workshop; this includes information that is not formalised, usually brief; and limited to the responses to questions and concerns that the caregivers verbalise, n = 100
Outcomes	Family outcome: understanding of the family member with schizophrenia - Patient Rejection Scale (PRS) Unable to use - Family stress: Schizophrenic Family Caregiver Stress Scale (SFCS) - non-peer-reviewed

Barber 1988* (*Continued*)

	scale	
Notes	*Due to high loss to follow-up, this study was subjected to a sensitivity analysis	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Simple random sampling - "using a table of random numbers, 200 patient code numbers were randomly selected and divided into 2 groups of 100 each, random assignment of subjects to control and experimental group was determined by a flip of a coin such that 'heads' represented the control group and 'tails' represented the experimental group. The subjects were subsequently alternately assigned to the groups after the initial toss of coin so that the groups were equal" (p66)
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not stated.
Incomplete outcome data (attrition bias) All outcomes	High risk	Attrition: 65% - 200 participants were originally randomised - 100 each to receive either the family workshop or routine clinical information. Out of n = 100 assigned to workshop, n = 44 participants agreed to participate, however only n = 39 attended, and only n = 36 returned both pre-tests and post-tests and were included in the analysis. Out of n = 100 assigned to routine clinical information, only n = 38 agreed to participate in the study, and only n = 34 completed the study and were included in data and analysis
Selective reporting (reporting bias)	Low risk	All specified outcomes were reported.
Other bias	High risk	Funding: not stated. Rating scales: not clear whether raters were independent of treatment. SFCS developed by trial investigator

Shinde 2005

Methods	Allocation: random. Blindness: none. Duration: 1 month, 3-month follow-up. Setting: inpatient and outpatient, Department of Psychiatry, NIMHANS, Bangalore (IN)
Participants	Participants - people with schizophrenia: Diagnosis: schizophrenia (ICD-10), paranoid schizophrenia (n = 32), other subtypes (n = 8). n = 40. Age: brief family intervention - mean 29.95 years (SD ± 6.85); control - mean 30.05 years (SD ± 7.22). Sex: 11F, 29M. Ethnicity: not stated. History: n = 4 belonged to inpatient wards, n = 36 were on outpatient treatment; mean duration of treatment - brief family intervention 52.25 months (SD ± 27.43); control 45.45 months (SD ± 28.81); average number of relapses 1.6 in both groups; n = 14 receiving typical antipsychotics; n = 26 receiving atypical antipsychotics Included: diagnosis of schizophrenia (ICD-10); duration of illness 1-10 years; age 18-65 years Excluded: acute psychotic excitement or illness; co-morbid psychiatric or chronic medical illness; mental retardation [sic] Participants - 'primary caregivers'*: Age: brief family intervention - mean 47.60 years (SD ± 14.80); control - mean 47.05 years (SD ± 12.97). Sex: 16F, 24M. Ethnicity: not stated. History: in contact and residing with person with schizophrenia since previous 1 month Included: parent, spouse, sibling, child or relative; aged 18-65 years; maximum hours of contact and residing with person with schizophrenia since previous 1 month Excluded: having another relative with psychiatric illness; chronic medical or psychiatric illness
Interventions	1. Brief family intervention: 'family psychoeducation module' - X3 (weekly) one-hour sessions to be completed over a period of four weeks (45-minute session with a 15-minute discussion and queries session), n = 20 i) Session one: education about schizophrenia (including diagnosis; symptoms; course of illness and relapse; causes; treatment); ii) Session two: assessing and handling difficult problems (including identifying problems; listing solutions; weighing advantages and disadvantages; selecting the best solution; implementation; review; maintenance and generalisation of solutions); iii) Session three: handling communication and emotions (including improving communication techniques and patterns; non-verbal communication; expressing feelings; positive communication; handling expressed emotions) 2. Standard care: 'standard inpatient/outpatient treatment' (control group participants were informed that they were on a waiting list to receive the intervention program at the end of three months), n = 20

