# Appendix 22c: 2009 Psychological therapies and psychosocial interventions study characteristics tables[1]

**Please note that some of the references and the data in this appendix have been incorporated from the previous guideline and have therefore not been updated to reflect current house style.**

**Full terms of abbreviations are listed at the back of the guideline, except in some instances where they are explained in situ.**

**An asterisk next to an author's name indicates that their study is the primary study.**

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# Adherence therapy

**Characteristics of included studies (previous guideline)**

| | | | | | |
|---|---|---|---|---|---|
| Kemp1996 | Allocation: randomised using tables of random numbers.<br>Blinding: none.<br>Duration: 2-3 weeks (4-6 sessions in total), 18 months follow-up.<br>Frequency: 20-60 minutes twice a week. | Inpatients.<br>Diagnosis: 43 schizophrenia (DSM-III-R), remaining sample mood disorders N=74.<br>Age: CBT group mean 34 (SD 10.6), control group mean 37 (SD 11.9).<br>Sex: 39 M 35 F.<br>History: mean duration of illness: CBT group 8.5 years (SD 6.3), control group 10.7 years (SD 9.6). | 1. CBT + standard care: compliance therapy - reviewing history of illness, discussing the benefits and drawbacks of drug treatment, the stigma of drugs, the discrepancy between participant's action and beliefs. N=39.<br>2. Supportive counselling: therapists listening to participants' concerns but declined to discuss treatment. N=35. | 1. Death<br>2. Leaving the study early<br>3. Relapse<br>4. BPRS<br>5. Global Assessment of Functioning scale (GAF).<br>5. Extended Schedule for Assessment of Insight<br>6. Drug Attitudes Inventory<br>7. Attitudes to Medication Questionnaire<br><br>Unable to use:<br>1. Medication compliance (not a peer-reviewed published scale).<br>2. Attitudes to treatment questionnaire (not a peer-reviewed published scale). | Therapists: research psychiatrist and clinical psychologist. Both trained in CBT and attended a workshop on motivational interviews.<br>Supervision: therapists received regular supervision.<br>CBT type: compliance therapy. |

**References of included studies (previous guideline)**

**Kemp1996**

*Kemp R, Hayward P, Applewhaite G, Everitt B, David A. (1996) Compliance therapy in psychotic patients: a randomised controlled trial. *British Medical Journal;* 312:345-9.

Kemp R, Kirov G, Everitt B, Hayward P, David A. (1998) Randomised controlled trial of compliance therapy. *British Journal of Psychiatry* 1998;172:413-419.

**Characteristics of included studies (update)**

| **Study ID** | **GRAY2006** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer - Although the analysis was ITT, the figures presented in the paper are for completers. |
| | **Type of analysis:** ITT with pro-rating used to deal with missing sub-scale data as long as fewer than 20% of items were missing. Imputation was used in a sensitivity analysis but not in the results presented in the paper |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - Study was conducted over 52 weeks, participants could have sessions of therapy for up to 20 weeks of this time. |
| | **Duration:** No. weeks of treatment - Up to a maximum of 20 weeks |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Range of psychiatric inpatient and community outpatient settings in four study sites: Amsterdam, The Netherlands; Leipzig, Germany; London, England and Verona, Italy. |
| | **Number of people screened, excluded & reasons:** 1218 people were referred with 809 being excluded from the study due to the following reasons: Not diagnoses with schizophrenia, not meeting other inclusion criteria, refusal to participate and other reasons. |
| | **Notes about study methods:** Randomisation was performed by the independent clinical trials unit, where allocation was carried out by permuted blocks of random size, stratified by centre. The therapist was notified of the participants' allocation but the researcher conducting the assessments remained masked to allocation throughout the trial. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** ICD-10 |
| | **Inclusion criteria:**<br>- Confirmed diagnosis of schizophrenia<br>- Needing continued medication for at least 1 year<br>- Clinical instability in year before baseline defined as >=1 hospital admission, change in dose or type of medication, increased frequency of contact with services and indication of clinical instability reported by relatives, carer or clinical teams. |
| | **Exclusion criteria:**<br>- Moderate to severe mental handicap/ learning disability; organic brain disorders;<br>- Currently treated by forensic services; |

- alcohol or drug dependence;
- inability to speak the language of host country to a sufficient standard to receive the intervention or assessment - lacking capacity to give valid consent

**Total sample size:** No. randomised 409

**Total sample size:** ITT population 372

**Gender:** % female 40%

**Age:** Mean 41

**Ethnicity:** White European - 75%

**Setting:** Outpatient

**Setting:** Inpatient

**History:**
[Adherence therapy completers / Adherence therapy non-completers / Health education completers / Health education non-completers]
Mean psychiatric inpatient days in previous year: 26.9(62.5) / 41.2(77.1) / 24.2(54.8) / 51.2(67.5)

**Baseline stats:**
[Adherence therapy completers / Adherence therapy non-completers / Health education completers / Health education non-completers]
BPRS: 44.3(12.8) / 44.3(12.6) / 45.9(13.2) / 47.0(14.7)

**Interventions** **Intervention - group 1.:** Adherence therapy, 8 sessions over a maximum of 5 months, N = 204

**Intervention - group 2.:** Health Education, 8 sessions over a maximum of 5 months, N = 205

**Notes about the interventions:**
Adherence Therapy
An individual cognitive–behavioural approach based on a manual which describes a collaborative, patient centred phased approach to promoting treatment adherence in people with schizophrenia. There are six elements that form the core of the therapy: assessment; medication problem-solving; a medication timeline; exploring ambivalence; discussing beliefs and concerns about medication; and using medication in the future.

Health Education
Acted as a control condition which was not expected to enhance medication adherence, but which did control for the time spent with the therapist. The didactic intervention consisted of eight individual sessions. The sessions included presentations on health education-related topics such as diet and healthy lifestyle.

Both interventions were provided in addition to TAU.

| | |
|---|---|
| | Training<br>Treatment fidelity was assured as follows:<br>- both treatments were manualised which were translated and back translated into the appropriate languages<br>- All therapists met for 7 days to receive intensive training,<br>- Randomly selected therapy sessions were audiotaped and independently rated using the Adherence Therapy Checklist<br>- Throughout intervention period, therapists attended monthly group telephone clinical supervision, focusing on case presentations, the resolution of clinical problems, and adherence to therapy manuals. |
| **Outcomes** | **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS |
| | **Non-adherence to study medication:** Non-adherence - MAQ; SAI-C |
| | **Quality of Life:** Average score/change in quality of life - SF-36 |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Well covered |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **MANEESAKORN2007** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Results were analysed on an ITT basis with missing values being replaced by the patient's last measure or LOCF |

**Type of analysis:** LOCF

**Blindness:** Only raters blind

**Duration:** No. weeks of treatment 8 weeks

**Raters:** Independent of treatment

**Design:** Single-centre - Muang Chiang Mai District, Thailand

**Number of people screened, excluded & reasons:** 86 patients were assessed for eligibility, 54 were excluded due to: drug and alcohol dependence (n=24), severe symptoms, (n=11), cannot speak Thai (n=5) and learning disabilities (n=4). 10 patients refused to participate

**Notes about study methods:** Patients were assigned via an independent randomisation service

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** Other method case note diagnosis of schizophrenia

**Inclusion criteria:**
- case note of schizophrenia
- aged 20+

**Exclusion criteria:**
- Primary diagnosis of drug or alcohol dependence
- Organic brain disease or moderate or severe learning disabilities.

**Total sample size:** No. randomised 32

**Total sample size:** ITT population 28

**Gender:** % female 28%

**Age:** Mean 40.85

**Ethnicity:** Thais - 100%

**Setting:** Inpatient

**History:**
[Adherence therapy / TAU]
duration of illness, years: 9.64(6.89) / 9.25(6.21)
Number of admissions: 8.69(5.75) / 8.63(5.82)

**Baseline stats:**
[Adherence therapy / TAU]
PANSS: 56.81(10.86) / 61.25(15.58)
GAF: 56.63(15.61) / 59.00(18.44)

**Notes about participants:**
[Adherence therapy / TAU]
Drug use
Abstinent: 14 / 15
Use without impairment: 2 / 1
Alcohol use
Abstinent: 10 / 12
Use without impairment: 3 / 1
Abuse: 1 / 2
Dependence: 2 / 1
Antipsychotic dose (mg/d chlorpromazine equivalent.): 337(43.55) / 344(39.71)

**Interventions**

**Intervention - group 1.:** Adherence Therapy, 8 weekly sessions; n=16

**Intervention - group 2.:** TAU; n=16

**Notes about the interventions:**
TAU
standard care including medication treatment, occupational therapy, group counselling and recreational therapy.

Adherence therapy
In addition to TAU, participants received 8 one-to-one sessions between 15-60 minutes long. Intervention is a brief cognitive behavioral approach evolved from compliance therapy. The key therapeutic techniques used are exchanging information, developing discrepancy and effectively dealing with resistance. The phases of adherence therapy are engagement, assessment, rating of readiness to take medication, intervention and evaluation working through in a flexible patient-centered way.

**Outcomes**

**Death:** Natural causes

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - PANSS - change in symptoms of >=25% as a definition of clinically meaningful improvement/deterioration.

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - GAF

**Adverse events:** Average score/change in specific adverse effects - Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS)

**Satisfaction with treatment:** Service user satisfaction DAI, SWAM

**Other:** drug and alcohol abstinence/use/dependency

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| **Study ID** | **ODONNELL2003** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Funding source:** Pharmaceutical industry |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment: 5 sessions – does not state time period |
| | **Duration:** Length of follow-up: Study period was 1 year in which participants received 5 sessions of therapy. |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Dublin, Ireland |
| | **Number of people screened, excluded & reasons:** 94 people approached, 6 were excluded due to IQ < 80 (5) and not fluent in English (1). Of the 88 people eligible for the study 32 declined. |
| | **Notes about study methods:** Randomisation done using odd and even digits from a standard table of random numbers. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |

**Inclusion criteria:**
- Meeting DSM-IV criteria for schizophrenia
- Aged 18-65
- Fluent English speakers
- No evidence of organic disturbance

**Total sample size:** No. randomised 56

**Total sample size:** ITT population 50

**Gender:** % female 27%

**Age:** Mean 32

**Ethnicity:** Details not reported

**Setting:** Inpatient

**History:**
[Adherence therapy / Non-specific counselling]
Mean no. of years of illness: 6(7) / 4(5)
Mean no. of bed days in psychiatric hospital in previous 2 years: 77(64) / 83(52)
First episode of schizophrenia, n: 5 / 7
Detained under Mental Treatment Act, n: 4 / 5

**Baseline stats:**
[Adherence therapy / Non-specific counselling]
PANSS: 71(22) / 66(17)
GAF: 36(14) / 31(12)

**Notes about participants:**
[Adherence therapy / Non-specific counselling]
Mean neuroleptic dose (in chlorpromazine equivalents): 835(507) / 883(715)

**Interventions** **Intervention - group 1.:** Adherence therapy, 5 sessions; N = 28

**Intervention - group 2.:** Non-specific counselling, 5 sessions; N = 28

**Notes about the interventions:**
Adherence therapy
Cognitive behaviour intervention with techniques adapted from motivational interviewing and other cognitive therapies as well as psychoeducation. The intervention used a manual and covered a review of the patient's illness history and understanding of illness and his or her ambivalence to treatment, maintenance medication, and stigma.

| | |
|---|---|
| | Non-specific counselling<br>Patients used sessions to raise matters relating to medication and discussed them with their treating teams. |
| **Outcomes** | **Death:** Natural causes |
| | **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) |
| | **Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAF |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS |
| | **Non-adherence to study medication:** Non-adherence; DAI, SAI |
| | **Quality of Life:** Average score/change in quality of life - QoL |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Not reported adequately |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **TSANG2005** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 6 months |

**Duration:** No. weeks of treatment: Unclear from paper

**Raters:** Independent of treatment

**Design:** Single-centre - Hong Kong

**Number of people screened, excluded & reasons:** 135 subjects fulfilled the inclusion criteria, 17 subjects refused consent and 40 subjects requested that they be switched to the alternate group contrary to randomisation.

**Notes about study methods:** Randomisation procedure not reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** ICD-10

**Inclusion criteria:** - Male inpatients

**Total sample size:** No. randomised - 78

**Total sample size:** ITT population 60 - completer sample

**Gender:** % female 0%

**Age:** Mean 37

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[Adherence therapy / control]
No. of admissions, n(%):
< or = 5 times: 22(77) / 10(53)
> 5 times: 6(23) / 9(47)
History of mental illness, N(%):
<3 years: 7(25) / 3(16)
3-10 years 8(29) / 8(42)
>10 years 8(42) / 13(46)

**Baseline stats:**
[Adherence therapy / Control]
BPRS: 43.9(8.72) / 44.84(7.27)

**Notes about participants:** 88% of participants were currently taking neuroleptics

**Interventions**

**Intervention - group 1.:** Adherence therapy, 5 sessions; N = 38

**Intervention - group 2.:** TAU; N = 40

**Notes about the interventions:**

Adherence therapy
Consisted of semi-structured cognitive-behavioural activities. The therapist adopted motivational interviewing techniques throughout the programme. Each session was marked by distinctive highlights and the exploration of personal feelings, experiences, and beliefs over the treatment regime were cardinal. The programme consisted of 5 sessions to allow for adequate exploration whilst offsetting the possibility of mild cognitive impairment.

Control
All participants received treatment as usual.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS

**Non-adherence to study medication:** Non-adherence DAI; self reported drug compliance scale, compliance with follow up appointments

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**References of included studies (update)**

**GRAY2006**

Gray,R.; Leese,M.; Bindman,J.; Becker,T.; Burti,L.; David,A.; Gournay,K.; Kikkert,M.; Koeter,M.; Puschner,B.; Schene,A.; Thornicroft,G.; Tansella,M. (2006) Adherence therapy for people with schizophrenia: European multicentre randomised controlled trial. *British Journal of Psychiatry*. 189: 508-14

**MANEESAKORN2007**

Maneesakorn,S.; Robson,D.; Gournay,K.; Gray,R. (2007) An RCT of adherence therapy for people with schizophrenia in Chiang Mai, Thailand. *Journal of Clinical Nursing*. 16(7): 1302 - 1312.

**ODONNELL2003**

O'Donnell,C.; Donohoe,G.; Sharkey,L.; Owens,N.; Migone,M.; Harries,R.; Kinsella,A.; Larkin,C.; O'Callaghan,E. (2003) Compliance therapy: a randomised controlled trial in schizophrenia. *British Medical Journal;* 327(7419): 834.

**TSANG2005**

Tsang,H.W.; Wong,T.K.S. (2005) The effects of a compliance therapy programme on Chinese male patients with schizophrenia. *Asian Journal of Nursing Studies* 8(2): 47 - 61.

## Characteristics of excluded studies (update)

### FRANGOU2005

**Reason for exclusion:** Does not meet definition for adherence therapy

### GRAY2004

**Reason for exclusion:** Only nurses were randomised into the intervention and not the patients. Nurses were able to select cases for the intervention. The intervention was aimed at improving adherence but was targeted at the nursing staff and not an intervention targeted at the patients.

### ODONNELL2002

**Reason for exclusion:** Conference abstract

## References of excluded studies (update)

Frangou,S.; Sachpazidis,I.; Stassinakis,A.; Sakas,G. (2005) Telemonitoring of medication adherence in patients with schizophrenia. *Telemedicine Journal and E-Health* 11(6): 675 - 683.

Gray,R.; Wykes,T.; Edmonds,M.; Leese,M.; Gournay,K. (2004) Effect of a medication management training package for nurses on clinical outcomes for patients with schizophrenia: cluster randomised controlled trial. *British Journal of Psychiatry* 185: 157 - 162.

O'Donnell,C.; Sharkey,L.; O'Donohue,G.; Owens,N.; Migone,M.; Harris,R.; Kinsella,T.; Tobin,A.; O'Callaghan,E. (2002) Influence of compliance therapy and carer education on the outcome of schizophrenia. *Schizophrenia Research* 53 (3 Suppl.1): 253.

## Arts therapies

**Characteristics of included studies (update)**

| **Study ID** | **GREEN1987** |
|---|---|
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind -The patients' therapist completed the rating scales. they were not informed of the patients group allocation (unless the patient specifically informed them) |
| | **Duration:** No. weeks of treatment - 20 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Central Psychiatric clinic, Cincinnati, US |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 50% |
| | **Diagnosis:** Other [%] 21% - major affective disorder or psychotic diagnosis<br>18% - neurotic diagnosis |
| | **Diagnostic tool:** Other method - Not reported |
| | **Inclusion criteria:** Attended the medical support service a minimum of once every 4 weeks. |
| | **Total sample size:** No. randomised 47 |
| | **Gender:** % female 64% |
| | **Age:** Mean 40 |
| | **Ethnicity:** Not reported |
| | **Setting:** Outpatient |
| | **History:** Not reported |
| | **Baseline stats:** Not reported |

**Notes about participants:** On average the 28 completers had had 3 psychiatric hospitalisations and had been receiving aftercare services in the outpatient setting for several years

**Interventions**

**Intervention - group 1.:** Art therapy, 10 fortnightly 1.5 sessions, n=24

**Intervention - group 2.:** TAU; n=23

**Notes about the interventions:**
Art therapy
Art therapy was conducted in two groups of 12. During the sessions participants were given art material to use in one of a variety of session projects with carefully predetermined gaols. Conversation and interaction were encouraged. Self-expression, rather than drawing out and identifying conflict, was encouraged in a supportive atmosphere with the goal of mastery and resolution. Other objectives were to promote overall group cohesion, increase tolerance of disclosing emotionally significant material and encourage group interaction, support and positive feedback.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) >50% left study so leaving study early only outcome to be extracted

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** >50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**NITSUN1974**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Blindness:** Open

**Duration:** No. weeks of treatment 22

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre - Not reported

**Design:** Multi-centre - Not reported

**Number of people screened, excluded & reasons:** Not reported

**Notes about study methods:** Patients were matched in two groups according to age, intelligence and length of hospitalisation. The groups were then randomly assigned. No further details reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** Other method - Not reported

**Inclusion criteria:**
- Aged 25-46
- Hospitalised for >=2years
- Diagnosis of schizophrenia with no organic disorder and manifesting some of the symptoms of flatness of affect, thought disorder, emotional incongruity, social withdrawal, body image disturbance, poverty and incoherence of speech and impaired psychomotor functioning
- intelligence not subnormal.

**Total sample size:** No. randomised 24

**Gender:** % female 41%

**Age:** Mean 38

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[Experimental / control]
Length of hospitalisation, years: 12.08 / 13.66

**Baseline stats:**
[Movement and drama group / group psychotherapy]
Global rating of illness: 4.0 / 3.40

| | |
|---|---|
| **Exclusion status** | **Reason for exclusion:** No usable data |

| | |
|---|---|
| **Study ID** | **RICHARDSON2007** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind. The rater had no involvement in therapy groups and was not aware of the arm to which the participant had been allocated. However the authors not that since assessments involved interviewing participants it is highly unlikely that the rater would be completely blind to group allocation. |
| | **Duration:** No. weeks of treatment 12 |
| | **Duration:** Length of follow-up 6 months |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Participants were in contact with a number of CMHTs in an inner city mental health NHS trust. |
| | **Number of people screened, excluded & reasons:** 452 patients were identified by the CMHTs as potential recruits. 90 participants were randomised to treatment (of the original 453, 206 patients refused to consent, 101 DNA'd twice, 49 were excluded, 1 lost to follow-up, 2 died) |
| | **Notes about study methods:** Randomisation was conducted using the minimisation procedure to limit variation between the treatment arms on: CPA level, chronicity, gender and ethnicity. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] |
| | **Diagnostic tool:** Other method not stated |
| | **Inclusion criteria:**<br>- diagnosis of chronic schizophrenia<br>- duration of illness > 2 years. |
| | **Exclusion criteria:**<br>- organic illnesses<br>- prior referral to arts therapy in the previous 2 years<br>- currently receiving another formal psychological treatment<br>- currently admitted to inpatient care |
| | **Total sample size:** ITT population - 74 participants were interviewed within 2 weeks of the completion of therapy with 40 being followed up |

at 6 months

**Total sample size:** No. randomised 90

**Gender:** % female 35%

**Age:** Mean 41

**Ethnicity:** Details not reported, only that there was no difference between the two groups in terms of ethnicity

**Setting:** Outpatient

**History:**
[experimental / control]
chronicity, years: 13.4 / 12.6]

**Baseline stats:**
[TAU / Arts therapy]
BPRS: 16.0(9.6) / 15.1(7.8)

**Interventions**

**Intervention - group 1.:** Arts therapy, 12 weekly 1.5 hour sessions; n=43

**Intervention - group 2.:** TAU; n=47

**Notes about the interventions:**
TAU
Standard psychiatric care was the regular contact with the CMHT CPN, regular medication review and CPA review meetings. Patients had access to a variety of psychiatric day treatment facilities which varied according to the local sector facilities and arrangements.