Outcomes	Clinical global response: relapse (clinical judgement); antipsychotic dose increased Leaving the study early. Mental state: positive symptoms; negative symptoms; total score (PANSS) Family outcome: expressed emotion score (Family Emotional Involvement and Criticism Scale (FEICS)); burden (Burden Assessment Schedule (BAS)); family coping (Family Crisis Oriented Personal Evaluation Scales (FCOPES)) Unable to use - Knowledge acquisition (Knowledge Interview (KI)) - no usable data
Notes	All participants continued medication management from their parent-treatment unit *Defined as a 'family member who lives in the same household as the index patient, who spends time with him/her, and/or is directly and actively involved in the care of the patient (supervising medication, bringing him/her to hospital for follow-up) for at least one month' (p31-2)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised - "random number table was used to assort 20 patients and their caregivers" - no further information
Allocation concealment (selection bias)	High risk	Non-blinded.
Blinding (performance bias and detection bias) All outcomes	High risk	Non-blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Follow-up: 88%. Brief family intervention group - all participants attended the first session; n = 16 attended the second session; n = 15 attended the third session. Three-month follow-up assessment was obtained from n = 18 patients and their caregivers Control group - n = 17 people with schizophrenia and their caregivers completed the 3-month follow-up assessment
Selective reporting (reporting bias)	Low risk	None detected.
Other bias	Unclear risk	Funding: not stated. Rating scales: FEICS described as a self-report scale - unclear whether raters of remaining scales were independent of treatment

Smith 1987

Methods	Allocation: random. Blindness: not stated. Duration: 6 months. Setting: inpatient and outpatient (UK).
Participants	People with schizophrenia: Diagnosis: evidence of one or more first rank symptoms of schizophrenia (Schneider 1959). n = 23 (total of 23 families). Age: mean 36.4 years (SD + 14). Sex: 18F, 5M. Ethnicity: not stated. History: mean duration of illness 7.9 years (SD + 6.8); mean number of hospital admissions 3.7 (SD + 3.8). Included: evidence of one or more 'first-rank' symptoms of schizophrenia (Schneider 1959); living at home or in close contact with the family (5 or more days a week); stabilised on depot or oral antipsychotic medication. Out of the people with schizophrenia who participated, n = 6 were in hospital at the time of the study Excluded: not stated. Participants - 'family members': n = 40 (28 parents; 7 spouses; 5 'other relatives'). Ethnicity: not stated. Included: English-speaking. Excluded: not stated.
Interventions	1. Brief family intervention: 'brief education intervention', the therapy was administered by the primary therapist in a semi-structured seminar format involving oral presentation of the information as well as audiovisual aids, delivered at weekly intervals for 4 weeks (4 sessions). Family participation was encouraged through question and answer discussions. At the end of each session, each family member received a booklet corresponding to the material covered in that section with homework they were invited to complete, n = 20. 2. Brief family intervention by post: 'postal information booklet', delivered at weekly intervals for 4 weeks (4 sessions). Family members received a typed information booklet, corresponding to what the group education intervention group received. A covering letter was also distributed, inviting family members to complete corresponding homework exercised attached, n = 20
Outcomes	Family outcome: stress (measured using the symptom rating scale - SRT, skewed, Kellner 1973); burden (measured using the Family Distress Scale - FDS, skewed, Pasamanick 1967). Unable to use - Beliefs about schizophrenia and its treatment - measured using a non-peer-reviewed scale Knowledge acquisition: clinical information survey - non-peer reviewed scale Worry and fear - measured using a non-peer-reviewed scale. Behavioural disturbance - not specified in protocol.
Notes	

Risk of bias

Smith 1987 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised - no further details.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not stated.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote, "there were no drop-outs during the intervention period" (p646)
Selective reporting (reporting bias)	Unclear risk	All data were reported.
Other bias	Unclear risk	Funding: not stated. Rating scales: not clear whether raters were independent of treatment