Arts therapy
In addition to SPC participants received 12 weekly group sessions of art therapy as conducted according to the guidelines. Through the availability and use of art material and associated imagery the therapist promotes a climate in which the participant can learn about and understand those patterns of behaviour which are causing distress. Here the specific presence of the image as a crucial part of art therapy can triangulate and temper problematic feeling of the patient toward the therapist.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS; SANS; BSI

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SFS; IIP

**Quality of Life:** Average score/change in quality of life HONOS; Per QoL

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis):** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **ROHRICHT2006** |
| **General info** | **Funding source:** Non-industry support |
| | **Funding source:** Pharmaceutical industry |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Participants were included in the analysis if they provided a post-therapy assessment regardless of their participation in the interventions. |
| | **Blindness:** Only raters blind. All screening, baseline and outcomes assessments were made by an experienced psychiatrist blind to treatment allocation. Patients were requested not to reveal any details of the treatment during post-therapy and follow-up assessments in an attempt to maintain rater blinding. |
| | **Duration:** No. weeks of treatment - 10 |
| | **Duration:** Length of follow-up - 4 months |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre East London, UK |
| | **Number of people screened, excluded & reasons:** 67 participants were referred for possible inclusion, 22 were excluded due to: not meeting the inclusion criteria (n=22) and withdrawal from the assessment (10). In total 45 were randomised |
| | **Notes about study methods:** Eligible patients were randomly allocated to one of the treatment conditions following the opening of a sealed envelope by the project co-ordinator, who had no involvement in data collection or assessments. |

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:** -age 20–55 years
- an established diagnosis of schizophrenia according to DSM-IV, with >=2 acute psychotic symptoms;
-currently an outpatient with time since last inpatient treatment >than 1 month;
-suffering from persistent symptoms of schizophrenia for >=6 months with a high degree of negative symptoms at baseline, i.e. PANSS negative score >=20 and/or one of the Anergia items ('emotional withdrawal', 'motor retardation' or 'blunted affect') >=6
-stable medication prior to entering the study.

**Exclusion criteria:** -evidence of organic brain disease
-severe or chronic physical illness
-substance misuse as primary diagnosis.

**Total sample size:** No. randomised 45

**Total sample size:** ITT population 42

**Gender:** % female 50%

**Age:** Mean 38

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** [Body-orientated psychological therapy (BPT) / Supportive counselling (SC)]
Duration of illness, years: 12.1(10.5) / 10.8(7.3)
No. of previous hospitalisations: 3.7(2.8) / 4.4(3.8)

**Baseline stats:** [BPT / SC]
PANSS total: 79.0(13.9) / 76.3(21.1)

**Notes about participants:** [BPT / SC]
Chlorpromazine equivalent: 497.9(289.1) / 440.5(324.8)

**Interventions**

**Intervention - group 1.:** BPT, 20 sessions of 60-90 minutes over 120 weeks; n=24

**Intervention - group 2.:** SC, 20 sessions of 60-90 minutes over 120 weeks; n=21

**Notes about the interventions:**
BPT
The treatment manual used in the intervention was defined by the first author and aimed to integrate different techniques into a clinically focused and syndrome specific method. The protocol manual was designed to achieve the following aims:
1) overcome communication barriers through introduction of non-verbal techniques
2) refocus cognitive and emotional awareness towards the body

3) stimulate activity and emotional responsiveness
4) promote exploration of self-potentials focusing on body strength and capability, experiencing the body as a source of creativity, reliability, pleasure and self-expression
5) modify dysfunctional self-perceptions
6) to address common psychopathological features.

SC
The therapist focused on individual differences and corresponding problem-solving strategies regarding the core negative symptoms.

Training
A part-time dance movement therapist conducted BPT. Two nurse therapists, also with previous training and experience in providing psychological therapies for schizophrenia
patients, delivered SC. All therapists had many years' experience of working with patients with schizophrenia and attended specific training sessions before the trial. Each received three supervision sessions to ensure adherence to the given treatment manual (on the basis of written records of each session).

TAU
Both BPT and SC were in additional to TAU provided by community psychiatrists. Treatment plans were not substantially altered during the trial period. In both treatment conditions, group size was limited to a maximum of 8

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state PANSS - primary outcome focused on the negative PANSS subscale

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state no. with symptom reduction >=20%

**Adverse events:** Average score/change in specific adverse effects - SAS

**Satisfaction with treatment:** Service user satisfaction - Client's Assessment of Treatment Scale; Helping Alliance Scale

**Quality of Life:** Average score/change in quality of life - Manchester Short Assessment of Quality of Life (MANSA)

**Other:** Medication change, number of treatment sessions attended

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed - special attention was paid to ensuring the blindness of the rater.

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **TALWAR2006** |
| **General info** | **Funding source:** None declared |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Multiple imputation was used to account for the missing data in outcome measures at follow-up |
| | **Blindness:** Only raters blind. Therapists and patients were instructed not to talk to the researcher about which arm of the trial they were in. |
| | **Duration:** No. weeks of treatment - 12 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - four hospitals in central and inner London, UK |
| | **Number of people screened, excluded & reasons:** 123 participants were assessed for suitability, of these 10 were excluded for the following reasons: unable to leave ward (6), unable to communicate in English (2) and already receiving music therapy (2). Of the 113 that met inclusion criteria 31 declined to participate in the study and 1 participant was considered unsuitable for therapy leaving a total of 81 randomised participants. |
| | **Notes about study methods:** Participants were allocated to groups by block randomisation stratified for hospital sites, using randomisation lists from a computer program. Randomisation was conducted by a person independent of the researcher. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 79% |
| | **Diagnosis:** Other [%] 21% |
| | **Diagnostic tool:** ICD-10 diagnosis of schizophrenia or schizophrenia-like psychoses |
| | **Inclusion criteria:** - inpatients with a primary diagnosis of schizophrenia or schizophrenia-like psychoses<br>- aged 18+ |

**Exclusion criteria:** -secondary diagnosis of organic psychoses or dementia
-spoke insufficient English to complete the baseline interview without the help of an interpreter

**Total sample size:** No. randomised 81

**Total sample size:** ITT population 66

**Gender:** % female 27%

**Age:** Mean 37

**Ethnicity:** White British: 29%

**Setting:** Inpatient

**Baseline stats:**
[Music therapy / control]
PANSS total: 73.1(13.4) / 70.8(12.8)
GAF: 54.2(11.4) / 55.7(9.8)

**Notes about participants:**
[Music therapy / control]
Medication (CPZ equiv): 417.8(340.8) / 478.5(396.5)
Mental health act 1983 status compulsory*, n(%): 18(54.5) / 29(58.3)

*Patients being treated on a compulsory basis or lacking capacity were also included providing assent and those involved in their care were happy for them to participate.

**Interventions**

**Intervention - group 1.:** Music therapy, 12 weekly sessions; n=33

**Intervention - group 2.:** TAU; n=48

**Notes about the interventions:**
TAU
All participants received routine standard care including nursing care and access to a range of occupational, social and other activities as part of the inpatient programme. Those randomised to TAU were placed on a waiting list and offered music therapy as the end of the trial

Music therapy
In addition to TAU, participants received up to 12 individual sessions of music therapy. During sessions participants were given access to a range of musical instruments and encouraged to use these to express themselves. The focus on therapy was co-creating improvised music, with talking used to guide, interpret or enhance the music experience.

All participants involved in the trial were excluded from music and other arts therapies (art, dance and movement and drama therapy) during the trial.

| | |
|---|---|
| | Therapist training<br>Five music therapist took part in the trial. All had trained on courses approved by the HPC and received fortnightly supervision from a senior music therapist throughout the study period. A random sample of the session recordings was examined at the end of the trial in order to assess treatment fidelity. |
| **Outcomes** | **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) |
| | **Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAF |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS |
| | **Satisfaction with treatment:** Service user satisfaction - Client satisfaction questionnaire |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Well covered |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **ULRICH2007** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Unclear from description |
| | **Blindness:** Only raters blind - Raters were blind to the aim of the study but it is unclear whether they were blind to the allocation of participants. |

**Duration:** No. weeks of treatment - 5 (conducted over a period of 8 months for the whole study)

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre - Rhenish Clinic, Germany

**Number of people screened, excluded & reasons:** After participants were assigned, they were asked whether they were willing to take part in the study. 10 patients refused to take part, leaving 37 participants.

**Notes about study methods:** Participants were randomly assigned to either the control or experimental group by throwing a die.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 73%

**Diagnosis:** Other schizophrenia related [%] Schizoaffective psychosis - 11%
Schizotypal disorder - 3%

**Diagnosis:** Other [%] Drug-induced psychosis - 8%
Depression with psychotic symptoms - 5%

**Diagnostic tool:** ICD-10 code F20-29

**Inclusion criteria:** ICD-10 code F20-F29 diagnosis

**Exclusion criteria:**
- acute psychotic symptoms
- not being able to mingle in a group.

**Total sample size:** No. randomised 47

**Total sample size:** ITT population 37 agreed to participate in their randomised interventions.

**Gender:** % female 45%

**Age:** Mean 38

**Ethnicity:** not reported

**Setting:** Inpatient

**History:**
[Experimental / control]
Time between admission and pretest (weeks): 2.75(2.22) / 3.13(6.68)

**Baseline stats:**
[Experimental / control]
SANS total: 1.09(0.66) / 0.7(0.59)

**Notes about participants:**
[Experimental / control]
Chlorpromazine equivalent: 539.75 / 338.14(258.69)

**Interventions**

**Intervention - group 1.:** Music therapy, average 7.5 sessions; n=26

**Intervention - group 2.:** TAU; n=21

**Notes about the interventions:**
The music therapy group was provided in addition to TAU.

TAU
Most participants were involved in another activity during the time the experimental group underwent music therapy.

Music therapy
Each session lasted 45 minutes, during which the main activity was playing together on rhythm instruments, where the sound stops as soon as the player stops playing. This was used to imply that the player is responsible for their actions. Besides playing music, there were group discussions used for reflection. In the sessions, orthopedagogical techniques and a supportive way of working were used. An important issue during the sessions was stimulating social interaction and learning to deal with problems in a social setting.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - SANS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - GieBentest - (GTS and GTFm)

**Quality of Life:** Average score/change in quality of life - SPG

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Poorly addressed - Randomisation - throwing a die

**1.3 An adequate concealment method is used.:** Poorly addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| Study ID | YANG1998 |
|---|---|
| General info | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| Method | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 12 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Multi-centre study was conducted in China, paper does not report number of centres |
| | **Design:** Single-centre study was conducted in China, paper does not report number of centres |
| | **Number of people screened, excluded & reasons:** No details reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| Participants | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** Other method - CCMD-2 |
| | **Inclusion criteria:**<br>- Chronic in-patients who met CCMD-2 criteria for schizophrenia<br>- demonstrated social disability with the following characteristics: duration of illness >2 years, prescribed antipsychotic drugs in sufficient dose during past 6 months but symptoms had not fully remitted<br>- free from any physical disease |
| | **Total sample size:** No. randomised 72 of which 70 completed and are used in the analysis |
| | **Gender:** % female 42% |
| | **Age:** Mean 38.5 |
| | **Ethnicity:** Not reported |
| | **Setting:** Inpatient |
| | **History:**<br>[Experimental group / Control]<br>Duration of illness, years: 12.78(6.40) / 13.06(7.50) |
| | **Baseline stats:**<br>[Experimental group / control]<br>SANS: 68.15(17.68) / 57.50(17.78) |

BPRS: 40.98(8.45) / 40.10(8.69)

**Interventions**

**Intervention - group 1.:** Music Therapy , 6 2-hour sessions per week for 12 weeks; n=41

**Intervention - group 2.:** Control (TAU); n=31

**Notes about the interventions:**
Music therapy
Involved a combination of small group (containing 10-15 participants) and individual therapy. Discussion sessions were conducted after listening to music or after musical improvisation performance. The main emphasis was on participation, social communication and emotional expressions. Music therapy was given in addition to neuroleptic medication.

Control
Neuroleptic medication alone.

Training
Two therapists who were musicians were responsible for teaching the patients singing and musical knowledge.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Clinically significant response in global state no. categorised as in remission (90% reduction in symptoms), marked improvement (60% reduction), somewhat improved (30% reduction) and no response (<30% reduction)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - SANS; BPRS; PSE

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning- SDSI (Social Disability Schedule for In-patient)

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**References of included studies (update)**

**GREEN1987**

Green,B.L; Wehling,C; Talsky GJ. (1987) Group art therapy as an adjunct to treatment for chronic outpatients. *Hospital and Community Psychiatry.* 38(9): 988 - 991.

**NITSUN1974**

Nitsun,M.; Stapleton,J.H.; Bender,M.P. (1974) Movement and drama therapy with long-stay schizophrenics. *British Journal of Medical Psychology*. 47(2): 11 - 119.

**RICHARDSON2007**

Richardson,P.; Jones,K.; Evans,C.; Stevens,P.; Rowe,A. (2007) Exploratory RCT of art therapy as an adjunctive treatment in schizophrenia. *Journal of Mental Health*. 16(4): 483-491.

**ROHRICHT2006**

Rohricht, F., Priebe, S. (2006) Effect of body-oriented psychological therapy on negative symptoms in schizophrenia: a randomised controlled trial. *Psychological Medicine* 36: 669-678.

**TALWAR2006**

Talwar,N.; Crawford,M.J.; Maratos,A.; Nur,U.; McDermott,O.; Procter,S. (2006) Music therapy for in-patients with schizophrenia: exploratory randomised controlled trial. *British Journal of Psychiatry*. 189: 405 - 409.

**ULRICH2007**

Ulrich,G.; Houtmans,T.; Gold,C. (2007) The additional therapeutic effect of group music therapy for schizophrenic patients: A randomized study. *Acta Psychiatrica Scandinavica*. 116(5): 362-370.

**YANG1998**

Yang,W.Y.; Zheng,L.; Yong-Zhen,W.; Zhang,H.Y.; Bio,M. (1998) Psychosocial rehabilitation effects of music therapy in chronic schizophrenia. Hong Kong Journal of Psychiatry. 8(1): 38-40.

**Characteristics of excluded studies (update)**

**APTER1978**

**Reason for exclusion:** Participants <18 years

**CASSITY1976**

**Reason for exclusion:** - N <10
- Does not meet definition: participants were involved in a group guitar lesson

**COELHO2007**

**Reason for exclusion:** Not an RCT

**DURAISWAMY2007**

**Reason for exclusion:** - Intervention does not meet definition for art therapy

**GLICKSOHN2000**

**Reason for exclusion:** - N<10 in each arm
- Does not fit definition: compared two types of music only.

**GRAINGER1992**

**Reason for exclusion:** Not an RCT

**HAYASHI2002**

**Reason for exclusion:** Not randomised - allocation based on ward (within each ward participants were selected for participation) intervention does not fit criteria - no focus on self-expression only improving enjoyment of music.

**KRAJEWSKI1993**

**Reason for exclusion:** Conference abstract

**MENG2005**

**Reason for exclusion:** Paper not in English

**ODELLMILLER2006**

**Reason for exclusion:** - Less than 50% diagnosed with schizophrenia
- 4 different types of arts therapy used (participants could be allocated to 4 different types depending on therapist opinion)

**QU2000**

**Reason for exclusion:** Paper not in English

**RABINER1967**

**Reason for exclusion:** - Not an RCT
- no control comparison

**SCHMID2007**

**Reason for exclusion:** Not an RCT

**SPENCER1983**

**Reason for exclusion:** Not randomised

**TANG1994**

**Reason for exclusion:** - Does not meet definition for art therapy

**TSELIKAS1997**

**Reason for exclusion:** Not an RCT

**WHETSTONE1986**

**Reason for exclusion:** does not meet intervention definition

**ZHOU2002**

**Reason for exclusion:** Paper not in English

**References of excluded studies (update)**

Apter, A., Sharir, I., Tyano, S. & Wijsenbeek, H. (1978) Movement therapy with psychotic adolescents. *British Journal of Medical Psychology*. 51: 155-159.

Cassity, M.D. (1976) The influence of a music therapy activity upon peer acceptance, group cohesiveness, and interpersonal relationships of adult psychiatric patients. *Journal of Music Therapy* 13(2): 66 - 76.

Coelho,H.F.; Crawford,M. (2007) A randomised clinical trial of music therapy should be feasible for acute inpatients with schizophrenia or schizophrenia-like illness: Commentary. *Focus on Alternative and Complementary Therapies*. 12(2).

Duraiswamy,G.; Thirthalli,J.; Nagendra,H.R.; Gangadhar,B.N. (2007) Yoga therapy as an add-on treatment in the management of patients with schizophrenia--a randomized controlled trial. *Acta Psychiatrica Scandinavica*. 116(3): 226 - 232.

Glicksohn,J.; Cohen,Y. (2000) Can music alleviate cognitive dysfunction in schizophrenia? *Psychopathology*. 33(1): 43 - 47.

Grainger, R. 1992 Dramatherapy and thought disorder. In: S. Jennings (ed) (2007) *Dramatherapy: Therapy and Practice*. London: Routledge,

Hayashi,N.; Tanabe,Y.; Nakagawa,S.; Noguchi,M.; Iwata,C.; Koubuchi,Y.; Watanabe,M.; Okui,M.; Takagi,K.; Sugita,K.; Horiuchi,K.; Sasaki,A.; Koike,I. (2002) Effects of group musical therapy on inpatients with chronic psychoses: a controlled study. *Psychiatry and Clinical Neurosciences*. 56(2): 187 - 193.

Krajewski,C.; Classen,W.; Boesken,S. (1993) Comparison of art and cognitive therapy (IPT) with simultaneous cognitive and art therapy for schizophrenic patients regarding the change of cognitive processes. *Pharmacopsychiatry* 26: 171.

Meng, P, Zheng, R., Cai, Z. *et al.* (2005) Group intervention for schizophrenia inpatients with art as a medium. *Acta Psychologica Sinica,* 37, 403-412.

Odell-Miller,H.; Hughes,P.; Westacott,M. (2006) An investigation into the effectiveness of the arts therapies for adults with continuing mental health problems. *Psychotherapy Research.* 16(1) ; 122-139.

Qu, Y., Li, Y., Xian, G. (2000) The efficacy of dramatherapy in chronic schizophrenia. *Chinese Journal of Psychiatry* 33: 237-239.

Rabiner, C.H.A.R. & Drucker, M.A.R.V. (1967) Use of psychodrama with hospitalised schizophrenia patients. *Diseases of the Nervous System*. 28(1): 34-38.

Schmid,G.B.; Wanderer,S. (2007) Phantasy therapy: Statistical evaluation of a new approach to group psychotherapy for stationary and ambulatory psychotic patients. *Forschende Komplementarmedizin*.14(4): 216-223.

Spencer,P.G.; Gillespie,C.R.; Ekisa,E.G. (1983) A controlled comparison of the effects of social skills training and remedial drama on the conversational skills of chronic schizophrenic inpatients. *British Journal of Psychiatry*. 143: 165 - 172.

Tang-W, Yao-X, Zheng-Z. (1994) Rehabilitative effect of music therapy for residual schizophrenia. A one-month randomised controlled trial in Shanghai. *The British Journal of Psychiatry*. Supplement (24): 38-44.

Tselikas, E. & Burmeister, J. (1997) The drum, the mouse and the boy in the glass palace. In: S. Jennings (Ed) (2007) *Dramatherapy: Therapy and Practice*. London: Routledge.

Whetstone, W.R. (1986) Social dramatics: social skills development for the chronically mentally ill. *Journal of Advanced Nursing* 11: 67-74.

Zhou, Y., Tang, W. (2002) A controlled study of psychodrama to improve self-esteem in patients with schizophrenia. *Chinese Mental Health Journal* 16: 669-671.

## Cognitive behavioural therapy

| Previous guideline review | 1. Review type<br>2. Funding<br>3. Period covered<br>4. Data analysis<br>5. No. of studies<br>6. No. participants randomised | Interventions | Reported outcomes |
|---|---|---|---|
| Pilling S, Bebbington P, Kuipers E, Garety P, Geddes J, Orbach G, Morgan C. (2002)<br><br>Psychological treatments in schizophrenia I: meta-analysis of family intervention and cognitive behaviour therapy.<br><br>*Psychological Medicine*, 32, 783-791. | 1. Systematic review of RCTs.<br>2. Intramural sources of support to the review: University College London. Extramural sources of support to the review: Department of Health, UK.<br>3. Database origin to 1999.<br>4. Meta-analysis of Odds Ratio and standardised mean difference.<br>5. 8 (13 after removing one trial and adding six new studies).<br>6. 393 (1297 after including new trials). | 1. CBT: to meet the criteria for CBT, interventions had to have a component which involved recipients establishing links between their thoughts, feelings or actions with respect to the target symptoms; and the correction of their misperceptions, irrational beliefs or reasoning biases related to those symptoms. At least one of the following was also required: self-monitoring of the treated person's thoughts, feelings or behaviours with respect to the target symptoms; and the promotion of alternative ways of coping with the target symptoms.<br>2. Standard care.<br>3. Other active treatments. | 1. Death by suicide.<br>2. Leaving the study early.<br>3. Relapse/ readmission.<br>4. Mental state: I. No important improvement<br>5. Mental state: II. Continuous measures.<br>6. Global assessment of function.<br>7. Quality of life.<br>8. Social functioning<br>9. Psychological well-being.<br>10. Occupational status. |
| **Update** | **Existing studies reclassified:** 1 RCT (Kemp1996) was reclassified as adherence therapy.<br>**Existing studies excluded:** 3 RCTs (Garety1994; Levine1996; Turkington2000).<br>**Follow-up to existing studies:** 6 papers: Sensky 2000 (2 papers); Turkington 2002 (2 papers); Lewis 2002 (2 papers).<br>**New studies:** 22 RCTs. | | **Notes:**<br>Definition updated |

**Characteristics of included studies (previous guideline)**

| Study | Methods | Participants | Interventions | Outcomes | Notes |
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| **Bradshaw1996** | Allocation: random (no further details).<br>Duration: 24 weeks.<br>Frequency: weekly 90 minute sessions. | Outpatients.<br>Diagnosis: schizophrenia (DSM III-R).<br>N=16.<br>Age: CBT mean 31(SD 12), control mean 29 (SD 10). Sex: 6 M 8 F. History: mean duration of illness - CBT 11 years (SD 8), control 10 years (SD 7). | 1. CBT: coping skills treatment model, including physiological arousal management, time management, cognitive restructuring, social skills training. N=8.<br>2. Problem solving group: orienting to the problem, generating and evaluating alternative solutions using brainstorming techniques, choosing and implementing a solution and assessing the result. N=8. | 1. Leaving the study early.<br>2. Relapse.<br>3. Global assessment of function: attainment of treatment goals (Goal Attainment Scaling). | Therapists: each group was led by 2 therapists with masters degrees and an average of 10 years of experience in the mental health field.<br>Training: each pair of therapists received 20 hours of training in their respective treatment methods.<br>Supervision: each therapy pair met separately weekly in group supervision to review procedures used in the group. Ongoing observation of the groups was done to ensure implementation of the treatment methods.<br>CBT type: coping skills. |

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| **Bradshaw2000** | Allocation: consecutively referred service users "randomly assigned." Blinding: all assessments carried out by two independent raters, "blind to the subjects' treatment condition." Duration: 3 years. Frequency: weekly 90 minute sessions. | Outpatients in day treatment programme. Diagnosis: schizophrenia (DSM-IV). N=24. Age: not given, but in range 18-60. Sex of study completers: 6 M 9 F. History of completers: mean duration of illness 11 years (SD 6). | 1. CBT + Day Treatment Programme (DTP): CBT - same model of CBT used in Bradshaw1996. Treatment divided into three phases (length varied among clients, and some overlap occurred). Phase I = Engagement and Education (~months 1-5). Aimed to develop therapeutic alliance regarding roles, goals and rationale of treatment, and to educate clients about schizophrenia and the process of CBT. Phase II = Behavioral Treatment (~months 6-20). Involved identifying stresses and teaching behavioral skills (for example, meditation, exercise) to deal with them. Phase III = Cognitive Treatment (~months 20-36). Utilised cognitive strategies to understand and cope with habitual stressful situations. Three techniques used: thought stopping, cognitive restructuring and positive self-appraisal training.<br>DTP - based on psychiatric rehabilitation model. Clients participated 3 days/week for 6 hours/day. Programme consisted of social skills training, independent living skills groups, goal groups, occupational and recreational therapy, prevocational employment training and medication management.<br>2. DTP only. | 1. Leaving the study early.<br>2. Mental state: Global Pathology Index (GPI).<br>3. Mental state: improved (score of 3 or less on GPI).<br>4. Social functioning: Role Functioning Scale (RFS).<br>5. Social functioning: living independently.<br>6. Social functioning: returned to education.<br>7. Occupational status: employed part-time.<br><br>Unable to use:<br>1. Readmission (no usable data). | Therapists: CBT - administered by two experienced social workers trained in the CBT model. DTP - three masters level social workers, three psychiatric nurses, an occupational therapist and consulting psychiatrist. "Clients also seen monthly for medication monitoring by their psychiatrists and monthly by their county case managers to monitor treatment needs and progress." Supervision: CBT therapists received weekly supervision by the programme director. Fidelity to CBT model also monitored by review of case materials and periodic review of audiotapes of sessions.<br>CBT type: coping skills. |

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| **Drury1996** | Allocation: random allocation using stratified sampling technique. Blinding: all service users rated by one author, and a random subset of service users blindly rated by two others.<br>Duration: up to 6 months, 9 month and 5 year follow-ups.<br>Frequency: 8 hours per week (3 hours CT, 5 hours other structured activities). | Inpatients.<br>Diagnosis: schizophrenia, schizoaffective, or delusional disorder (DSM-IV). N=62.<br>Age: mean 30 (SD 9), range 20-55.<br>Sex: 25 M 15 F 22 unknown.<br>History: mean duration of illness 6 years, mean number of episodes 3. | 1. CBT: individual - challenging and testing key beliefs. Group cognitive therapy - coping strategy enhancement and standard care. N = 30.<br>2. Recreation and support: leisure and social activities away from ward and standard care. N=32. | 1. Leaving the study early.<br>2. Mental state: improved, based on personal recovery from positive symptoms (lowest Psychiatric Assessment Scale score achieved over the follow-up and maintained for at least three consecutive points), recovery of insight (score >9 on Insight Scale), and recovery of prepsychotic symptoms (score <30 on Early Signs Scale).<br>3. Specific symptom clusters: Psychiatric Assessment Scale.<br>4. Delusional beliefs: Beliefs and Convictions Scale.<br>5. Insight: Insight Scale.<br><br>Unable to use:<br>1.Relapse (no usable data).<br>2. Readmission (no usable data).<br>3. Insight: Personal Beliefs about Illness Questionnaire (not a published, peer-reviewed scale). | Therapists and supervision: not clear.<br>CBT type: meaning. |

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| **Haddock1998** | Allocation: "randomly allocated." Blinding: raters blind.<br>Duration: 5 weeks or until participant discharged if this period was shorter, booster sessions at 1, 2, 3,4 months post-discharge, 2 year follow-up.<br>Frequency: mean no. CBT sessions 10.2 (SD 5.1), 1.67 booster sessions. Mean no. SC sessions 9.1 (SD=4.36), 0.91 booster sessions. | Inpatients.<br>Diagnosis: schizophrenia or schizoaffective disorder (DSM-IV).<br>N=21.<br>Age: ~29.<br>Sex: 19 M 2 F.<br>History: First treatment for schizophrenia less than 5 years ago, currently admitted to acute ward for onset or relapse of psychotic symptoms. | 1. CBT: manual-based. 4 treatment stages: i) engagement and assessment of mental state and symptoms to allow cognitive-behavioural analysis of how symptoms might relate to cognitions, behaviour and coping strategies. Stress-vulnerability model used to link biological and psychological mechanisms; ii) prioritised problem list developed collaboratively with participant. Problems assessed for trigger situations and cognitions; iii) and iv) intervention and monitoring.<br>2. Supportive counselling (SC): manual-based – no further description. | 1. Leaving the study early.<br>2. Number of days in hospital.<br>3. Relapse.<br>4. BPRS.<br><br>Unable to use:<br>1. Readmission (no usable data).<br>2. PSYRATS scale (no usable data). | Therapists: two clinical psychologists.<br>CBT type: mixed. |

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| **Hogarty1997** | Allocation: random assignment - two concurrent trials (with/without families).<br>Blinding: none.<br>Duration: 3 years.<br>Frequency: weekly for personal therapy, with less contact in year 3 for those who completed treatment objectives; biweekly for supportive therapy in all years. | Outpatients.<br>Diagnosis: schizophrenia or schizoaffective disorder (DSM-IV).<br>N=101.<br>Age: with family mean 28.6 (SD 7.5), living independently of family mean 33.0 (SD 7.6).<br>Sex: with family 56 M 41 F, living independently of family 24 M 30 F.<br>History: mean duration of illness living with family 6.2 years (SD 6.5), living independently of family 10.2 (SD 8.2). | 1. Personal therapy: focus on "modifying model of person," environmental and emotional monitoring - internal coping strategies. N=48.<br>2. Supportive therapy: active listening, correct empathy, appropriate reassurance, reinforcement of participant health-promoting initiatives, and reliance on the therapist for advocacy and problem solving in times of crisis. N=53. | 1. Leaving the study early.<br>2. Relapse.<br><br>Unable to use:<br>1. Social adjustment (no usable data).<br>2. Mental state (no usable data).<br>3. Family rating (no usable data). | Therapists: Masters level psychiatric nurse, clinical specialists and doctoral level clinical psychologists.<br>Supervision: fidelity to therapy was facilitated by explicit treatment manuals as well as by weekly individual and peer-group supervision provided by two senior (doctoral level) clinical supervisors and/or the principal investigator and by treatment process ratings that identified the practice principles used and the goals achieved.<br>CBT type: coping, stress-vulnerability/problem solving. |

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| **Kuipers1997** | Allocation: randomised, permuted block (size 6).<br>Blinding: none.<br>Duration: 9 months, 9 months follow-up.<br>Frequency: 1 hour weekly/fortnightly sessions | Outpatients.<br>Diagnosis: 29 schizophrenia, 2 schizoaffective, 13 delusional disorder, 6 unknown (DSM III-R). N=60.<br>Age: CBT mean 38.5, range 19-65, control mean 41.8, range 18-63.<br>Sex: 38 M, 22 F.<br>History: mean duration of illness - CBT 12.1 years (range 1-26), control 14.0 years (range 1-33). | 1. CBT + standard care: coping strategies enhancement, modifying dysfunctional beliefs, managing social disability and relapse. N=28.<br>2. Standard care: routine care, case management and medication. N=32. | 1. Death.<br>2. Leaving the study early.<br>3. Relapse.<br>4. Improved: 20% cut off on BPRS; 40% cut off on BPRS; clinically significant response in participant's primary presenting problem, measured by Personal Questionnaire.<br>5. Mental state: BPRS.<br><br>Unable to use:<br>1. Insight (no data).<br>2. Depression (no data)<br>3. Anxiety (no data).<br>4. Hopelessness (no data).<br>5. Social functioning (no data).<br>6. Self-esteem (no data).<br>7. Dysfunctional Attitudes (no data).<br>8. Delusional conviction, preoccupation and distress (no usable data).<br>9. Hallucination frequency, intensity and distress (no usable data).<br>10. participant satisfaction (incomplete data). | Therapists: experienced clinical psychologists.<br>Supervision: at least monthly peer/therapy supervision. Strenuous attempts made to follow procedures as laid down in the treatment manual.<br>CBT type: mixed. |

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| **Lewis2002** | Allocation: "independent, concealed randomisation of individuals with minimisation." Stratification according to first or second admission, inpatient or day patient, M or F, 1st episodes further stratified for duration of symptoms of more or less than 6 months. Blinding: "all outcome assessments were made blind to treatment allocation." Duration/frequency: 15-20 hours within 5-week treatment envelope, plus booster sessions at a further 2 weeks, and 1, 2, 3 months. Follow-up at 1-5 weeks. | Inpatients (N=264) and day patients (N=45). Diagnosis: schizophrenia, schizophreniform, schizoaffective, or delusional disorder (DSM-IV). N=309. Age: median 27.4. Sex: 216 M, 93 F. History: all service users either first episode (N=257) or second episode (N=52) admissions, positive psychotic symptoms for 4 weeks or more, moderate or severe score (4 or more) on PANSS target item for delusions or hallucinations. | 1. CBT: manual-based. 4 treatment stages: i) engagement and assessment of mental state and symptoms to allow cognitive behavioural analysis of how symptoms might relate to cognitions, behaviour and coping strategies. Stress-vulnerability model used to link biological and psychological mechanisms; ii) prioritised problem list developed collaboratively with participant; problems assessed for trigger situations and cognitions; iii) and iv) intervention and monitoring.<br>2. Supportive counselling (SC): manual-based – no further description.<br>3. Routine care. | Leaving the study early. Death. PANSS (Positive and Negative Syndrome Scale): total and positive scale scores. Delusions Scale (DS). Auditory Hallucinations Scale (AHS). | Therapists: "CBT was manual-based and conducted by one of five therapists trained in CBT in psychosis supervised by experienced cognitive therapists." CBT type: mixed. |

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| **Sensky2000** | Allocation: "simple randomization applied independently" for two sets of participants, one from London and another from the north of England. Blinding: "assessors were independent of the randomization procedure and remained blind to each participant's assigned group throughout the study." Duration: 9 months, 9 months follow-up. Frequency: number and length of sessions "were flexible to accommodate the needs of individual participants, but the initial aim was to offer each participant at least 45 minutes of therapy each week. After this phase, which could last up to 2 months, the session frequency could be reduced." | Outpatients. Diagnosis: schizophrenia (ICD-10 RDC & DSM-IV). N=90. Age: mean 39 (CBT), 40 (befriending). Sex: 53 M 37 M. History: mean duration of illness 14 years, mean number of previous admissions 14. | 1. CBT: began by examining the antecedents of emergence of psychotic disorder, developing a normalising rationale, generating shared case formulation. Thereafter, coping strategies for positive symptoms developed. Finally, interventions for negative symptoms attempted "using paced activity scheduling and diary recording of mastery and pleasure." N=46.<br>2. Befriending: designed to provide participants with approximately the same amount of therapist contact as CBT group, with sessions spaced at similar intervals. Intervention was empathic and nondirective. "Psychotic or affective symptoms were not directly tackled in any way." Sessions focused on neutral topics (for example, hobbies, sports, current affairs). N=44. | 1. Leaving the study early.<br>2. CPRS endpoint.<br>3. SANS endpoint.<br>4. MADRS endpoint.<br>5. Clinical improvement (50% cut off) on CPRS, MADRS, and SANS.<br><br>Unable to use:<br>1. Participant satisfaction (no usable data). | Therapists: two experienced psychiatric nurses. Supervision: therapists provided with regular supervision. Interviews were audiotaped for supervision and for quality control. CBT type: mixed. |

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| **Tarrier1998** | Allocation: random, stratified sample technique.<br>Blinding: blinded raters.<br>Duration: 10 weeks, 1 and 2 year follow-up.<br>Frequency: 20 sessions altogether, 1 hour twice a week. | Outpatients.<br>Diagnosis: schizophrenia, schizoaffective psychosis, delusional disorder (DSM III R). N=87.<br>Age: mean 39 (SD 11).<br>Sex: 69 M 18 F.<br>History: median duration of illness 11 years, persistent positive symptoms. | 1. CBT: coping strategy enhancement, training in problem solving, strategies to reduce relapse + standard care. N=33.<br>2. Supportive counselling: emotional support, unconditional regard, general counselling + standard care. N=26.<br>3. Standard care. N=28. | 1. Leaving the study early.<br>2. Relapse.<br>3. Mental state: important improvement (BPRS).<br><br>Unable to use:<br>1. BPRS change scores (SD not reported).<br>2. Positive and negative symptom severity (PAS, SANS scales - no usable data).<br>3. Depression (Beck Depression Inventory - no usable data).<br>4. Hopelessness (Beck Hopelessness Scale - no usable data). | Therapists: three experienced clinical psychologists.<br>Supervision: the therapists met on a regular basis to discuss cases. Sessions were taped.<br>CBT type: coping/problem solving. |

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| **Turkington**<br><br>**2002** | Allocation: random, but in 2:1 ratio (CBT group: control group). Blinding: assessors blind to randomisation. Duration: 2-3 months. Frequency: 6 1-hour sessions. If the participant's carer agreed to take part in programme, they received a total of 3 sessions over the same time period. participants attending <3 sessions classed as dropouts. | Patients "receiving treatment within psychiatric secondary care services," lists compiled from in- and outpatient case lists, depot and clozapine clinics, mental health key workers and Care Programme Approach registers.<br>Diagnosis: schizophrenia (ICD-10). N=422.<br>Age: mean 40.47 years.<br>Sex: 23% F(CBT group).<br>Exclusions: participants who were deteriorating and who needed inpatient care or intensive home treatment, primary diagnosis of drug or alcohol dependence, organic brain disease or severe learning disability. History: 4.71 mean previous admissions CBT group, 5.18 mean previous admissions control; 48.53 mean previous days in hospital CBT group, 52.01 mean previous days in hospital control. | 1. CBT: based on same manual used in Turkington2000. Included "assessment and engaging, developing explanations, case formulation, symptom management, adherence, working with core beliefs and relapse prevention." N=257.<br><br>2. Standard care: "treatment as usual" from CMHTs. N=165. | 1. Leaving the study early.<br>2. Mental state (CPRS, Schizophrenia Change Scale)<br>3. Depression (MADRS)<br>2. Insight (Insight Rating Scale).<br>3. Burden of care (Burden of Care Questionnaire).<br><br>Unable to use:<br>1. Participant and carer satisfaction (no usable data). | Therapists: CPNs who received 10 days of intensive training, based on manual developed by authors DT and DK. Supervision: "individual, group and telephone." Sessions were taped. Treatment fidelity analysis "revealed that the vast majority of sessions" were above the level "indicating acceptable quality of therapy analysis." |

**References of included studies (previous guideline)**

**Bradshaw1996**

*Bradshaw W. (1996) Structured group work for individuals with schizophrenia: a coping skills approach. *Research on Social Work Practice*; 6(2):139-154.

**Bradshaw*2000***

*Bradshaw W. (2000) Integrating cognitive-behavioral psychotherapy for persons with schizophrenia into a psychiatric rehabilitation program: results of a three year trial. *Community Mental Health Journal*; 36(5):491-500.

**Drury1996**

*Drury V, Birchwood M, Cochrane R, Macmillan F. (1996) Cognitive therapy and recovery from acute psychosis: a controlled trial. I. Impact on psychotic symptoms. *British Journal of Psychiatry*; 169:593-601.

Drury V, Birchwood M, Cochrane R, Macmillan F. (1996) Cognitive therapy and recovery from acute psychosis: a controlled trial. II. Impact on recovery time. British Journal of Psychiatry; 169:602-607.

Drury V, Birchwood M, Cochrane R. (2000) Cognitive therapy and recovery from acute psychosis: a controlled trial. III. Five-year follow-up. *British Journal of Psychiatry*; 177: 8-14.

**Haddock1999**

*Haddock G, Tarrier N, Morrison AP, Hopkins R, Drake R, Lewis S. (1999) A pilot study evaluating the effectiveness of individual inpatient cognitive-behavioural therapy in early psychosis. *Social Psychiatry and Psychiatric Epidemiology*; 34:254-8.

**Hogarty1997**

*Hogarty G, Kornblith S, Greenwald D, DiBarry A, Cooley S, Ulrich R, Carter M, Flesher S. (1997) Three year trials of personal therapy among schizophrenic patients living with or independent of family, I: Description of study and effects on relapse rates. *American Journal of Psychiatry*; 154(11):1504-1515.

Hogarty G, Greenwald D, Ulrich R, Kornblith S, DiBarry A, Cooley S, Carter M, Flesher S. (1997) Three year trials of personal therapy among schizophrenic patients living with or independent of family, II: Effects on adjustment of patients. *American Journal of Psychiatry*;154(11):1514-1524.

**Kuipers1997**

*Kuipers E, Garety P, Fowler D, Dunn G, Freeman D, Bebbington P, Hadley C. (1997) London East-Anglia randomised controlled trial of cognitive behavioural therapy for psychosis: I Effects of treatment Phase. *British Journal of Psychiatry*; 171: 319-27.

Garety P, Fowler D, Kuipers E, Freeman D, Dunn G, Bebbington P, Jones S. (1997) London East-Anglia randomised controlled trial of cognitive behavioural therapy for psychosis: II Predictors of outcome. *British Journal of Psychiatry*; 171:420-6.

Kuipers E, Fowler D, Garety P, Chisholm D, Freeman, D, Dunn G, Bebbington P, Hadley C. (1998) London East-Anglia randomised controlled trial of cognitive behavioural therapy for psychosis. *British Journal of Psychiatry*; 173:61-68.

Garety P, Kuipers E, Fowler D, Chamberlain F, Dunn G. (1994) Cognitive behavioural therapy for drug resistant psychosis. *British Journal of Psychiatry*; 67:259-271.

**Lewis2002**

*Lewis S, Tarrier N, Haddock G, Bentall R, Kinderman P, Kingdon D, Siddle R, Drake R, Everitt J, Leadley K, Benn A, Grazebrook K, Haley C, Akhtar S, Davies L, Palmer S, Faragher B, Dunn G. Randomised, controlled trial of cognitive-behaviour therapy in early schizophrenia: acute phase outcomes. *British Journal of Psychiatry* (in press).