Youssef 1987

Methods	Allocation: random. Blindness: non-blinded. Duration: 12 months follow-up*. Setting: inpatient, psychiatric unit of a general hospital, Virginia (US)
Participants	Participants - people with schizoaffective disorder; Diagnosis: schizoaffective disorder. n = 30. Age: range 28-52 years, mean 37. Sex: 12F, 18M. Ethnicity: not stated. History: mean length of illness 8 years; mean previous hospital admissions 3.7; mean length of hospitalisations 5.4 weeks Included: not stated. Excluded: refusal to participate; reluctance to join all three education sessions
Interventions	1. Brief family intervention: patient-family** teaching programme, twice weekly, participants were required to attend 3 consecutive sessions lasting one hour. Discussion based, question and answer sessions to explain the meaning of the illness, causes and treatments: i) To provide knowledge, clarification and support for patients and families (including diagnosis; medication; signs of relapse; community resources available for patients and families); ii) Help the family understand the meaning of hospitalisation for the patient, and remain aware of 'problem areas' to be aware of after discharge, n = 15 2. Standard care: 'did not receive the patient-family teaching programme', n = 15

Outcomes	Global state: improved (defined as a marked increase on the Global Assessment Scale (GAS) scores between the time of admission and the time of discharge) Service utilisation: hospital admission. Unable to use - Global state: average change/endpoint score (GAS) - no usable data
Notes	*The study was carried out in a psychiatric unit of a general hospital, with an average length of stay of 4 weeks. The patient-family teaching program was implemented prior to discharge (length of intervention not specified) **For this study, quote, "'family' was defined as a 'family member or significant others such as room mates, friends, or any other person with whom the patient has any type of enduring relationship"' (p613)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomised - no further details.
Allocation concealment (selection bias)	Unclear risk	Not stated.
Blinding (performance bias and detection bias) All outcomes	High risk	Quote: "subjects were approached by the investigator and informed verbally of the purpose of the study" (p613)
Incomplete outcome data (attrition bias) All outcomes	High risk	It is stated that, quote, "initially a total of 42 patients with affective disorders were approached for possible inclusion in this investigation. Of this number, 12 patients were excluded from the initial sample for the following reasons: families' refusal to participate in this study, reluctance to join all three education sessions, and/or difficulties in tracing some patients and their families during the follow-up period" (p613). It is unclear whether these participants had been randomised into either the intervention or control group, or whether data were collected for these participants
Selective reporting (reporting bias)	High risk	Statistical data for the GAS were not reported.
Other bias	Low risk	Funding: not stated. Rating scales: not clear whether raters were independent of treatment

BAS - Burden Assessment Scale.

DSM - Diagnostic Statistical Manual.
FCOPES - Family Crisis Oriented Personal Evaluation Scale.
FDS - Family Disress Scale.
FEICS - Family Emotional Involvement and Criticism Scale.

GAS - Global Assessment Scale.
ICD - International Classification of Diseases.
PRS - Patient Rejection Scale.

SFCS - Schizophrenia Family Gare Give Stress Scale.
SRT - Symptom Rating Test.
PANSS - Positive and Negative Syndrome Scale.
PRS - Patient Rejection Scale.
SD: standard deviation

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Berkowitz 1984	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care. Outcomes: no usable data.
Birchwood 1992	Allocation: sequential.
Chen 2000	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Chen 2002	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Cozolino 1988	Allocation: quasi-randomised.
Dixon 2011	Allocation: randomised. Participants: 'serious mental illness' - not specific to schizophrenia
Gassmann 2011	Allocation: randomised. Participants: people with schizophrenia. Intervention: psychoeducative family intervention vs standard care - not brief family intervention
Kane 1990	Allocation: not randomised.

(*Continued*)

Koolaee 2009	Allocation: randomised. Participants: mothers of people with schizophrenia. Intervention: psychoeducation vs behavioural family management vs standard care - not brief family intervention
Li 2003	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Ling 1999	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Pickett-Schenk 2006	Allocation: randomised. Participants: mixed diagnosis (schizophrenia, schizoaffective disorder, bipolar disorder, depression, OCD, other) - majority bipolar disorder Intervention: psychoeducation vs standard care - not brief family intervention
Rotondi 2005	Allocation: randomised. Participants: people with schizophrenia. Interventions: 'telehealth' family intervention (via Internet-based guide to schizophrenia) vs standard care - duration of family intervention not measured
Spiegel 1987	Allocation: randomised. Participants: people with schizophrenia. Interventions: 'family case consultation' vs standard care - duration of family intervention optional up to 15 sessions
Tarrier 1988	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - not brief family intervention
Wang 1997	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Yang 2002	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Zhang 2001	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Zhao 2000	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified

(*Continued*)

Zhu 1998	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified
Zhu 2002	Allocation: randomised. Participants: people with schizophrenia. Interventions: family intervention vs standard care - duration of family intervention not specified

vs: versus

DATA AND ANALYSES

Comparison 1. BRIEF FAMILY INTERVENTION vs STANDARD CARE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Service utilisation: 1. hospital admission	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 long term (by 1 year)	1	30	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.22, 1.11]
2 Global state: 1. relapse	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.1 medium term (by 3 months)	1	40	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.10, 2.43]
3 Global state: 2. improved (GAS)	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 long term (by 1 year)	1	30	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.91, 1.78]
4 Global state: 3. antipsychotic dose increased	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 medium term (by 3 months)	1	40	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.29, 1.52]
5 Mental state: 1. positive symptoms, average score (PANSS, high score = worse)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1 medium term (by 3 months)	1	35	Mean Difference (IV, Random, 95% CI)	-0.89 [-2.84, 1.06]
6 Mental state: 2. negative symptoms, average score (PANSS, high score = worse)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
6.1 medium term (by 3 months)	1	35	Mean Difference (IV, Random, 95% CI)	-0.62 [-3.35, 2.11]
7 Mental state: 3. total average score (PANSS, high = worse)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
7.1 medium term (by 3 months)	1	35	Mean Difference (IV, Random, 95% CI)	-2.72 [-9.79, 4.35]
8 Family outcome: 1. understanding, average score for understanding of family member with schizophrenia (PRS, high score = greater acceptance)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
8.1 medium term (by 3 months)	1	70	Mean Difference (IV, Random, 95% CI)	14.90 [7.20, 22.60]
9 Family outcome: 2. burden/ stress, average score (BAS, high score = greater burden)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
9.1 medium term (by 3 months)	1	35	Mean Difference (IV, Random, 95% CI)	-2.52 [-10.43, 5.39]
10 Family outcome: 3. family coping, average score (FCOPES)			Other data	No numeric data

10.1 medium term (by 3 months)			Other data	No numeric data
11 Family outcome: 4. expressed emotions, average score (FEICS, high score = greater EE)	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
11.1 medium term (by 3 months)	1	35	Mean Difference (IV, Random, 95% CI)	-1.88 [-5.61, 1.85]
12 Leaving the study early	1		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
12.1 medium term (by 3 months)	1	40	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.12, 3.57]

Comparison 2. BRIEF FAMILY INTERVENTION vs BRIEF FAMILY INTERVENTION BY POST

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Family outcome: 1. Stress - average score (SRT, high score = worse, skew)			Other data	No numeric data
1.1 short term (by 1 month)			Other data	No numeric data
1.2 long term (by 6 months)			Other data	No numeric data
2 Family outcome: 2. Burden - average score (FDS, high score = worse, skew)			Other data	No numeric data
2.1 short term (by 1 month)			Other data	No numeric data
2.2 long term (by 6 months)			Other data	No numeric data

ADDITIONAL TABLES

Table 1. Brief versus standard care Versus non-brief versus standard care

Outcome	Brief vs standard care (by one year)	Non-brief vs standard care (by one year)
Relapse	n = 40, 1 RCT, RR 0.50, 95% CI 0.10 to 2.43	n = 2981, 32 RCTs, RR 0.55, 95% CI 0.48 to 0.62
Hospital admission	n = 30, 1 RCT, RR 0.50, 95% CI 0.22 to 1.11	n = 532, 9 RCTs, RR 0.78, 95% CI 0.63 to 0.98
Family burden	n = 35, 1 RCT, MD -2.52, 95% CI -10.43 to 5.39	n = 48, 1 RCT, MD -7.01, 95% CI -10.77 to -3.25
Family understanding of patient	n = 70, 1 RCT, MD 14.90, 95% CI 7.20 to 22.60	n = 39, 1 RCT, RR 1.11, 95% CI 0.45 to 2.70