Tarrier,N.; Haddock,G.; Lewis,S.; Drake,R.; Gregg,L.; SoCRATES Trial Group (2006) Suicide behaviour over 18 months in recent onset schizophrenic patients: the effects of CBT. *Schizophrenia Research* 83(1): 15 - 27.

Tarrier,N.; Lewis,S.; Haddock,G.; Bentall,R.; Drake,R.; Kinderman,P.; Kingdon,D.; Siddle,R.; Everitt,J.; Leadley,K.; Benn,A.; Grazebrook,K.; Haley,C.; Akhtar,S.; Davies,L.; Palmer,S.; Dunn,G. (2004) Cognitive-behavioural therapy in first-episode and early schizophrenia. 18-month follow-up of a randomised controlled trial. *British Journal of Psychiatry* 184: 231 - 239.

**Sensky2000**

Bateman,K.; Hansen,L.; Turkington,D.; Kingdon,D. (2007) Cognitive behavioral therapy reduces suicidal ideation in schizophrenia: results from a randomized controlled trial. *Suicide and Life-Threatening Behavior*.37(3): 284 - 290.

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**Characteristics of included studies (update)**

| **Study ID** | **BACH2002** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer data was available for 70/80 participants who completed the study. The other 10 participants either moved out of the hospital area or died. |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 4 months |
| | **Duration:** No. weeks of treatment - Up to 2 weeks (4 sessions with up to 72 hours between each session) |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - State psychiatric hospital, Nevada, US |
| | **Number of people screened, excluded & reasons:** Approx. 1 in 5 of those approached agreed to participate. Participants, in comparison with non-participants, were less likely to have a secondary substance misuse diagnosis and were more likely to have had previous hospitalisations at the study centre. |
| | **Notes about study methods:** Randomisation procedures not reported |
| **Participants** | **Diagnosis:** Other schizophrenia related [%] Schizoaffective 24%<br>Mood disorder with psychotic features 15%<br>Delusional disorder 4%<br>Psychosis NOS 4% |
| | **Diagnosis:** Schizophrenia [% of sample] 54% |
| | **Diagnosis:** Other [%] Secondary diagnoses:<br>Substance-related disorder 19%<br>Borderline intellectual functioning 13%<br>Personality disorder 15% |
| | **Diagnostic tool:** Other method Diagnosis at hospital intake |
| | **Inclusion criteria:** |

- Experiencing auditory hallucinations or delusions at admission
- Would be receiving outpatient treatment following discharge

**Exclusion criteria:**
- Diagnosis of substance-induced psychosis
- Symptoms occurred as part of dementia, delirium or medical condition
- Diagnosis of mental retardation by DSM-IV.

**Total sample size:** No. randomised 80

**Gender:** % female 36%

**Age:** Mean 39

**Ethnicity:** Caucasian 75%
Hispanic 11%
African American 4%
Southeast Asian 1%
Native American 3%

**Setting:** Inpatient

**Setting:** Outpatient

**History:** Time since previous release from hospital (days): 77
Duration of previous hospitalisation (days): 33

**Baseline stats:** Frequency of hallucinations and delusions rating: 6.0 ("more than once a day")

**Interventions** **Intervention - group 1.:** ACT, 4 sessions; n=40

**Intervention - group 2.:** TAU; n=40

**Notes about the interventions:**
ACT (acceptance and commitment therapy)
Followed a larger ACT treatment manual. Focus of the therapy was to try to just notice thoughts, without attempting to communicate with them, and to behave regardless of what these thoughts might say; to learn to accept symptoms even though one may not like them; and to consider coping strategies to these symptoms that would not interfere with one's goals.

TAU
Medication, attendance at three or more psychoeducational groups (once or twice daily ~40min sessions), and for those hospitalised for more than a few days, individual psychotherapy sessions with psychologist or intern at least once a week. After discharge, TAU included case management and medication management meetings. Rehabilitation classes, psychotherapy and assertive community treatment were available but not all participants (60%) made use of them.

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| | Training<br>The ACT sessions were conducted by a psychology intern who had been trained to the point of competence by the developer of the treatment approach. |
| **Outcomes** | **Death:** Natural causes |
| | **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) |
| | **Global state & service outcomes (e.g. CGI):** Re-hospitalisation |
| | **Global state & service outcomes (e.g. CGI):** Time to relapse |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - Frequency of reported symptoms (hallucinations and delusions): No. reporting symptoms at all<br>- Distress associated with symptoms<br>- self-rated believability of symptoms: |
| | **Non-adherence to study medication:** Non-adherence |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **BARROWCLOUGH2006** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT - All analyses were reported on an intention-to-treat basis, whereby all participants who agreed to assessment were included.

**Blindness:** Only raters blind

**Duration:** No. weeks of treatment - 24

**Duration:** Length of follow-up - 6 months

**Raters:** Independent of treatment

**Design:** Multi-centre - 5 NHS trust sites

**Number of people screened, excluded & reasons:** 127 screened, 113 eligible and randomised

**Notes about study methods:** Within each site, sufficient participants to form one CBT group and an equal number for the control condition (approximately 12 people) were identified. They were then allocated to the two conditions using a programme operated by an individual independent of the research team, following the minimisation method of stratification for chronicity (3 years or less vs. greater than 3 years).

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 89%

**Diagnosis:** Other schizophrenia related [%] Schizoaffective 11%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- DSM-IV diagnosis of schizophrenia or schizoaffective disorder verified by case note review
- Substance misuse and learning disability not identified as the primary problem
- Age 18–55
- Persistent and clinically significant positive symptoms, i.e. having either item P3 (hallucinatory behaviour) or item P1 (delusions) from the PANSS scored 4 (moderate) or above, with the symptom having been present at this level for at least 50% of the last 2 months
- At least 1 month of stabilisation if the patient had experienced a symptom exacerbation in the last 6 months (i.e. at least 1 month since discharge after an acute admission; no change in psychotropic medication prescribed in the last 4 weeks).

**Total sample size:** No. randomised 113

**Gender:** % female 27%

**Age:** Mean 38.8 (8.6)

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** Years of illness: 13.7 (8.0)

**Baseline stats:**
[TAU / CBT]

PANSS: 66.02 (13.86) / 61.61 (11.27)
SFS: 109.42 (22.44) / 111.69 (24.01)
HADS: 18.32 (7.24) / 18.83 (7.48)
GAF Symptoms: 28.84 (5.71) / 28.25 (5.07)

**Interventions** **Intervention - group 1.:** Group CBT, 18 sessions, + TAU; n=57

**Intervention - group 2.:** TAU; n=56

**Notes about the interventions:**
Group CBT
The group intervention covered themes including: identification of patient problems (delusional beliefs and voices were the main focus); formulating problems in terms of thoughts, feelings and behaviours; negative thinking patterns and thought monitoring; thought challenging; behavioural strategies: experiments and action plans; stress, arousal and medication; staying-well plans; emergency staying-well plans. Sessions lasted 2 hours including breaks, and followed a detailed plan and timetable contained in the therapy manual. The session plan included setting the day's agenda, introducing the main topic, reviewing homework, applying the topic to individuals' own experiences, problem formulations in small groups, discussion and comparison of group members' experiences, setting homework and eliciting feedback on the session.

TAU
All participants received standard psychiatric care in the UK based on the care programme approach to case management, and including maintenance antipsychotic medication, outpatient and community follow-up, and access to community-based rehabilitative activities such as day centres and drop-in centres.

Training
Two therapists conducted each session, and at least one therapist per group had training in CBT meeting the British Association of Behavioural and Cognitive Psychotherapy accreditation standards, plus experience in using CBT with people with psychosis. All therapists were provided with an initial training programme, and supervision sessions occurred monthly. A measure of treatment adherence was devised; checklists were completed at each session by both therapists and participants independently, to assess whether key elements of the CBT protocol were adhered to. Independently completed checklists from all therapists and participants present were collected on random session dates.

**Outcomes** **Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Days in hospital

**Global state & service outcomes (e.g. CGI):** Relapse - defined as hospital admission identified from hospital record systems, or exacerbation of symptoms lasting longer than 2 weeks and requiring a change in patient management (increased observation or medication change made by clinical team as assessed from hospital case notes)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

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|---|---|
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS<br>- HADS<br>- RSE |
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SFS, GAF: |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Well covered |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed |
| | **2.1 How well was the study done to minimise bias?:** + |
| **Study ID** | **BECHDOLF2004** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 8 |
| | **Duration:** Length of follow-up - 6 and 24 months |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre- Cologne, Germany |
| | **Number of people screened, excluded & reasons:** During the study period, 189 patients fulfilled inclusion criteria. 57 patients were not |

approached, either because they were involuntary admissions, formally detained under the Mental Health Act and could therefore not be included in RCTS or because during their inpatient stay, patient flow was too small to form a group of eight patients to start a group intervention. Of the remaining 132 subjects whose consent to enter the trial was sought, there was a 33.4% non-participation rate (n = 44) due to refusal, non-German speaking, inability to complete assessment or rapid discharge.

**Notes about study methods:** Randomisation by computer-generated random numbers for blocks of 8 participants. Results were placed in sealed envelopes and only opened at the time of treatment allocation

**Participants**

**Diagnosis:** Schizophrenia [% of sample] ICD-10: F 20, F 23, F 25
[CBT / Psychoeducation (PE)]
ICD-10 diagnoses, n (%)
F 20: 32 (80.0) / 37 (77.1)
F 23: – (0.0) / 2 (4.1)
F 25: 8 (20.0) / 9 (18.8)

**Diagnosis:** Other schizophrenia related [%]

**Diagnostic tool:** ICD-10

**Exclusion criteria:** - primary diagnosis of drug or alcohol dependence, organic brain disease, learning disability or hearing impairment

**Total sample size:** No. randomised 88

**Gender:** % female 55

**Age:** Mean 32

**Age:** Range 18-64

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[CBT / psychoeducation]
Time since diagnosis, months: 56.7 (65.4) / 50.0 (58.7)
Mean number of admissions: 2.6 (3.8) / 2.4 (3.2)

**Baseline stats:**
[CBT / Psychoeducation]
PANSS total: 13.6 (5.3) / 15.1 (5.6)

**Notes about participants:** Medication use: The mean dosages of typical antipsychotics converted to chlorpromazine equivalents were nearly the same at baseline and follow-up evaluations, although there was a wide range of dosage within the treatment groups [pretreatment [mg mean (SD)]: CBT 431.7 (201.0), PE 375.0 (349.5); posttreatment: CBT 158.8 (73.3), PE 520.0 (413.3); follow-up: CBT 358.3 (340.4), PE 361.4 (340.9)]. All patients were treated with neuroleptics, most with atypicals (pretreatment: CBT 80%, PE 85%; post-treatment: CBT 93.5%, PE 87.8%; follow-

up: CBT 88.9%, PE 89.2%). Around one-third of patients studied also received antidepressive medication (pretreatment: CBT 26.3%, PE 25.0%; posttreatment: CBT 25.8%, PE 38.9%; follow-up: CBT 31.0%, PE 28.9%). No significant differences emerged between treatment groups at pre- and post-treatment or follow-up.

**Interventions** **Intervention - group 1.:** Group CBT, 16 sessions, n=40

**Intervention - group 2.:** Group psychoeducational programme, 8 sessions, n=48

**Notes about the interventions:**
All interventions were an adjunct to routine hospital care and patients remained under the medical supervision of the responsible consultant psychiatrist who alone determined the pharmacological regime, timing of discharge and readmission.

Group CBT
The group CBT treatment was based on a manualised approach which used coping strategy enhancement, problem solving and relapse prevention in patients with psychosis.

Group psychoeducational (PE) programme.
The PE programme was similar to a manualised PE group training for patients

Training
Groups of both interventions were led by an experienced and CBT trained psychiatrist or clinical psychologist

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Relapse defined by a rating of at least 5 and a 2-point increase compared with the previous assessment in at least one of the items of the positive syndrome subscale of the PANSS

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation defined as a 36-hour full hospitalisation or a 5-day partial hospitalisation because of an exacerbation of acute psychotic symptoms.

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS general, positive, negative.

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - change was calculated by a two-fold criterion: (i) improvement of PANSS global score >2 SD beyond the mean of the intake sample at follow-up and (ii) reliable change index exceeds 1.96.

**Non-adherence to study medication:** Compliance with medication

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| **Study ID** | **CATHER2005** |
|---|---|
| **General info** | **Funding source:** Pharmaceutical industry |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT defined as having completed at least 4 out of 16 sessions |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 16 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Two outpatient clinics in Boston |
| | **Notes about study methods:** Randomisation performed by independent member of the research team and stratified by PANSS and gender |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 61% |
| | **Diagnosis:** Other schizophrenia related [%] Schizoaffective 39% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- 18–65 years of age<br>- English speaking<br>- Treated with olanzapine for at least 6 months and at a stable dose for at least 30 days<br>- Exhibiting residual psychotic symptoms as defined by two ratings of mild or one rating of moderate on psychosis items of PANSS. |
| | **Exclusion criteria:**<br>- Known or suspected organic brain disorder<br>- Substance use disorder in the past 3 months |

- A conceptual disorganisation rating on the PANSS of moderate or higher
- Previous exposure to the study treatments.

**Total sample size:** ITT population 28

**Total sample size:** No. randomised 30

**Gender:** % female 43%

**Age:** Mean 40.4 (11.96)

**Ethnicity:** White 68%
Hispanic 4%
Black 29%

**Setting:** Outpatient

**History:** Mean years of illness: 18 (13.1)

**Baseline stats:**
Average for the whole sample:
PANSS total: 51.1 (12.6)
PSYRATS-total: 33.3 (13.7)
Auditory hallucinations: 85.7%
SFS: 118.5 (21.5)

**Notes about participants:** Medication: Olanzapine doses ranged from 5 to 40mg with a mean daily dose of 19.7 (8.6) mg. 33% of participants were taking another antipsychotic in addition to olanzapine.

**Interventions**

**Intervention - group 1.:** Functional CBT: 16 weekly sessions; n=15

**Intervention - group 2.:** Psychoeducation; n=13

**Notes about the interventions:**
Functional CBT
Comprises several modules: education, coping skills, cognitive restructuring, behavioural experiments and goal-setting. Patients are taught skills for managing persistent positive symptoms that interfere with accomplishing certain activities or goals. For example, rather than discussing hallucinations or delusions as 'real' or 'unreal', functional CBT focuses on whether psychotic symptoms and responses to these symptoms block attainment of specific goals. This approach helps ensure that therapists always have a context for challenging maladaptive responses to symptoms.

Psychoeducation
Team Solutions is a psychoeducational intervention developed and sponsored by Eli Lilly & Co. to teach patients about schizophrenia and the principles of its management, with the aim of promoting reintegration. The program is not medication-specific and includes a video, patient workbook and instructor's manual and was delivered in an individual format. The program is organized into 10 modules including:

| | |
|---|---|
| | promoting understanding of the illness and of symptoms of schizophrenia, identifying members of the treatment team and their roles, learning about medication and side effects, preventing relapse, and coping with symptoms.<br><br>Training<br>Treatment was delivered by nine therapists with an average of 7.8 years (SD=4.77) of experience conducting CBT. Weekly supervision meetings were held to discuss cases and ensure protocol adherence. |
| **Outcomes** | **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - Clinically significant improvement defined as 20% reduction in PANSS Positive subscale |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS, PSYRATS |
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SFS |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Adequately addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed |
| | **2.1 How well was the study done to minimise bias?:** + |

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|---|---|
| **Study ID** | **DURHAM2003** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial (effectiveness/pragmatic) |
| | **Type of analysis:** LOCF |

**Type of analysis:** ITT - All participants who started allocated treatment were analysed. For missing values, LOCF and imputation from group means were also applied, these had no impact on significant outcomes.

**Blindness:** Only raters blind

**Duration:** Length of follow-up - 3 months

**Duration:** No. weeks of treatment - 36

**Raters:** Independent of treatment

**Design:** Multi-centre - Two adjacent mental health services in Tayside and Fife

**Number of people screened, excluded & reasons:** A total of 274 people were referred for possible inclusion in the trial, of whom 95 (35% of initial referrals) fulfilled the initial criteria, entered the baseline assessment phase and were offered a further screening interview 3 months later. Of these, 66 (24% of initial referrals, 38% of 171 potentially suitable referrals) entered the study and were randomised to treatment conditions.

**Notes about study methods:** Randomisation (sealed envelope technique) administered centrally by non-clinical project coordinator, carried out separately at each treatment centre by permuted blocking

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 89%

**Diagnosis:** Other schizophrenia related [%] Delusional disorder 3%
Schizoaffective 8%

**Diagnostic tool:** ICD-10

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- Psychosis with a diagnosis of schizophrenia, schizoaffective disorder or delusional disorder
- Aged 16–65 years
- Known to the psychiatric services as suffering from positive symptoms of persistent and distressing hallucinations or delusions
- Stabilised on antipsychotic medication for at least a 6-month period under the care of a consultant psychiatrist.

**Exclusion criteria:**
- Primary diagnosis of alcoholism or drug misuse
- Evidence of organic brain disease
- History of violence.

**Total sample size:** No. randomised 66

**Total sample size:** ITT population 60

**Gender:** % female 32%

**Age:** Mean 36 (10.4)

**Ethnicity:** Not reported

**Setting:** Inpatient

**Setting:** Outpatient

**History:** Mainly middle-aged men with a long history of illness (mean 13 years, range 2-31)

**Baseline stats:**
[CBT / SPT / TAU]
PANSS total score: 101.2 (14.7) / 95.0 (17.7) / 92.4 (17.5)
PSYRATS delusions: 14.1 (4.5) / 12.3 (5.8) / 11.2 (5.6)
PSYRATS hallucinations: 23.0 (11.3) / 23.6 (10.0) / 20.8 (10.9)
Global Assessment Scale: 32.0 (4.8) / 34.9 (7.2) / 34.8 (8.1)

**Notes about participants:**
Medication [CBT / SPT / TAU]
Chlorpromazine equivalents, mg/day [mean (95% CI)]: 604 (392-816) / 747 (527-967) / 630 (333-927)

Four of the fifteen patients who were started on an atypical were prescribed clozapine.

**Interventions** **Intervention - group 1.:** CBT; n=22

**Intervention - group 2.:** SPT; n=23

**Intervention - group 3.:** TAU; n=21

**Notes about the interventions:**
CBT
Drew on best practice as exemplified by the treatment manuals. The essential elements were as follows: engagement; analysis of problems; development of a normalising rationale for psychotic experiences; exploration of current coping strategies; acquisition of additional coping strategies for hallucinations and delusions; and focus on accompanying affective symptomatology using relaxation training, personal effectiveness training and problem-solving as appropriate. The overall aims were: to enhance knowledge and acceptance of illness; to encourage the acquisition of specific coping skills for managing hallucinations and delusions; and to develop an understanding of personal vulnerability and how to mitigate its effects.

SPT
Supportive psychotherapy using an established framework. The approach is psychodynamic in orientation and seeks to understand psychotic experience as a function of being overwhelmed and unable to bear intensely charged emotional experiences. The essential elements of therapy were as follows: provision of non-specific emotional support and empathy; opportunity for the patients to describe the narrative of their lives and the impact of the illness; and working through of transference.

TAU
All participants received usual treatment, focused on community mental health teams. Services include regular psychiatric consultation and contact with a keyworker (typically a trained community psychiatric nurse), with emergency assessment and hospital admission available as required. Facilities in the community include day care, sheltered work, supported accommodation and volunteer befriending. Specialist psychological intervention for psychosis within a cognitive–behavioural framework, although a limited resource, is offered through clinical psychology and clinical nurse specialists.

Training
The CBT arm of the trial was delivered by five clinical nurse specialists with extensive professional experience of severe mental disorder. All had completed a recognised post-registration training in Dundee that mainly focuses on standard CBT for common mental disorders but includes a module on psychosis. All were registered as therapists with the British Association of Behavioural and Cognitive Psychotherapy. One of these five had developed a specialist interest in CBT for psychosis and took the lead role in developing the treatment protocol, training and supervising the other therapists and treating the majority of patients.

None of the CBT therapists saw patients in the supportive psychotherapy arm of the trial, which was delivered by 16 mental health professionals (mainly nursing but also psychiatry and occupational therapy) who were attached to the clinical teams responsible for the patients referred to the trial. All had expressed an interest in developing clinical skills in psychotherapy for patients with psychosis and none had received any formal training in CBT. They were given training and supervision by a consultant psychotherapist, who has consultant responsibility for one of the day hospitals in Dundee and is director of psychotherapy training in Tayside. She took responsibility for developing the supportive psychotherapy protocol and for training and supervising the therapists. All therapists in both treatment conditions were offered bi-weekly supervision for the duration of their contact with patients in the trial.