Table 1. Brief versus standard care Versus non-brief versus standard care (*Continued*)

Family conflicts/expressed emotions	n = 35, 1 RCT, MD -1.88, 95% CI -5.61 to 1.85	n = 164, 3 RCTs, RR 0.68, 95% CI 0.54

CI: confidence interval
MD: mean difference
RCT: randomised controlled trial
RR: risk ratio

Table 2. Suggested design of study

Methods	Allocation: randomised, fully explicit description of methods of randomisation and allocation concealment. Blinding: single, tested. Setting: community rather than hospital. Duration: 12 weeks intervention, and then follow-up to at least 52 weeks
Participants	Diagnosis: schizophrenia (ICD). N = 300.* Age: adults. Sex: both.
Interventions	1. Brief family intervention (five sessions or less, of less than three months duration) n = 150 2. Standard care, n = 150.
Outcomes	General: time to all-cause treatment failure marked by its discontinuation, relapse, general impression of clinician (CGI), career/other, compliance with treatment., healthy days, Mental state: BPRS and PANSS. Global state: CGI (Clinical Global Impression). Quality of life. QOL (Quality of Life Questionnaire). Family burden: FBQ (Family Burden Questionnaire). Social functioning: return to everyday living for 80% of time.* Adverse events: any adverse event recorded. Economic outcomes.
Notes	* Powered to be able to identify a difference of ~ 20% between groups for primary outcome with adequate degree of certainty

BPRS: Brief Psychiatric Rating Scale
ICD: Internation Classification of Diseases
PANSS: Positive and Negative Syndrome Scale

Table 3. Future reviews

Intervention	Study
Internet-based family interventions for schizophrenia.	Rotondi 2005

CONTRIBUTIONS OF AUTHORS

Okpokoro Uzuazomaro - instigated and wrote the protocol and review.

Clive E Adams - helped with the protocol and review.

Stephanie Sampson - helped write the review; checked data-extraction and helped construct the summary of findings table.

DECLARATIONS OF INTEREST

Okpokoro Uzuazomaro - none.

Clive E Adams - none.

Stephanie Sampson - none.

SOURCES OF SUPPORT

Internal sources

- The University of Nottingham, UK.
- Institute of Mental Health, Nottingham, UK.

External sources

- National Institute for Health Research (NIHR), UK.

Cochrane Collaboration Programme Grant 2011: Cost effective treatments and diagnostic approaches for people with schizophrenia within the NHS (ref: 10/4001/15)

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Major changes	Minor changes
i. Change from published protocol from "[A]dults, however defined, with schizophrenia or related disorders, including schizophreniform disorder, schizoaffective disorder and delusional disorder - again, by any means of diagnosis", to "[A]dults, however defined, with schizophrenia or related disorders, including schizophreniform disorder, schizoaffective disorder and delu-	i. Difference between presentation of Types of interventions; protocol stated comparisons as: *1. any intervention described as 'family intervention' for people with schizophrenia of longer duration;* *2. any other non-family psycho-social or educational package of brief duration;*

(*Continued*)

sional disorder, by any means of diagnosis, and their families/ caregivers/supporters (however defined in each study)" (see Types of participants). By nature, any type of family intervention has a likelihood that family members will be involved in studies as well as participants with the above mentioned disorders	*3. any other non-family psycho-social or educational package of longer duration; or* *4. standard care.* The current review states comparisons as: *1. Standard care: as defined in each study.* *2. Non-brief family intervention: any intervention described as 'family intervention' for people with schizophrenia of longer duration.* *3. Any other non-family psycho-social or educational package: of brief duration or longer duration.* The review authors recognise the difference in structure; however, there have been no changes as to the meaning of how the comparisons are defined. The authors feel that the current format is more concise and all-encompassing

INDEX TERMS

Medical Subject Headings (MeSH)

*Expressed Emotion; Family Therapy [*methods]; Patient Education as Topic [methods]; Psychotherapy, Brief [*methods]; Psychotic Disorders [*therapy]; Randomized Controlled Trials as Topic; Schizophrenia [*therapy]; Secondary Prevention

MeSH check words

Humans