**Outcomes**

**Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Average score/change in global state GAS

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state PANSS Total, PSYRATS Delusions, PSYRATS Hallucinations

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state Clinically worthwhile improvement: 25% reduction in PANSS

Clinically important improvement: 50% reduction in PANSS

**Satisfaction with treatment:** Service user satisfaction

**Other:** Antipsychotic use (CPZ equivalents), increase/decrease in antipsychotic doses, discontinuation/change in antipsychotic

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** ++

| **Study ID** | **ENGLAND2007** |
|---|---|
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 16 |
| | **Duration:** Length of follow-up - 54 weeks after initiation of treatment |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - 4 clinical sites near a regional research centre, Canada |
| | **Number of people screened, excluded & reasons:** 70 volunteers were referred to the study, 65 candidates met the inclusion criteria, 3 declined and 2 were excluded due to being unable to make an informed choice about treatment |
| | **Notes about study methods:** participants were randomly assigned using a random number table |
| **Participants** | **Diagnosis:** Other schizophrenia related [%] Schizoaffective disorder - not reported |
| | **Diagnosis:** Schizophrenia [% of sample] Not reported |
| | **Diagnostic tool:** DSM-IV |

**Inclusion criteria:**
- ability to speak and understand English
- a DSM-IV label of schizophrenia or schizoaffective disorder
- negative voices in the previous 6 months
- adherence to prescribed medication
- neuroleptic medication regimen >=80% of the time
- competence to give informed consent as rated by the MacArthur Competence Assessment Tool.

**Total sample size:** No. randomised 65

**Gender:** Not stated

**Age:** Mean 41

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** Not reported

**Baseline stats:**
[Cognitive Nursing + TAU / TAU]
BPRS: 51.0(9.8) / 51.1(7.9)
RSCQ: 113.5(20.1) / 115.5(14.5)

**Notes about participants:** The participants reported a history of emotional (n=25, 38.5%), physical and emotional (n=13, 20.0%) or sexual (n=27, 41.5%), self-harm (n=49, 75.4%), or abuse of alcohol (n=52, 80.0%) or drugs (n=37, 56.9%). Most used nicotine (n=59, 90.8%) or marijuana (n=5, 7.7%).

All participants reported more than 80% adherence to a prescribed neuroleptic medication regimen.

**Interventions** **Intervention - group 1.:** Cognitive nursing intervention (CNI), 12, 90-minute sessions; n=44

**Intervention - group 2.:** TAU; n=21

**Notes about the interventions:**
TAU
Operationalised as a healthcare or service provider's routine use of communication strategies while providing psychiatric or primary care services including medication to voice hearers.

CNI
12, 90-minute sessions of individualised counselling to voice hearers over a period of 4 months. The intervention was flexibly structured to accommodate real-time learning needs and requirements of each participant. The sessions involved A CBT approach including techniques of Socratic learning, verbal challenging, empirical reality testing, and home work assignments.

| | |
|---|---|
| | Training<br>CBT was delivered by an experienced psychiatric clinical nurse with specialist training at the graduate level. This person was blinded as to the nature of the UC participants received. |
| **Outcomes** | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS, RSCQ |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Poorly addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **GARETY2008** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 36 |
| | **Duration:** Length of follow-up - data collected at 12 months (after treatment) and 24 months (end of treatment + 12 months follow-up) |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - 5 locality mental health services in London and East Anglia: inner city London (2), suburban outer London (1), county town (Norwich) and rural centre (Norfolk) |

**Number of people screened, excluded & reasons:** 683 patients meeting inclusion criteria were identified, 382 patients withheld consent. A total of 301 patients provided informed consent, of whom 218 entered pathway 1 (individual pathway) and 83 pathway 2 (carer pathway)

**Notes about study methods:** Randomisation was stratified within each of the centres, and within inpatient or outpatient status at the time of relapse. Randomisation schedules were independently generated by a trial randomisation service in a separate location from all trial centres, using randomised permuted blocks with a block size randomly varying between 2-10 for the individual pathway and 3-9 in the carer pathway.

If patients had no carer they were invited to participate in the individual study. Those who identified a carer, a relative or friend with whom they lived or were in close contact >-10 hours per week, the patient was asked to give informed consent for the carer pathway study. The carers were then approached for their consent. At the trial recruitment midpoint it became apparent that otherwise eligible patients with carers had been excluded from the study because their carer had refused to participate. From this point in cases where patients or carers refused carer participation, participants with carers were offered entry to the individual pathway.

**Participants**

**Diagnosis:** Other schizophrenia related [%] schizoaffective disorder = 13.3%
Delusional disorder = 1.3%

**Diagnosis:** Schizophrenia [% of sample] 85.4%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- current clinical diagnosis of non-affective psychosis (F2 in the ICD-10 and DSM-IV)
- aged 18-65
- second subsequent psychotic episode starting <=3 months before they agreed to enter trial
- Rating >=4 for at least one positive symptom on the PANSS

**Exclusion criteria:**
- primary diagnosis of alcohol or substance dependency, organic syndrome or learning disability
- a command of spoken English inadequate for engaging in psychological therapy
- unstable residential arrangements such that the likelihood of being available for the duration of the trail was low.

**Total sample size:** No. randomised 301

**Total sample size:** ITT population Primary outcome data at 24 months available for 295 participants

**Gender:** % female 30%

**Age:** Mean 37

**Ethnicity:** White - 72.3%
Black Caribbean - 7.6%
Black African - 9.2%
Black - other - 2.3%
Indian - 1.6%

Other - 7%

**Setting:** Inpatient

**Setting:** Outpatient

**History:**
Non carer pathway:
[TAU / CBT]
Inpatient, n: 78 / 76
Outpatient, n: 34 / 30
Mean length of illness, years: 9.9(8.7) / 10.9(8.1)
Mean no. admissions: 4.4(4.4) / 5.0(5.6)
History of violence:
No: 79 / 66
Yes: 30 / 35
history of suicide or self-harm:
No: 65 / 65
Yes: 42 / 35

Carer Pathway:
[TAU / CBT / FI]
Inpatient, n: 18 / 16 / 16
Outpatient, n: 10 / 11 / 12
Mean length of illness, years: 10.5(8.6) / 10.9(9.7) / 13.3(11.8)
Mean no. admissions: 4.6(5.50 / 3.4(3.2) / 6.5(9.2)
History of violence:
No: 23 / 20 / 21
Yes: 5 / 7 / 7
History of suicide or self-harm:
No: 15 / 16 / 14
Yes: 13 / 11 / 12

**Baseline stats:**
Non-carer pathway:
[TAU / CBT]
PANSS total: 66.26(15.91) / 62.32(13.49)

Carers pathway:

[TAU / CBT / FI]
PANSS total: 64.11(15.28) / 66.89(14.26) / 70.93(13.36)

**Interventions** **Intervention - group 1.:** CBT, 12-20 sessions; non-carers pathway n=106; carer pathway n=27

**Intervention - group 2.:** FI, 12-20 sessions; carer pathway n=28

**Intervention - group 3.:** TAU; non-carers pathway n=112; carer pathway n=28

**Notes about the interventions:**
TAU
Consisted of good standard care, delivered according to national and local service protocols and guidelines, including the prescription of antipsychotic medication. TAU did not preclude the provision of psychological intervention, although in practice this was relatively rare.

CBT
Adaptation of generic CBT for psychosis manual. It was specifically aimed at targeting key aspects of relapse prevention. The first stage focused on engagement and assessment. A central focus of the work was developing a shared formulation of relapse, including where appropriate a new model of disorder emphasising alternatives to delusional thinking. therapists then attempted to target the key problems associated with vulnerability to relapse. The last stage involved developing a set of self regulatory strategies to manage relapse.

FI
Followed a manualised approach with an emphasis on improving communication, offering discussion of up-to-date information about psychosis, problem solving, reducing criticism and conflict, improving activity, and emotional processing of grief, loss and anger. Sessions focused on one problem at a time and were aimed at an individual formulation of each family's problem as they defined them. There was a particular focus on relapse prevention.

Training for CBT
Five lead trial therapists, all doctorate level or equivalent clinical psychologists provided therapy to 72% of total treatment cases. A further 37 CBT treatment cases were seen by therapists employed by the local mental health services, these were a mixture of doctoral clinical psychologists and nurses who had received specialist training in CBT. All therapists were required to demonstrate competence in CBT. This was followed by a period of intensive training in workshops with both the expert CBT therapists on the trial and external experts. Lead therapists from each centre met monthly for case discussion and supervision with the expert CBT therapists.

Training for FI
FI involved a lead and co-therapist working together. The five lead therapists for CBT also acted as the lead FI therapists. All lead therapists were required to show in-depth knowledge of evidence-based FI in psychosis and to demonstrate key techniques in role-play. They also attended intensive training from an expert FI therapist. All co-therapists attended FI training workshops or received individual training from a trial lead therapist. The local therapists were a mix of doctorate level clinical psychologists and nurses who had received training in FI. The trial lead therapists were provided with specialist expert monthly supervision throughout the trial, and attended advanced skills workshops

by experts. The lead therapists also meet fortnightly for peer supervision and case presentations.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes**

**Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Relapse following full remission: Data reported but because number of people achieving remission was low, data difficult to interpret.

Relapse ratings were made using a published method employed in a previous RCT. Relapse ratings are based on evidence of the re-emergence of, or significant deterioration in, positive psychotic symptoms of at least moderate degree persisting for at least 2 weeks

**Global state & service outcomes (e.g. CGI):** Remission ratings were made using a published method employed in a previous randomised controlled trial. Ratings are based on changes in positive psychotic symptoms. Evidence is required of improvement in (for partial remission) or absence of (for full remission) positive psychotic symptoms continuing for at least 4 weeks.

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Global state & service outcomes (e.g. CGI):** Days in hospital

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS total, positive and negative

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Social and Occupational Functioning Assessment Scale & Time Budget

**Quality of Life:** Average score/change in quality of life - EUROQOL

**Other:** Beck Depression Inventory

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed

**2.1 How well was the study done to minimise bias?:** ++

| | |
|---|---|
| **Study ID** | **GRANHOLM2005** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - analyses were used to examine all outcome variables. Missing data were replaced by within-group means of the missing values. |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 24 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - All centres were based in the US |
| | **Number of people screened, excluded & reasons:** 87 participants were screened; 11 were excluded due to: refusal to complete baseline assessment (n=4), disabling medical illness (n=4), current substance abuse (n=3) |
| | **Notes about study methods:** A stratified randomisation procedure was used to assign participants to treatments within sites, with the constraint of equal numbers of patients from each site would be assigned to the two conditions according to a sequential list of random numbers. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 63% |
| | **Diagnosis:** Other schizophrenia related [%] Schizoaffective disorder = 37% |
| | **Diagnostic tool:** DSM-IV |
| | **Exclusion criteria:**<br>- disabling medical problems that would interfere with testing<br>- absence of medical records to inform diagnosis<br>- diagnosis of dependence on substances other than nicotine or caffeine within the past 6 months |
| | **Total sample size:** No. randomised - 76 |
| | **Total sample size:** ITT population - 76 |
| | **Gender:** % female 73.5% |
| | **Age:** Mean 54 |

**Age:** Range 42-74

**Ethnicity:** 78% were of Caucasian ethnicity

**Setting:** Other community-dwelling patients

**History:**
[TAU +CBSST / TAU]
Age at onset: 26.4(10.9) / 24.7(10.0)
Illness duration: 30.1(11.3) / 28.4(10.5)

**Baseline stats:**
[TAU + CBSST / TAU]
Beck cognitive insight scale: 4.1(5.3) / 5.9(4.7)
PANSS: 51.5(13.2) / 56.1(14.8)
HAM-D: 13.5(9.0) / 14.2(8.8)
Independent Living Skills Survey: 0.69(0.10) / 0.71(0.09)
ICSD Performance-based skills assessment: 0.73(0.18) / 0.67(0.17)

**Notes about participants:**
Participant mediation
1+ Atypical antipsychotics = 46
Typical antipsychotics = 17
Both typical and atypical = 7
No antipsychotic medication = 6

**Interventions** **Intervention - group 1.:** TAU + CBSST (Cognitive behavioural social skills training); n=37

**Intervention - group 2.:** TAU control; n=39

**Notes about the interventions:**
TAU
Patients continued in whatever ongoing care they were receiving. No medication guidelines were provided as part of this protocol. To characterise TAU, a standardised service utilisation interview was administered to all participants. 82% reported a psychotropic medication visit in the 6 weeks preceding study entry. 19% reported receiving any form of psychotherapy.

CBSST
CBSST was conducted in 24 weekly 2-hour group sessions. The treatment manual included a patient workbook that contained homework forms. CBSST targeted the multidimensional deficits that lead to disability in aging patients with schizophrenia. The social skills training modules were based on modules in the UCLA social and independent living skills series, whilst the cognitive components were developed specifically for patients with schizophrenia. The age-relevant content modifications included identifying and challenging ageist beliefs, age-relevant role-playing situations and age-specific problem solving. The modules were repeated to compensate for cognitive impairment.

| | |
|---|---|
| **Outcomes** | **Global state & service outcomes (e.g. CGI):** Re-hospitalisation |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS; HAM-D; Beck Cognitive Insight Scale; Comprehensive Module Test. |
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Independent living Skills Survey; UCSD Performance-Based Skills Assessment |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Adequately addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Well covered |
| | **2.1 How well was the study done to minimise bias?:** ++ |

| | |
|---|---|
| **Study ID** | **GUMLEY2003** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Missing data not imputed |
| | **Blindness:** Open |
| | **Duration:** Length of follow-up 52 weeks |
| | **Duration:** No. weeks of treatment - 12 with an additional intensive targeted phase (2 to 3 sessions per week) at the appearance of early signs of relapse. |
| | **Raters:** Not stated to be independent of treatment |

**Design:** Multi-centre - 6 CMHTs in Ayrshire and 2 CMHTs in Glasgow

**Number of people screened, excluded & reasons:**
742 case notes screened
237 fulfilled initial criteria
93 failed entry criteria (not approached by keyworker, excluded by RMO, refused, or diagnosis incorrect)
144 randomised

**Notes about study methods:**
Randomisation: After the interview the patient was randomised according to predetermined envelopes containing the treatment group to which participants would be allocated (TAU or CBT) devised by one of the authors, which was unbeknown to the assessors, therapist or participants. A member of the research team opened an envelope that informed as to which group individual participants were to be allocated. Another member of the team witnessed this procedure, and the envelope was placed in the participant's case file.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 82%

**Diagnosis:** Other schizophrenia related [%] Schizoaffective 15%
Schizophreniform 1%
Delusional disorder <1%
Psychotic disorder NOS <1%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- DSM-IV criteria for schizophrenia or a related disorder confirmed by SCID
- Aged between 18 and 65
- Receiving antipsychotic medication
- Considered relapse prone by one or more of the following characteristics : (1) a history of relapse in the last 2 years; (2) their keyworker viewed them as living in a stressful environment (e.g. a home environment characterized by high levels of expressed emotion); (3) living alone or socially isolated ; (4) nonadherence with antipsychotic medication (where this was viewed as problematic by the participant's keyworker and/or prescribing psychiatrist) ; and (5) being on a neuroleptic dosage reduction programme.

**Exclusion criteria:**
- Non-English speaker
- Had organic brain disorder
- Presence of significant learning disability
- Severe positive psychotic symptoms (PANSS Positive subscale >=5)
- Primary drug or alcohol dependence disorder (based on the opinion of the key worker)
- In receipt of a concurrent psychotherapy outside the study.

**Total sample size:** No. randomised - 144

**Total sample size:** ITT population 144

**Gender:** % female 27%

**Age:**
Mean
CBT: 35.8 (9.6)
TAU: 36.7 (10.1)

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
[CBT / TAU]
Duration of illness (months): 113 (81) / 114 (84)
History of relapse: 53% / 57%
History of admission: 39% / 52%

**Baseline stats:**
[CBT / TAU]
PANSS Global: 31.7 (7.5) / 29.3 (6.6)
BSI GSI: 1.32 (0.80) / 1.05 (0.70)

**Interventions** **Intervention - group 1.:** CBT: 5 sessions over 12 weeks, then 2-3 sessions/week at the appearance of early signs of relapse; n=72

**Intervention - group 2.:** TAU; n=72

**Notes about the interventions:**
CBT
Engagement phase centred on cognitive model of relapse and monitoring early signs of relapse. Targeted phase at first signs of relapse consisted of detailed assessment, identifying negative beliefs, developing alternative beliefs and reinforce through behaviour change.

TAU
All participants received usual treatment, i.e. ongoing medication, regular psychiatric review, follow-up from keyworker, access to wider multidisciplinary CMHT

Training
A clinical psychologist provided all CBT sessions.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Time to relapse

**Global state & service outcomes (e.g. CGI):** Relapse: hospital admission or increase in positive symptoms ( defined as 50% increase in PANSS

over 7 days where baseline PANSS >=3, or a 3 point increase in PANSS over 7 days where baseline PANSS <3)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SFS

**General and psychosocial functioning (e.g. SFS):** Clinically significant response in general functioning - SFS: any movement of +-2 SDs (only reported for the 7 individual subscales and not the SFS total)

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**JACKSON2005**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT- All randomised were included in analyses. Missing data imputed by EM method in SPSS.

**Blindness:** Only raters blind

**Duration:** Length of follow-up - Hospital admission data was follow-up for 4 years after the end of treatment

**Duration:** No. weeks of treatment - 52

**Raters:** Independent of treatment

**Design:** Single-centre - Western Melbourne, Australia

**Number of people screened, excluded & reasons:** 118 referred, 25 met exclusion criteria, 2 missed pre-test; 91 randomised

**Notes about study methods:** Randomisation by trial co-ordinator by sequential assignment

**Participants**

**Diagnosis:** Other schizophrenia related [%] Schizophreniform 12%
Schizoaffective 15%
Delusional/Psychotic 9%

**Diagnosis:** Schizophrenia [% of sample] 31%

**Diagnosis:** Other [%] Bipolar/depressive 32%

**Diagnostic tool:** Other DSM

**Inclusion criteria:**
- Aged 15–29 years
- Experiencing a first episode of psychosis
- Fluent English
- Live within EPPIC's catchment area.

**Exclusion criteria:**
- Organic cause for psychosis (e.g. cerebral tumour revealed on MRI scan)
- Epilepsy
- Evidence of IQ <70
- Diagnosis of substance dependence.

**Total sample size:** No. randomised - 91

**Total sample size:** ITT population - 91

**Gender:** % female 23%

**Age:** Mean
COPE: 22.49 (3.40)
TAU: 22.50 (3.27)

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
[COPE / TAU]
Age of onset: 22.11 (3.47) / 21.93 (3.39)
Length of psychosis (days): 160.29 (149.76) / 164.63 (238.39)
Length of hospitalisation (days): 22.16 (34.08) / 12.72 (14.40)

**Baseline stats:**
[COPE / TAU]
BPRS: 16.51 (6.94) / 17.85 (8.21)
SANS: 19.73 (13.00) / 20.76 (13.73)

**Notes about participants:**
Medication administered in line with a low-dose protocol.
Chlorpromazine equivalents:
COPE: 246.89 (275.72)
TAU: 280.76 (287.18)

**Interventions** **Intervention - group 1.:** COPE: n=45

**Intervention - group 2.:** No COPE (TAU only): n=46

**Notes about the interventions:**
COPE (cognitively oriented psychotherapy for early psychosis)
Sessions were approx. 40 minutes in duration and were held weekly or fortnightly, although this was somewhat flexible. COPE consists of four phases: engagement, assessment, adaptation, and secondary morbidity. The therapy was manualised. The therapist typically spent the initial 3–4 sessions assessing and engaging with the patient. A therapeutic agenda was developed with the patient, usually by session 4 (engagement and assessment phases) which formed the basis for targeting issues of adaptation and secondary morbidity. Typically, the COPE agenda would include psychoeducation, stigma and identity issues, and focus on the patient's problems with motivation and confidence. Such issues were dealt with using techniques derived from a cognitive behavioral framework.
Participants also received usual treatment from EPPIC.

TAU
Standard EPPIC (Early Psychosis Prevention and Intervention Centre) treatment include: early detection, mobile assessment and home-based treatment, inpatient unit, outpatient case management, family work, accommodation, prolonged recovery programmes, tailored group programmes and mobile outreach team for 'difficult to engage' youth.

Training
There were five therapists comprising two consultant psychiatrists and three clinical psychologists. All received weekly group supervision and also weekly peer supervision on a rotational basis. The COPE therapist was an ' auxiliary therapist ' in the treating team, but was never also the treating medical doctor or case manager.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation No. re-admitted each year - time to re-admission

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS, SANS, BDI, GSI,

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SOFAS

| | |
|---|---|
| | **Quality of Life:** Average score/change in quality of life - QLS |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Poorly addressed |
| | **1.3 An adequate concealment method is used.:** Poorly addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **JACKSON2007** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Analyses were performed on all 62 participants and follow-up interviews were conducted where possible, regardless of whether they had withdrawn.<br><br>Ten multiply imputed datasets were generated to deal with missing responses |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - Up to 14 weeks maximum |
| | **Duration:** Length of follow-up 1 year |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Early Psychosis Prevention Centre (EPPIC), Melbourne, Australia |
| | **Number of people screened, excluded & reasons:** 427 people screened, of which 111 were excluded due to ineligibility, a further 126 people |

referred within the time-frame could not be approached e.g. no response to telephone calls/ letters, DNA at appointments. Therefore 190 people were approached for inclusion into the study. Of these 128 refused to participate.

**Notes about study methods:** Randomisation was stratified according to affective and non-affective psychotic diagnosis to ensure equal distribution across therapists and treatment conditions. The randomisation process was conducted by an independent statistician.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 13%

**Diagnosis:** Other schizophrenia related [%] schizophreniform - 40%
schizoaffective - 11%

**Diagnosis:** Other [%] bipolar / depressive - 21%
Delusional / psychotic (NOS) - 15%

**Diagnostic tool:** DSM-IV

**Exclusion criteria:**
- inability to speak English
- intellectual disability (IQ<70)
- psychosis due to a medical condition
- change to non-psychotic diagnosis
- left the EPPIC catchment area
- treatment from a private psychiatrist/ psychologist
- participating in a first-episode mania trial
- exhibiting violent behaviour or being incarcerated

**Total sample size:** No. randomised 62

**Total sample size:** ITT population 53 at end of treatment, 55 at follow-up

**Gender:** % female 27%

**Age:** Range EPPIC age range = 15-25

**Age:** Mean 22

**Ethnicity:** Not reported

**Setting:** Other EPPIC - a comprehensive treatment service which included an inpatient unit, an outpatient case management system, family work, accommodation, prolonged recovery programmes and tailored group programmes.

**History:**
[ACE / befriending]
Mean age of onset of psychosis: 21.58(3.49) / 21.67(4.20)
Median length of psychosis (untreated) in days: 83 / 107
Number of inpatient hospitalisation: 12 / 14

**Baseline stats:**
[ACE / Befriending]
Positive symptoms (psychotic subscale of BPRS): 11.68(4.17) / 12.29(4.50)
Negative symptoms (SANS): 22.55(11.66) / 25.55(14.86)
SOFAS: 52.10(11.77) / 51.84(7.09)

**Notes about participants:**
[ACE / Befriending]
Mean neuroleptic dosage in CPZ equiv: 224(112) / 297(136)
Number who received ECT: 4 / 1

**Interventions** **Intervention - group 1.:** ACE (Active Cognitive Therapy for Early Psychosis), Maximum of 20 sessions of therapy over 14 weeks; n=31

**Intervention - group 2.:** Befriending; n=31

**Notes about the interventions:**
ACE
-The ACE manual utilised an adapted approach derived form other manualised CBT interventions
-Involves the assessment of presenting psychotic and non-psychotic symptoms followed by the formulation of the relationship between these complaints and the participant's life history. Problems are prioritised according to a flowchart that directed the ACE therapy.

Befriending
-based on the befriending therapy used in previous studies
-aimed to control for time in therapy, participant expectations and positive experiences of therapy.
-consisted of talking about neutral topics that interested the participant or engaging in activities such as board games, walking or playing sport. The therapist's primary goal was to keep the participant engaged for the full duration of the session and to keep the conversation or activity as close to a neutral chat as possible.

Training
The therapists received 3 months of training in the treatments and were supervised throughout the trial.

**Outcomes** **Death:** Suicide

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Global state & service outcomes (e.g. CGI):** Days in hospital

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state Positive symptoms - measured using the psychotic subscale of the BPRS, SANS

| | |
|---|---|
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning SOFAS |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Well covered |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **JENNER2004** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All participants randomised and who gave consent |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - The Netherlands |
| | **Number of people screened, excluded & reasons:** 100 approached, 22 ineligible, 2 more which were excluded after randomisation as one was found to have concealed primary substance abuse and the other was assigned to control but erroneously received experimental treatment. |
| | **Notes about study methods:** Randomisation by minimisation procedure, conducted by independent medical technology unit of the university hospital. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] Paranoid schizophrenia 78% |

**Diagnosis:** Other schizophrenia related [%] Schizoaffective 15%
Psychosis NOS 7%

**Diagnostic tool:** Other method - SCAN interview

**Inclusion criteria:**
- Experiencing auditory hallucinations for >2 years after adequate treatment
- Diagnosis of non-affective psychosis, including schizophrenia, schizoaffective and psychotic disorder NOS
- Former use of at least two antipsychotics in adequate doses or period according to Dutch Psychiatric Association guidelines
- No previous CBT for auditory hallucinations
- No current misuse of psychoactive drugs or alcohol (moderate use of cannabis or alcohol was allowed)
- Estimated IQ >80.

**Total sample size:** No. randomised - 80

**Total sample size:** ITT population - 69

**Gender:** % female 46%

**Age:** Mean 36 (11.2)

**Ethnicity:** No mention

**Setting:** Outpatient

**History:** Duration of hallucinations (years): 12 (10.4)
Lifetime admissions: 3

**Baseline stats:**
[HIT / TAU]
PANSS Total: 60.0 (15.6) / 60.4 (12.5)

**Interventions**

**Intervention - group 1.:** HIT; n=37

**Intervention - group 2.:** TAU; n=39

**Notes about the interventions:**
Hallucination-focused integrated treatment (HIT)
Multimodal intervention focusing on regaining control and command over persistent hallucinations, integrating motivational, behavioural, cognitive, psychoeducational and rehabilitative elements. The approach is a directive style of single family therapy that integrates motivational interventions, training in coping skills, CBT, psychoeducation and operant conditioning regarding medication. Positive outreach crisis intervention was available around the clock. Programme comprised of approx. 20 1-hour sessions over 9 to 12 months.

TAU
Routine care delivered by community mental health teams, includes psychiatric, social, financial, occupational management, crisis

intervention, and day patient care (drop-in centres and rehabilitation activities).

Where possible, contact time was controlled in the two conditions to be similar.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS, PSYRATS, AHCL (Auditory Hallucinations Coping List)

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Social Disabilities Schedule

**Engagement with services (e.g. SES):** Average score/change in engagement with services - Adherence to treatment

**Other:** Use of medications (antipsychotics and adjuncts)

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** ++

**Study ID**

**LECLERC2000**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Type of analysis:** ITT - Those who dropped out were allocated to an ITT group although some never attended a single therapy sessions all

completed each of the evaluations at the 3 time points. The authors note that "the fact that they were paid for each of these evaluations may help to explain their assiduousness in this regard"

**Blindness:** Only raters blind

**Duration:** No. weeks of treatment - 12

**Duration:** Length of follow-up - 6 months follow-up

**Raters:** Independent of treatment

**Design:** Multi-centre - three different treatment setting in Montreal, Canada

**Number of people screened, excluded & reasons:** Not reported

**Notes about study methods:** Randomisation procedure not reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] % Not reported

**Diagnosis:** Other schizophrenia related [%] schizoaffective disorder - % not reported

**Diagnosis:** Other [%] paranoid psychosis - % not reported

**Diagnostic tool:** Other DSM DSM-III-R

**Inclusion criteria:**
- diagnosis of schizophrenia, schizoaffective disorder or paranoid psychosis.
- ability to speak, read and write French
- able to give informed consent

**Total sample size:** No. randomised - 99

**Gender:** % female 27%

**Age:** Mean 40.6(10.7)

**Ethnicity:** 89.2% were of French-Canadian origin

**Setting:** Inpatient

**Setting:** Outpatient

**History:**
Age of first hospitalisation = 24.2(6.8).
[CBT / control / ITT group]
number of years of lifetime hospitalisation: 17.83(11.74) / 11.80(8.65) / 11.88(7.66)
mean number of hospitalisations: 4.19(3.79) / 3.77(3.95) / 4.47(2.50)

**Baseline stats:**
[CBT / control group]
PANSS positive: 2.38(0.88) / 2.26(0.79)

PANSS negative: 2.34(1.01) / 2.49(1.13)
PANSS general: 1.89(0.54) / 1.89(0.57)

**Interventions** **Intervention - group 1.:** Coping Skills module, 24 group meetings over 12 weeks; n=55

**Intervention - group 2.:** Control; n=44

**Notes about the interventions:**
Coping skills module
The module developed by the first author comprises 24 group meetings over 12 weeks, each lasting 60 minutes. Paperwork, discussion and peer support are part of these sessions and the module includes a notebook containing the entire contents of the meetings. The module consists of seven steps each with their own goals and pencil-and-paper exercises. The module's training for coping and its subsequent use was designed to foster the development of competence and have a positive influence on self-esteem. The group leader helps participants use situations in their daily life and review the whole process as often as possible.

Training
The six groups were led by the first author and a women co-leader.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS negative, positive and general subscales; RSES

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - ILSS

**Other:** Stress appraisal measure
Cybernetic coping scale

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **LECOMTE2008** |
| **General info** | **Funding source:** Non-industry support<br>**Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial<br>**Type of analysis:** ITT analyses were performed on the entire sample<br><br>For the HLM model drop-outs were not excluded from the analyses as long as they had completed at least one assessment time.<br>**Blindness:** Only raters blind<br>**Duration:** Length of follow-up - 6 months<br>**Duration:** No. weeks of treatment - 12<br>**Raters:** Independent of treatment<br>**Design:** Multi-centre - Various early psychosis intervention programmes and community mental health clinics in Quebec and British Columbia, Canada<br>**Number of people screened, excluded & reasons:** Of the 210 people approached, 129 met inclusion criteria and gave informed consent. Of the 210 people approached, 38 refused consent, 7 were not eligible and 36 withdrew before randomisation.<br>**Notes about study methods:** Participants were randomised by cohort in one of two ways. The first cohorts were randomised between the three groups only once a sufficient number of clients were recruited in order to simultaneously run the two treatment groups and the control group from the same site. For the less populated sites, such as certain suburbs, once sufficient numbers were recruited to run one treatment group and half a control group, the clients were randomised between the two, and the chosen treatment was decided by randomisation as well. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] - 75% had a primary diagnosis in the schizophrenia spectrum<br>**Diagnosis:** Other [%] - 25% had a primary diagnosis of a mood disorder with psychotic features.<br>**Diagnostic tool:** DSM-IV<br>**Inclusion criteria:**<br>- aged 18 - 35,<br>- fluent (verbally as well as reading and writing skills) in one of the official languages (English and French),<br>- currently presenting with persistent or fluctuating psychotic symptoms (defined as delusions or hallucinations appearing occasionally, such as in periods of stress)<br>- consulted for the first time a mental health professional for psychotic symptoms in the past two years |

- non-affective psychosis was preferred but individuals with unclear diagnoses at the time of the referral were also accepted.

**Exclusion criteria:**
- experiencing an organic disorder
- already received one of the interventions
- not being able to give informed consent (verified by a true-false questionnaire)

**Total sample size:** No. randomised 129

**Total sample size:** ITT population 129 - (although table 2 used only those available at follow-up)

**Gender:** % female 27%

**Age:** Mean 24

**Ethnicity:** Caucasian - 66%
Asian - 10%
First Nation - 3%
Other - 21%

**Setting:** Outpatient - Individuals were only recruited once they had been discharged from hospital

**History:**
[CBT / SM / Control]
Age of first hospitalisation: 21.7 / 22.0 / 21.7

**Baseline stats:**
[CBT / SM / Control]
BPRS total: 42.7 / 41.0 / 41.3

**Notes about participants:** Participants had been diagnosed with a psychotic disorder for an average of 1.2 year (S.D. 0.44) prior to entering the study.

**Interventions** **Intervention - group 1.:** CBT, 24 sessions, twice weekly over 12 weeks; n= 48

**Intervention - group 2.:** Skills training symptom management (SM), 24 sessions, twice weekly over 12 weeks; n=54

**Intervention - group 3.:** Control; N=27

**Notes about the interventions:**
CBT
The CBT manual was developed by three of the authors and integrates the principles and philosophy of individual CBT for psychosis, but adapted to a group format and tailored for first episodes. The manual is in 4 parts: 1) Stress: how it affects me, 2) Testing hypotheses and looking for alternatives, 3) Drugs, alcohol and how I feel, 4) Coping and competence.

SM
The manual used in this study was the symptom management (SM) module developed by UCLA Psychiatric Rehabilitation Consultants. The treatment aims at building four skill areas: 1) Identifying warning signs of relapse, 2) Managing warning signs, 3) Coping with persistent symptoms and, 4) Avoiding alcohol and street drugs. Each section follows the exact same format: Introduction to skill area, Videotape questions and answers, Role-plays, Resource management, Outcome problems (problem solving), In vivo exercises and, Homework assignments. The therapists are instructed to model appropriate interaction styles and behaviors, and to teach clients how to effectively use the skills by using repetition and encouragements.

Control
Clients in the control group could receive on of the two treatments, should they still wish to, after being in the study for a minimum of 9 months.

Training
Each intervention was led by two co-therapists of different genders, one from the site's mental health team and one from the research team. The therapists all had previous experience working with individuals with psychosis (average: 6 years) and had a degree in occupational therapy (20%), nursing (50%), psychology (10%), or social work (20%). None had previous training in CBT, and less than one-third had experience in skills training or group experience. The therapists received 2 days of intensive training in the treatment they were to offer by one of the authors. Approximately 50% of the therapists offered both treatments; being trained in SM first and conducting a group before receiving the CBT training. All the sessions were videotaped for quality control.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS; RSES

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Social provision scale

**General and psychosocial functioning (e.g. SFS):** Clinically significant response in general functioning defined as a drop in BPRS scores of two or more on any BPRS item. (A drop of 10 on the total score for the CBT group reflects a significant improvement for most participants.)

**Other:** self-report measures on medication change
Cybernetic coping skills
Insight scale
Addiction Severity scale

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50% Although in total - 70% were not followed up in the SM group at 6 months.

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Well covered

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**MCLEOD2007**

**General info**

**Funding source:** Not mentioned

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** Completer - All participants completed the study

**Blindness:** No mention

**Duration:** Length of follow-up - 6 months - although data does not seem to be reported for 6 month follow-up. Data is reported for baseline and post-treatment only

**Duration:** No. weeks of treatment - 8

**Raters:** Independent of treatment

**Design:** Single-centre - No details

**Number of people screened, excluded & reasons:** 29 people were referred, 4 had benevolent voices and chose not to participate, 3 found the concept of a group too threatening and 2 did not want to travel to the group.

**Notes about study methods:** Randomisation procedure not reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:** DSM-IV diagnosis of schizophrenia and experiencing auditory hallucinations.

**Exclusion criteria:** Not stated

**Total sample size:** No. randomised 20

**Gender:** Not stated

**Age:** Mean - Details not reported
**Ethnicity:** Not reported
**Setting:** Inpatient
**Setting:** Outpatient
**History:** Not reported
**Baseline stats:** Not reported in either part 1 or 2

**Interventions**

**Intervention - group 1.:** CBT, 8 sessions; n=10
**Intervention - group 2.:** TAU; n=10
**Notes about the interventions:**
Experimental group
8-week programme utilising coping strategy enhancement, power and control cognitive behavioural interventions. The sessions were based upon a CBT approach and had a specific structure and format of aims and objectives. The techniques of traditional cognitive therapy, along with Socratic questioning, reflection and summarising were used.

Control group
Received TAU which included routine individual follow-up

Training
No details reported

**Outcomes**

**Other:** Frequency of voices; perceived power of voices and level of distress

NB: Outcomes were reported in part 2 [McLeod 2007a]

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed
**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately
**1.3 An adequate concealment method is used.:** Not addressed
**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed
**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed
**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed
**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed
**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **PENADES2006** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Missing data from dropouts were replaced by the baseline scores following the "carry forward" method. |
| | **Type of analysis:** LOCF |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 16 |
| | **Duration:** Length of follow-up - 6 months |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Participants were recruited from the hospital clinic mental health centre which serves part of the Barcelona area |
| | **Number of people screened, excluded & reasons:** 52 patients screened, 12 excluded from the randomised study due to: not meeting inclusion criteria (8) and refusal to participate (4) |
| | **Notes about study methods:** Randomisation was independently conducted. Researcher took no part whatsoever in the implementation of assignments. A random number table was used to generate lots that were drawn for sealed envelopes which assigned patients to CRT to CBT groups. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- age <55<br>- presence of negative symptoms confirmed by the PANSS,<br>- presence of cognitive impairments confirmed by a battery of neuropsychological tests. |
| | **Exclusion criteria:**<br>- IQ < 85<br>- organic cerebral diseases or primary diagnosis of substance misuse, psychiatric comorbidity |

- psychotic exacerbation in the previous 6 months, plans to change medication during the treatment phase.

**Total sample size:** No. randomised - 40

**Total sample size:** ITT population - 40

**Gender:** % female 42%

**Age:** Mean 35

**Ethnicity:** not reported

**Setting:** Other - Not stated

**History:** the participants on average had an illness duration of 13 years,

**Baseline stats:**
[CRT / CBT / TAU]
PANSS positive: 11.13(3.0) / 11.41(2.6) / 10.85(2.5)
PANSS negative: 19.87(8.1) / 20.47(6.0) / 19.01(7.1)
PANSS psychopathology: 35.69(6.3) / 35.41(7.1) / 35.40(8.7)

**Notes about participants:**
[CRT / CBT / TAU]
Medication (n)
Risperidone: 5 / 10 / 10
Olanzapine: 12 / 8 / 10
Clozapine: 3 / 2 / 0

**Interventions** **Intervention - group 1.:** CRT; n=20

**Intervention - group 2.:** CBT, n=20

**Intervention - group 3.:** TAU, n=20

**Notes about the interventions:**
CRT
This was set out in the Frontal/Executive programme. The programme was implemented on an individual basis, using mainly paper and pencil tasks. An errorless learning approach was adopted in tasks of progressive complexity and the problem was set, as far as was possible, at the subject's own pace. The main instructional technique was scaffolding. The patients received 40 1-hour sessions two or three times a week over 4 months.

CBT
A similar number of CBT hours were conducted on an individual basis following a manualised approach.

TAU
All the patients reported a psychotropic medication visit in the 8 weeks preceding study entry and none reported receiving any type of individual psychotherapy.

Training
Not reported

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state PANSS positive, PANSS negative

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - LSP

**Cognitive functioning:** Average score/change in cognitive functioning comprehensive battery of neuropsychological subtests which of which composite scores were obtained in the following domains: Working memory, psychomotor speed, verbal memory, nonverbal memory, executive function.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

| | PINTO1999 |
|---|---|
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Naples, Italy |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia<br>- No evidence of current substance abuse or organic pathology<br>- Treatment-refractory schizophrenia as documented by >=2 previous neuroleptic drug trials of at least 6 weeks at a dose of >600mg chlorpromazine equivalent |
| | **Total sample size:** No. randomised 41 |
| | **Total sample size:** ITT population - 37 completers |
| | **Gender:** % female 31% |
| | **Age:** Mean 34 |
| | **Ethnicity:** Not reported |
| | **Setting:** Inpatient |
| | **Setting:** Outpatient |
| | **History:**<br>[CBT+SST / Supportive therapy]<br>Illness duration, years: 9.2(3.3) / 8.2(2.9)<br>Hospital admissions: 11.6(7.9) / 11.7(6.6) |

**Baseline stats:**
[CBT+SST / Supportive therapy]
BPRS: 83.1(21.7) / 81.7(20.6)

**Notes about participants:**
All participants were on Clozapine
[CBT+SST / supportive therapy]
Clozapine dose, mg: 552.6(129.6) / 547.2(109.1)

**Interventions** **Intervention - group 1.:** CBT+SST, 6 months; N = 20

**Intervention - group 2.:** Supportive therapy, 6 months; N=21

**Notes about the interventions:**
CBT+SST
The CBT intervention focussed on improving clients' abilities to manage their current psychotic symptoms and was based on the manual by Fowler et al. Skills training methods were used to improve social behaviours including self-case, medication self-management, social conversation, interpersonal problem solving, self-directed recreation, family communication and management of personal resources. Both the CBT and SST components involved rehearsal, positive reinforcement, in vivo exercises and homework assignments.

Supportive therapy
Individual supportive therapy sessions included basic psychoeducation about the nature and treatment of schizophrenia, active listening, empathy and reassurance, reinforcement of the clients; health-promoting initiatives, help in managing a crisis and advocacy of the clients' needs.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS, SANS, SAPS

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**

**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| **Study ID** | **RECTOR2003** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Weak - only those who completed >4 treatment sessions were kept in analysis |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 24 |
| | **Duration:** Length of follow-up - 6 months |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Two large outpatient psychiatric facilities in Toronto and Ontario, Canada |
| | **Number of people screened, excluded & reasons:** Of the patients who completed assessment and were successfully randomized (n= 50), the dropout rate was equivalent in the two treatment groups: five patients (17%) did not complete the assessment phase of CBT, dropping out after three sessions or fewer, and three patients (14%) assigned to the standard treatment condition dropped out within the first 4 weeks of treatment, v2(1,50) = 0.79, p>0.78. |
| | **Notes about study methods:** Randomisation was performed by members of the research team who were not involved in either the baseline, posttreatment or follow-up assessments or in patient treatment. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] Not reported |
| | **Diagnosis:** Other schizophrenia related [%] Not reported |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia or schizoaffective disorder based SCID-I<br>- Presence of persistent positive and negative psychotic symptoms in the past 6 months as determined by the SCID-I interview<br>- Stable treatment with antipsychotic medications<br>- Age 18–65 |
| | **Exclusion criteria:**<br>- Suspected organic brain pathology |

- Concurrent substance misuse or dependence
- Past treatment with either behavioral or CBT in either individual or family format

**Total sample size:** No. randomised - 50

**Total sample size:** ITT population - 42 completed at least 4 sessions

**Gender:** % female
CBT: 38%
TAU: 62%

**Age:** Mean
CBT: 37.5 (8.3)
TAU: 41.2 (10.9)

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
[CBT / TAU]
Age first psychotic symptoms: 21.0 (5.7) / 19.2 (7.9)
Age first diagnosed: 25.3 (6.4) / 23.2 (7.0)
No. of hospitalisations: 5.1 (4.9) / 5.8 (6.3)
Years on neuroleptics: 13.9 (9.4) / 17.9 (10.0)

**Baseline stats:**
[CBT / TAU]
PANSS General: 31.0 (7.5) / 34.3 (11.2)
BDI: 17.6 (11.8) / 18.9 (12.1)

**Notes about participants:** Patients were on a range of conventional and atypical neuroleptics as well as antidepressant medications throughout the duration of the study. Patient groups did not differ in terms of the degree of use of atypical medications (CBT-ETAU= 63%; ETAU = 56%), v2(1,42) = 0.39, p>0.76, or in terms of antidepressant use (CBT-ETAU = 46%; ETAU = 56%). Only two patients (one in CBT-ETAU, one in ETAU) changed class of medications from treatment with a conventional to an atypical neuroleptic over the duration of the study.

**Interventions** **Intervention - group 1.:** CBT: 20 sessions on a weekly basis for 6 months; n=24

**Intervention - group 2.:** ETAU; n=18

**Notes about the interventions:**
CBT
Delivered on an individual basis for 6 months, guided by the principles and strategies developed by Beck in the treatment of the emotional disorders and tailored to treat the specific symptoms of schizophrenia within a diathesis-stress framework. Unlike the step-by-step

manualisation of the CT of the emotional disorders, the preferred approach here has been to develop specific modules that can be flexibly employed to treat selective symptoms of psychosis depending on the patient's presentation.

Enhanced TAU (ETAU)
Comprehensive psychiatric management with optimised medication and case management from social worker, nurse and/or OT. Patients also attended psychoeducational groups and received housing help and home-based outreach during crises. ~2hour/month contact time with services. This is considered enriched management compared with routine community care.

Both treatment groups received ETAU.

Training
The principal author, two doctoral level psychologists and one psychiatrist, all with formal training and practice in cognitive–behavioral interventions, provided CBT. Each therapist had worked in this therapeutic modality exclusively for an average of 4.5 years (S.D. = 1.7). Therapists met in regular supervision meetings and assessed adherence to the treatment protocol by reviewing audiotaped sessions and discussing cases.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS general, PANSS negative, PANSS positive, BDI

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - PANSS: 20% reduction represents a clinically significant change

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** +

| Study ID | STARTUP2004 |
|---|---|
| General info | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| Method | **Type of study:** Individual randomised trial (effectiveness/pragmatic) |
| | **Type of analysis:** ITT - All participants who had completed >=12 sessions (CBT) were considered ITT - but not all such participants were followed up and attempts were not made to deal with missing data |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 25 |
| | **Duration:** Length of follow-up - 6 months |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Three acute psychiatric hospitals in England |
| | **Number of people screened, excluded & reasons:** The 279 patients who were considered to be eligible were invited to participate when their psychiatrists declared them to be capable of informed consent. The invitation was declined by 100, and 38 were excluded because, by that time, more than 28 days had passed since they had been admitted (one of the exclusion criteria). Those who accepted were then excluded if, during a baseline assessment, they were found not to be suffering an acute psychotic episode (N=13), their diagnoses could not be confirmed according to DSM-IV criteria (N=7), they had been dependent on alcohol or illicit drugs according to DSM-IV criteria during the past year (N=12), or their IQs, assessed by the Quick Test (Ammons & Ammons, 1962), were below 80 (N=19). |
| | **Notes about study methods:** Randomisation: 43 were assigned at random by inviting the patient to toss a coin in front of the assessor, to a TAU control group, and 47 were assigned to TAU plus CBT. |
| Participants | **Diagnosis:** Schizophrenia [% of sample] 87% |
| | **Diagnosis:** Other schizophrenia related [%] Schizoaffective 8%<br>Schizophreniform 6% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- Aged between 18 and 65 years<br>- Resident within the catchment area<br>- Had received a clinical diagnosis of schizophrenia, schizophreniform or schizoaffective disorder<br>- Appeared to be experiencing an acute psychotic episode<br>- Not already receiving psychological treatment<br>- Showed no evidence of organic mental disorder. |

**Exclusion criteria:**
- more than 28 days had passed since they had been admitted
- not to be suffering an acute psychotic episode
- dependent on alcohol or illicit drugs according to DSM-IV criteria during the past year
- IQs, assessed by the Quick Test <80

**Total sample size:** No. randomised 90

**Total sample size:** ITT population - 75 available to follow-up from informant interviews

**Gender:** % female 24%

**Age:** Mean CBT: 30.5 (8.7)
TAU: 31.3 (9.6)

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[CBT / TAU]
Age at onset: 23.5 (5.6) / 24.4 (6.0)

**Baseline stats:**
[CBT / TAU]
SAPS Psychotic: 7.4 (2.0) / 7.3 (2.0)
SAPS Disorganization: 3.3 (2.6) / 3.4 (2.2)
SANS total: 9.4 (3.5) / 8.4 (2.9)
BPRS total: 46.0 (7.4) / 45.5 (8.0)
SFS: 93.3 (8.9) / 96.2 (9.4)
GAF: 33.5 (10.0) / 38.0 (9.1)

**Interventions** **Intervention - group 1.:** CBT: ~25 weekly 90 minute sessions; n=47

**Intervention - group 2.:** TAU; n=43

**Notes about the interventions:**
TAU
Treatment as usual (TAU) in the three participating Trusts of the UK NHS consists of pharmacotherapy, nursing care during hospitalisation and community care after discharge. Each patient has a keyworker who devises and implements a care plan that might include any or all of the following: day hospital or day centre attendance, home visits with counselling, support worker involvement, sheltered work, social clubs and outings, help obtaining benefits and accommodation, carer support. No attempt was made to influence the course of psychiatric or community care.

CBT
Provided as an addition to TAU, followed the objectives, strategy and techniques of a manualised approach. This is a highly individualised, needs-based form of CBT for psychotic disorders and is based on collaborative empiricism and (evolving) cognitive-behavioural formulations. It has been shown to be an effective adjunct to standard treatment for outpatients with residual psychotic symptoms but has yet to be evaluated with acutely ill inpatients.

Training
CBT was provided by the first two authors and one other clinical psychologist. The authors were employed as specialists in serious mental illness and conducted CBT for schizophrenia on a routine basis. They had had 10 years and 2 years of post-qualification experience at the outset of the trial and had 28 and 17 clients, respectively, assigned to them for treatment in the current trial. The third therapist had recently undertaken 1-year specialist training in CBT for psychotic disorders. He had two clients assigned to him in the trial. The therapists met at least once a month for peer supervision and to maintain adherence.

**Outcomes**

**Death:** Suicide

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAF

**Global state & service outcomes (e.g. CGI):** Clinically significant response in global state - Clinically reliable change defined by a +-8.7 movement on GAF

Clinically significant change defined by a 57 point cut-off on GAF, or suicide

Above reversed to produce number for: No significant improvement (worst case scenario applied). For TAU the suicide has been counted as deterioration and as drop out, hence in the worst case scenario calculation, the total number deteriorated or no change + drop-out - 1 has been used)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - SAPS, SANS, BPRS

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - SAPS: proportion with residual disorganisation symptoms

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SFS

**Other:** Medication dosages, imprisonment - Does not state which group the imprisonment occurred in

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Poorly addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **TROWER2004** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 6 months |
| | **Duration:** No. weeks of treatment - 24 |
| | **Duration:** Mean duration (for each group) CT: median 16 sessions |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - The participants were recruited from local mental health services in Birmingham and Solihull, Sandwell and a West Midlands semi-secure unit for offenders with mental illness. |
| | **Number of people screened, excluded & reasons:** 224 referrals were screened, from which 69 patients were identified as being eligible for the study and were invited to participate. Of these, 31 refused consent, leaving a sample of 38 consenting to randomisation. |
| | **Notes about study methods:** Random assignment by means of a computerised random number generator administered by the Birmingham Clinical Trials Unit independent of the research team, to ensure the research associate was blind to the allocation at baseline and post-testing. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] CT for command hallucinations: 33% schizophrenia, 28% paranoid schizophrenia<br>TAU: 55% schizophrenia, 25% paranoid schizophrenia |
| | **Diagnosis:** Other [%] CT for command hallucinations: 6% personality disorder, 6% psychotic depression, 6% OCD |

TAU: 10% personality disorder, 10% psychotic depression

**Diagnosis:** Other schizophrenia related [%] CT for command hallucinations: 22% schizoaffective,

**Diagnostic tool:** ICD-10

**Inclusion criteria:**
- ICD–10 diagnosis of schizophrenia or related disorder with command hallucinations for at least 6 months
- Recent history of compliance with, and appeasement of, voices with 'severe' commands, including harm to self, others or major social transgressions.

**Exclusion criteria:** - Primary organic or addictive disorder

**Total sample size:** No. randomised 38

**Gender:** % female 37%

**Age:** Range 17-60

**Age:** Mean 35.5 (10.4)

**Ethnicity:** White 71%
Black 18%
Asian 5%
Other 5%

**Setting:** Inpatient

**Setting:** Outpatient

**History:**
CT for command hallucinations / TAU
Duration of voices (years) 13.4 (9.9) / 10.0 (5.7)
Duration of commands (years) 8.8 (7.9) / 8.6 (5.9)

**Baseline stats:**
CT for command hallucinations / TAU
PANSS Positive 21.9 (3.1) / 20.8 (3.2)
PANSS Negative 20.8 (6.4) / 21.5 (6.4)
PANSS General 36.3 (6.6) / 35.9 (6.7)

**Notes about participants:** Medication: At baseline, 13/18 (72%) in CT for command hallucinations were prescribed atypicals, including 5 patients taking clozapine; in TAU, 13/20 were prescribed atypicals (65%), including 7 patients taking clozapine.

**Interventions** **Intervention - group 1.:** CT for command hallucinations; n=18

**Intervention - group 2.:** TAU; n=20

**Notes about the interventions:**
CT for command hallucinations
Targets four core dysfunctional beliefs that define the client–voice (social rank) power relationship: that the voice has absolute power and control; that the client must comply or appease, or be severely punished; the identity of the voice (e.g. the Devil); and the meaning attached to the voice experience (e.g. the client is being punished for past bad behaviour). Using the methods of collaborative empiricism and Socratic dialogue, the therapist seeks to engage the client to question, challenge and undermine the power beliefs, then to use behavioural tests to help the client gain disconfirming evidence against the beliefs.

TAU
Delivered by CMHTs. TAU was extensive, involving 18 categories of service and admissions.

Training
CT for command hallucinations sessions were delivered by a clinical psychologist experienced in cognitive therapy and supervised in CTCH. A behavioural scientist independent of the trial rated a random selection of early, middle and late audiotaped sessions (13 in total) using the Cognitive Therapy Checklist.

**Outcomes**

**Death:** Natural causes

**Death:** Suicide

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) unsure

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - Voice Compliance Scale, Belief About Voices Questionnaire, Voice Power Differential Scale, Omniscience Scale, PANSS - means not reported, change score reported for only CBT group, PSYRATS, CDSS

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **VALMAGGIA2005** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All randomised participants, excluding 4 patients whose data were lost by assessor |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 6 months |
| | **Duration:** No. weeks of treatment - 22 weeks |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Various mental health hospitals across The Netherlands and one in Belgium |
| | **Number of people screened, excluded & reasons:** 66 assessed for eligibility: 2 did not meet inclusion criteria, 2 refused consent, 62 randomised |
| | **Notes about study methods:** For the randomisation procedure, the project coordinator had two baskets: a 'treatment' basket which contained sealed envelopes with lots for each of the two treatment conditions and a 'used' basket where the drawn lots could be placed. To ensure the anonymity of the participants, each individual was given a code, and the coordinator used a form to communicate the results of the random assignment to the local therapist. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- Age 18–70 years;<br>- DSM-IV diagnosis of schizophrenia<br>- Residual delusions or auditory hallucinations experienced for at least 3 months<br>- A stable medication regimen (last medication change more than 6 weeks prior to recruitment).<br>- A confirmed resistance to psychopharmacological treatment was established according to the following conventional criteria: symptoms unresponsive to at least two different antipsychotic compounds including an atypical antipsychotic, taken for enough time and in an acceptable dosage, as advised in the prescription guidelines. |
| | **Exclusion criteria:**<br>To exclude patients experiencing predominantly symptoms from the disorganisation dimension, the following exclusion criteria were also applied: |

- Conceptual disorganisation;
- Stereotypic thinking;
- Disorientation, measured by the PANSS, items P254, N753, and G1052;
- Drug or alcohol addiction as a primary diagnosis (patients using drugs or alcohol below the level of this criterion were included);
- Mental retardation (premorbid IQ580);
- Organic conditions;
- CBT given for persistent psychotic symptoms in the past.

**Total sample size:** No. randomised 62

**Total sample size:** ITT population - 58; 4 of 62 had data lost by assessor

**Gender:** % female 29%

**Age:** Range - 18-70

**Age:** Mean - 35.5 (10.8)

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:** Years of positive symptoms: 10.7 (7.5)
Years since diagnosis: 9 (7)

**Baseline stats:**
[CBT / Supportive counselling]
PANSS General: 33.81 (9.73) / 33.47 (7.03)
PSYRATS Auditory Hallucination (cognitive): 5.63 (5.34) / 7.83 (4.86)
PSYRATS Delusion (cognitive): 9.14 (4.64) / 7.09 (5.47)

**Notes about participants:** Participants had tried five different antipsychotics on average (if the same medication was taken twice, it was counted as one). All patients had taken at least one atypical antipsychotic and more than 2/3 had taken clozapine. All patients were taking antipsychotic medication during the trial, and the majority were on atypical antipsychotic regimens. Nine patients were using a typical compound during the trial because they had been given depot medication. The medication regimens were kept stable during the study. Three patients experienced a relapse and their medication had to be changed; these patients were considered to have withdrawn from the study.

**Interventions** **Intervention - group 1.:** CBT: 16 sessions in 22 weeks; n=36

**Intervention - group 2.:** Supportive counselling: 16 sessions in 22 weeks; n=26

**Notes about the interventions:**
CBT
A comprehensive treatment manual was written and the participating therapists were trained in using this protocol. CBT consisted of four phases: engagement, establishing links between thoughts, emotions and behaviour, reducing symptoms and associated distress, and relapse

prevention.

Supportive counselling
The supportive counselling protocol was a conventional method previously used in other studies. The therapist shows non-critical acceptance, warmth, genuineness and empathy.

Training
A comprehensive treatment manual was written and the participating therapists were trained in using this protocol.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Relapse

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - Relapse defined as >10 increase on PANSS positive symptom subscale with the deterioration in symptoms lasting >3 days

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state PANSS, PSYRATS

**Other:** Included number needed to treat

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** +

| Study ID | WYKES2005 |
|---|---|
| General info | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| Method | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Participants analysed in allocated group irrespective of whether they adhered to treatment. The analyses undertaken include all participants provided that their covariate measures and at least one post-treatment outcome measure were available. |
| | **Blindness:** No mention |
| | **Duration:** Length of follow-up - 26 weeks |
| | **Duration:** No. weeks of treatment - 10 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Rolling programme of referrals from CMHTs in defined geographical areas |
| | **Number of people screened, excluded & reasons:** 85 met entry criteria, consented to the trial and randomised |
| | **Notes about study methods:** Randomisation carried out independently in blocks of typically 12 |
| Participants | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV schizophrenia by chart review<br>- Persistent and distressing auditory hallucinations (Score 3 on PANSS hallucination item)<br>- No planned changes in medication during treatment period<br>- Age >=18<br>- Substance misuse or medical disorder does not significantly contribute to symptoms |
| | **Total sample size:** No. randomised 85 |
| | **Total sample size:** ITT population - Varied depending on outcome |
| | **Gender:** % female 41% |
| | **Age:** Mean 39.6 (10.4) |
| | **Ethnicity:** Not reported |
| | **Setting:** Outpatient |
| | **History:** 65% had first contact with services >=10 years ago<br>79% reported hearing voices at least daily and had little control over them |

**Baseline stats:**
[Group CBT / Control]
SBS: 11.6 (7.3) / 13.5 (9.7)
PSYRATS: 29.1 (5.3) / 26.8 (6.8)
Rosenberg self-esteem: 16.7 (3.9) / 18.2 (3.8)

**Notes about participants:** Medication: The most prescribed medications were clozapine (28%) and olanzapine (35%). 13 out of 85 participants were prescribed more than one neuroleptic.

17 people (20%) changed their medication during the trial; 10 people in the control group were provided with specific individual psychological therapy as part of their routine care thus contaminating the sample. The effect of these possible moderating effects was investigated in all analyses.

**Interventions**

**Intervention - group 1.:** Group CBT: 7 sessions; n=45

**Intervention - group 2.:** TAU; n=40

**Notes about the interventions:**
Group CBT
A manualised therapy for the positive symptoms of psychosis providing four key elements: engagement, collaborative discussion about an agreed model, cognitive restructuring of delusional beliefs and reducing negative self evaluation. A CBT group typically included 6-8 participants.

TAU
Treatment as usual (no details provided).

Training
The therapists who carried out this therapy were drawn from local services and then trained in group CBT techniques. Many but not all were experienced in providing individual CBT.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state PSYRATS Hallucinations Scale - Rosenberg self esteem

**Behaviour (e.g. NOSIE):** Average score/change in behaviour SBS (Social Behaviour Schedule), effective coping strategies

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**References of included studies (update)**

**BACH2002**

Bach, P & Hayes, S.C. (2002) The use of acceptance and commitment therapy to prevent the rehospitalization of psychotic patients: a randomized controlled trial. *Journal of Consulting and Clinical Psychology*. 70(5): 1129-1139.

**BARROWCLOUGH2006**

Barrowclough C, Haddock G, Lobban F, Jones S, Siddle R, Roberts C, Gregg L. (2006) Group cognitive-behavioural therapy for schizophrenia. Randomised controlled trial. *British Journal of Psychiatry*. 189: 527-532.

**BECHDOLF2004**

*Bechdolf,A.; Knost,B.; Kuntermann,C.; Schiller,S.; Klosterktter,J.; Hambrecht,M.; Pukrop,R. (2004) A randomized comparison of group cognitive-behavioural therapy and group psychoeducation in patients with schizophrenia. *Acta Psychiatrica Scandinavica* 110: 21 - 28.

Bechdolf,A.; Kohn,D.; Knost,B.; Pukrop,R.; Klosterkotter,J. (2005) A randomized comparison of group cognitive-behavioural therapy and group psychoeducation in acute patients with schizophrenia: outcome at 24 months. *Acta Psychiatrica Scandinavica* 112(3): 173 - 179.

**CATHER2005**

Cather,C.; Penn,D.; Otto,M.W.; Yovel,I.; Mueser,K.T.; Goff,D.C. (2005) A pilot study of functional Cognitive Behavioral Therapy (fCBT) for schizophrenia. *Schizophrenia Research* 74: 201 - 209.

**DURHAM2003**

Durham,R.C.; Guthrie,M.; Morton,R.V.; Reid,D.A.; Treliving,L.R.; Fowler,D.; Macdonald,R.R. (2003) Tayside-Fife clinical trial of cognitive-behavioural therapy for medication-resistant psychotic symptoms. Results to 3-month follow-up. *British Journal of Psychiatry* 182: 303 - 311.

**ENGLAND2007**

England,M. (2007) Efficacy of cognitive nursing intervention for voice hearing. *Perspectives in Psychiatric Care*. 43(2): 69 - 76.

**GARETY2008**

Garety, P.A., Fowler, D.G., Freeman, D., Bebbington, P., Dunn, G. & Kuipers, E. (2008) A randomised controlled trial of cognitive behavioural therapy and family intervention for the prevention of relapse and reduction of symptoms in psychosis. *British Journal of Psychiatry* 192: 412-423.

**GRANHOLM2005**

Granholm,E.; McQuaid,J.R.; Link,P.C.; Fish,S.; Patterson,T.; Jeste,D.V. (2008) Neuropsychological predictors of functional outcome in Cognitive Behavioral Social Skills Training for older people with schizophrenia. *Schizophrenia Research.* 100(1-3): 133-143.

*Granholm,E.; McQuaid,J.R.; McClure,F.S.; Auslander,L.A.; Perivoliotis,D.; Pedrelli,P.; Patterson,T.; Jeste,D.V. (2005) A randomized, controlled trial of cognitive behavioral social skills training for middle-aged and older outpatients with chronic schizophrenia. *American Journal of Psychiatry* 162(3): 520 - 529.

Granholm,E.; McQuaid,J.R.; McClure,F.S.; Link,P.C.; Perivoliotis,D.; Gottlieb,J.D.; Patterson,T.L.; Jeste,D.V. (2007) Randomized controlled trial of cognitive behavioral social skills training for older people with schizophrenia: 12-month follow-up. *Journal of Clinical Psychiatry* 68: 730 - 737.

**GUMLEY2003**

Gumley,A.; Karatzias,A.; Power,K.; Reilly,J.; McNay,L.; O'Grady,M. (2006) Early intervention for relapse in schizophrenia: impact of cognitive behavioural therapy on negative beliefs about psychosis and self-esteem. *British Journal of Clinical Psychology* 45(Pt 2): 247 - 260.

*Gumley,A.; O'Grady,M.; McNay,L.; Reilly,J.; Power,K.; Norrie,J. (2003) Early intervention for relapse in schizophrenia: results of a 12-month randomized controlled trial of cognitive behavioural therapy. *Psychological Medicine* 33(3): 419 - 431.

**JACKSON2005**

Jackson, H.J., McGorry, P.D., Killackey, E., Bendall, S., Allott, K., Dudgeon, P., Gleeson, J., Johnson, T., Harrigan, S. (2007) Acute-phase and 1-year follow-up results of a randomised controlled trial of CBT versus Befriending for first-episode psychosis: the ACE project. *Psychological Medicine*, in press.

**JACKSON2007**

Jackson,H.; McGorry,P.; Edwards,J.; Hulbert,C.; Henry,L.; Harrigan,S.; Dudgeon,P.; Francey,S.; Maude,D.; Cocks,J.; Killackey,E.; Power,P. (2005) A controlled trial of cognitively oriented psychotherapy for early psychosis (COPE) with four-year follow-up readmission data. *Psychological Medicine*. 35(9): 1295 - 1306.

**JENNER2004**

*Jenner,J.A.; Nienhuis,F.J.; Wiersma,D.; van de Willige, G (2004) Hallucination focused integrative treatment: a randomized controlled trial. *Schizophrenia Bulletin* 30(1): 133 - 145.

Jenner,J.A.; Nienhuis,F.J.; van de Willige,G; Wiersma,D. (2006) "Hitting" voices of schizophrenia patients may lastingly reduce persistent auditory hallucinations and their burden: 18-month outcome of a randomized controlled trial. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 51(3): 169 - 177.

Wiersma,D.; Jenner,J.A.; Nienhuis,F.J.; van de Willige,G. (2004) Hallucination focused integrative treatment improves quality of life in schizophrenia patients. *Acta Psychiatrica Scandinavica* 109(3): 194 - 201.

**LECLERC2000**

Leclerc, C., Lesage, A.D., Ricard, N., Lecomte, T., Cyr, M. (2000) Assessment of a new rehabilitative coping skills module for persons with schizophrenia. *American Journal of Orthopsychiatry* 70(3): 380-388.

**LECOMTE2008**

Lecomte, T., Leclerc, C., Corbiere, M., Wykes, T., Wallace, C.J., Spidel, A. (2008) Group cognitive behaviour therapy or social skills training for individuals with a recent onset of psychosis? Results of a randomised controlled trial. *Journal of Nervous and Mental Disease*, in press.

**MCLEOD2007**

McLeod, T., Morris, M., Birchwood, M. & Dovey, A. (2007) Cognitive behavioural therapy group work with voice hearers. Part 2. *British Journal of Nursing* 16(5): 292-295.

McLeod,T.; Morris,M.; Birchwood,M.; Dovey,A. (2007) Cognitive behavioural therapy group work with voice hearers. Part 1. *British Journal of nursing* 16: 248 - 252.

**PENADES2006**

Penades,R.; Catalan,R.; Salamero,M.; Boget,T.; Puig,O.; Guarch,J.; Gasto,C. (2006) Cognitive remediation therapy for outpatients with chronic schizophrenia: a controlled and randomized study. *Schizophrenia Research*. 87(1-3): 323 - 331.

**PINTO1999**

Pinto, A., La Pia, S., Mennella, R., Giorgio, D. & DeSimone, L. (1999) Cognitive-behavioural therapy and clozapine for clients with treatment-refractory schizophrenia. *Psychiatric Services* 50(7): 901-904.

**RECTOR2003**

Rector,N.A.; Seeman,M.V.; Segal,Z.V. (2003) Cognitive therapy for schizophrenia: a preliminary randomized controlled trial. *Schizophrenia Research*. 63:1-11.

**STARTUP2004**

Startup,M.; Jackson,M.C.; Bendix,S. (2004) North Wales randomized controlled trial of cognitive behaviour therapy for acute schizophrenia spectrum disorders: outcomes at 6 and 12 months. *Psychological Medicine* 34: 413 - 422.

Startup,M.; Jackson,M.C.; Evans,K.E.; Bendix,S. (2005) North Wales randomized controlled trial of cognitive behaviour therapy for acute schizophrenia spectrum disorders: two-year follow-up and economic evaluation. *Psychological Medicine* 35(9): 1307 - 1316.

Startup,M.; Jackson,M.C.; Startup,S. (2004) Insight and recovery from acute psychotic episodes: the effects of cognitive behavior therapy and premature termination of treatment. *Journal of Nervous and Mental Disease* 194(10): 740 - 750.

**TROWER2004**

Trower,P.; Birchwood,M.; Meaden,A.; Byrne,S.; Nelson,A.; Ross,K. (2004) Cognitive therapy for command hallucinations: randomised controlled trial. *British Journal of Psychiatry* 184: 312 - 320.

**VALMAGGIA2005**

Valmaggia,L.R.; van-der,Gaag M.; Tarrier,N.; Pijnenborg,M.; Slooff,C.J. (2005) Cognitive-behavioural therapy for refractory psychotic symptoms of schizophrenia resistant to atypical antipsychotic medication. Randomised controlled trial. *British Journal of Psychiatry* 186: 324 - 330.

**WYKES2005**

Wykes,T.; Hayward,P.; Thomas,N.; Green,N.; Surguladze,S.; Fannon,D.; Landau,S. (2005) What are the effects of group cognitive behaviour therapy for voices? A randomised control trial. *Schizophrenia Research* 77: 201 - 210.

**Characteristics of excluded studies (update)**

**Bechdolf 2002**

**Reason for exclusion:** Conference abstract

**DAVIS2005**

**Reason for exclusion:** CBT + vocational employment services - outside scope

**Gaudiano2006**

**Reason for exclusion:** -58% of participants had comorbid substance use disorder

**GRANHOLM2002**

**Reason for exclusion:** - letter to editor

**HALL2003**

**Reason for exclusion:** <50% schizophrenia

**JOLLEY2003**

**Reason for exclusion:** - <10 in TAU arm
- In final analysis only 8 participants were included in CBT group

**KINGSEP2003**

**Reason for exclusion:** - -ve quality assessment due to problems with randomisation, lack of allocation concealment, no ITT analysis etc.

**KRAJEWSKI1993**

**Reason for exclusion:** Conference abstract

**Levine1998**

**Reason for exclusion:** N<10

**LYSAKER2005**

**Reason for exclusion:** CBT + vocational employment services - outside scope

**LYSAKER2005B**

**Reason for exclusion:** CBT + vocational training - outside scope

**LYSAKER2007[LYSAKER2005]**

**Reason for exclusion:** Primary paper excluded
CBT + vocational training - outside scope

**MASTEROENI2005**

**Reason for exclusion:** Non-RCT

**MORRISON2004**

**Reason for exclusion:** Non-RCT

**MORRISON2007**

**Reason for exclusion:** Prevention study - outside scope

**OCONNOR2007**

**Reason for exclusion:** N<10 inattention placebo arm

**TAIT2002**

**Reason for exclusion:** - intervention arm <9 participants
- -ve quality assessment rating

**ZHANG2007**

**Reason for exclusion:** Paper is in Chinese

**References of excluded studies (update)**

Bechdolf,A.; Knost,B.; Kuntermann,C.; Schiller,S.; Hambrecht,M.; Klosterkotter,J.; Pukrop,R. (2002) Coping-oriented versus psychoeducational group therapy for post acute patients with schizophrenia: results of a 6 month follow-up. *Schizophrenia Research* 53: 264 - 265.

Davis, L.W., Laysaker, P.H., Lancaster, R.S., Bryson, G.J. & Bell, M.D. (2005) The Indianapolis Vocational Intervention Program: A cognitive behavioral approach to addressing rehabilitation issues in schizophrenia. *Journal of Rehabilitation Research and Development* 42(1): 35-46.

Gaudiano, B.A. & Herbert, J.D. (2006) Acute treatment of inpatients with psychotic symptoms using acceptance and commitment therapy: Pilot results. *Behaviour Research and Therapy*. 44: 415-437.

Granholm,E.; McQuaid,J.R.; McClure,F.S.; Pedrelli,P.; Jeste,D.V. (2002) A randomized controlled pilot study of cognitive behavioral social skills training for older patients with schizophrenia. *Schizophrenia Research* 53: 167 - 169.

Hall, P.L. & Tarrier, N. (2003) The cognitive-behavioural treatment of low self-esteem in psychotic patients: a pilot study. *Behaviour Research and Therapy*. 41: 317-332.

Jolley,S.; Garety,P.; Craig,T.; Dunn,G.; White,J.; Aitken,M. (2003 ) Cognitive therapy in early psychosis: A pilot randomized controlled trial. *Behavioural and Cognitive Psychotherapy*. 31(4): 473-478.

Kingsep, P; Nathan,P.; Castle,D. (2003) Cognitive behavioural group treatment for social anxiety in schizophrenia. *Schizophrenia Research* 63: 121 - 129.

Krajewski,C.; Classen,W.; Boesken,S. (1993) Comparison of art and cognitive therapy (IPT) with simultaneous cognitive and art therapy for schizophrenic patients regarding the change of cognitive processes. *Pharmacopsychiatry* 26: 171.

Levine, J., Narak, Y., & Granek, I. (1998) (1998) Cognitive group therapy for paranoid schizophrenics: Applying cognitive dissonance. *Journal of Cognitive Psychotherapy* 12(1): 3-12.

Lysaker,P.H.; Bond,G.; Davis,L.W.; Bryson,G.J.; Bell,M.D. (2005) Enhanced cognitive-behavioral therapy for vocational rehabilitation in schizophrenia: Effects on hope and work. *Journal of Rehabilitation Research and Development*. 42(5): 673 - 682.

Lysaker,P.H.; Davis,L.W.; Beattie,N. (2005) Effects of cognitive behavioral therapy and vocational rehabilitation on metacognition and coping in schizophrenia. *Journal of Contemporary Psychotherapy* 36(1): 25-30.

Lysaker,P.H.; Davis,L.W.; Beattie,N. (2007) "Effects of cognitive behavioral therapy and vocational rehabilitation on metacognition and coping in schizophrenia": Erratum. *Journal of Contemporary Psychotherapy* 37(2); 115.

Mastroeni,A.; Bellotti,C.; Pellegrini,E.; Galleti,F.; Lai,E.; Falloon,I.R.H. (2005) Clinical and social outcomes five years after closing a mental hospital: A trial of cognitive behavioural interventions. *Clinical Practice and Epidemiology in Mental Health*. 1: 25

Morrison,A.P.; French,P.; Parker,S.; Roberts,M.; Stevens,H.; Bentall,R.P.; Lewis,S.W. (2007) Three-year follow-up of a randomized controlled trial of cognitive therapy for the prevention of psychosis in people at ultrahigh risk. *Schizophrenia Bulletin*. 33(3): 682 - 687.

Morrison,A.P.; Renton,J.C.; Williams,S.; Dunn,H.; Knight,A.; Kreutz,M.; Nothard,S.; Patel,U.; Dunn,G. (2004) Delivering cognitive therapy to people with psychosis in a community mental health setting: An effectiveness study. *Acta Psychiatrica Scandinavica* 110(1): 36-44.

O'Connor,K.; Stip,E.; Pelissier,M.C.; Aardema,F.; Guay,S.; Gaudette,G.; Van Haaster,I; Robillard,S.; Grenier,S.; Careau,Y.; Doucet,P.; Leblanc,V. (2007) Treating delusional disorder: a comparison of cognitive-behavioural therapy and attention placebo control. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie*. 52(3): 182 - 190.

Tait,A.; McNay,L.; Gumley,A.; O'Grady,M. (2002) The development and implementation of an individualised early signs monitoring system in the prediction of relapse in schizophrenia. *Journal of Mental Health* 11(2): 141 - 153.

Zhang,L.; Kong,Y. (2007) Evaluation on cognitive behavior therapy applied in schizophrenia patients of convalescence stage with emotional disorder. *Chinese Nursing Research* 18(11A): 07 - 09.

## Cognitive remediation

| **Previous guideline review** | **1. Review type**<br>**2. Funding**<br>**3. Period covered**<br>**4. Data analysis**<br>**5. No. of studies**<br>**6. No. participants randomised** | **Interventions** | **Reported Outcomes** |
|---|---|---|---|
| Pilling S, Bebbington P, Kuipers E, Garety P, Geddes J, Martindale B, Orbach G, Morgan C.<br><br>Psychological treatments in schizophrenia II: meta-analyses of randomized controlled trials of social skills training and cognitive remediation.<br><br>*Psychological Medicine*, 2002, 32, 783-791. | 1. Systematic review of RCTs.<br>2. Intramural sources of support to the review: University College London. Extramural sources of support to the review: Department of Health, UK.<br>3. Database origin to 1999.<br>4. Meta-analysis of Odds Ratio and standardised mean difference.<br>5. 7.<br>6. 295. | 1. Cognitive remediation, defined as a programme focused on improving cognitive function using a procedure implemented with the intention of bringing about an improvement in the level of that specified cognitive function.<br>2. Occupational therapy.<br>3. The comparison group was matched with the experimental group, and differed only in that they were not receiving cognitive remediation. | 1. Verbal memory<br>a. Wechsler Memory Scale – Revised Logical Memory (Tompkins 1995; Medalia 2000)<br>b. Sentence span (Wykes 1999)<br>c. Word-list recall task (Benedict 1994)<br>2. Visual memory<br>a. Wechsler Memory Scale – Revised Visual Memory (Tompkins 1995)<br>b. Visual span (Wykes 1999)<br>3. Attention<br>a. Continuous Performance Test: degraded stimulus - perceptual sensitivity (Benedict 1994)<br>b. Continuous Performance Test: letter detection - absolute % correct (Medalia 1998)<br>4. Mental state: BPRS (Medalia 1998; Wykes 1999)<br>5. Planning (Tower of London task) (Wykes 1999)<br>6. Cognitive flexibility<br>a. Stroop task (Wykes 1999)<br>b. Wisconsin Card Sort Test (Wykes 1999; Bellack 2001)<br>c. Halstead Category Test (Bellack 2001)<br>7. Self esteem (Wykes 1999)<br>8. Drop out (Medalia 1998; Tompkins 1995; Wykes 1999; Medalia 2000) |
| **Update** | **Follow up to existing studies:** 3 papers provided follow-up data to existing RCTs: Wykes1999 (2 papers); Medalia2000 (1 paper)<br>**New studies:** 18 RCTs. | | **Notes:**<br>Definition updated |

**Characteristics of included studies (previous guideline)**

| Study | Methods | Participants | Interventions | Outcomes | Notes |
|---|---|---|---|---|---|
| **Benedict1994** | 14 sessions of 50 minutes.<br>Allocation: "randomly assigned, in sequence."<br>Blinding: not given.<br>Setting: outpatients day treatment centre, Buffalo, NY. | N=38. Diagnosis: schizophrenia (RDC).<br>History: no evidence of brain damage, mental retardation, or substance dependence, mean education level 11.2 (SD=2.1), average age at first hospitalisation 23.9 (SD=5.2), mean no. of days hospitalized 239.7, mean chlorpromazine equivalent level 330.5 mg/ml (SD=393.1). (SD=213.3).<br>Sex: 22 M, 16 F.<br>Age: mean 37.9 (SD=10.8). | 1. Guided practice on six computer-based attentional tasks: participants received a mean of 14.4 (SD=1.09) 50-minute sessions.<br>2. Control: no attention training. | Attention (Continuous Performance Test - CPT, Span of Apprehension Test - SAT).<br>Verbal memory (Word List Recall Task - WLRT).<br>Unable to use:<br>Scale for the Assessment of Negative Symptoms (SANS - no data).<br>Scale for the Assessment of Positive Symptoms (SAPS - no data). | |

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|---|---|---|---|---|---|
| **Hadas-Lidor2001** | Two to three 1-hour sessions/week for one year.<br>Allocation: "randomly assigned into two equal groups matched for gender, age, family status, education and subcategory of schizophrenia diagnosis."<br>Blinding: none.<br>Setting: community day rehabilitation centre, Israel. | N=71. Diagnosis: schizophrenia (DSM-IV).<br>History (completers): 5/58 had 1 previous admission, 14/58 had 2 previous admissions, 25/58 had 3 previous admissions, 14/58 had spent up to one year in rehabilitation, 16/58 had spent up to 2 years, 21/58 had spent >2 years.<br>Sex (completers): 35/58 M, 23/58 F. Age: mean 36 (SD 10.29). | 1. Dynamic cognitive intervention: a) regular Instrumental Enrichment (IE) sessions. IE is divided into 15 tools, each focusing on a specific cognitive deficiency. Treatment provided by OTs and adapted to each subject's abilities and needs. "The goals were to improve the subject's cognitive adaptive ability and independence and to sharpen their awareness of their abilities." Each session divided into three parts: i) paper and pencil exercises to improve skills (for example, categorization, organization in space);<br>ii) analysis of paper and pencil exercise performance by participant and therapist;<br>iii) included examples from participant's daily life (for example, work, residence, social skills) and demonstrated how skills tested in 1st exercise are relevant.<br>b) Group treatment also offered according to need every few weeks. Goals were "to enable subjects to share a common theme and enhance group belonging, develop their ability to see problems from different perspectives, and develop their communication skills."<br>2. Control: "traditional occupational therapy" (functional tasks and expressive activities), individually and in groups. | Dropout.<br>Ravens Progressive Matrices (RPM).<br>General Aptitude Test Battery (GATB).<br>Memory (Learning Potential Assessment Device - LPAD).<br>Employment status.<br>Residence status.<br>Unable to use:<br>Fitts Self-Concept Scale (no SD). | |

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|---|---|---|---|---|---|
| **Medalia1998** | 18 20-minute sessions, 3 times per week for 6 weeks. Allocation: pairs matched by test rankings and randomised.<br>Blinding: BPRS scored by blind rater.<br>Setting: inpatients, New York City. | N=60.* Diagnosis: schizophrenia (DSM-III-R).<br>History: IQ >70, impaired attention <99% correct on CPT, in hospital > 6 weeks before study, on neuroleptics, no diagnosed brain disease.<br>Sex: 47 M, 13 F.<br>Age: mean ~ 33 years (SD ~6.5). | 1. Cognitive rehabilitation (Orientation remedial module computer programme developed for people with head injuries emphasising "practice in a behavioral learning format that shapes and reinforces attentive behavior through engaging in computerized exercises"). N=30.*<br>2. Control: viewing National Geographic documentaries with a clinician. N=30.*<br>Both comprised three 20-minute sessions per week for 6 weeks. Orientation remedial module = computer based attentional remediation program. | Dropout.<br>Mental state (BPRS).<br>Attention (Continuous Performance Test - CPT).<br>Unable to use:<br>Reaction time (no usable data). | JADAD[2] score = 1.<br>* 6 participants dropped out, trialists analysed 54 (27 each group) - reviewers assumed 3 lost / group - unclear when attrition occurred. |

[2] JADAD scores relate to a quality assessment scale: the JADAD scale (Jadad, A.R., Moore, R.A., Carroll, D. *et al.* (1996) Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials, 17,* 1–12). The JADAD scale has not been applied to any papers in the update, instead the SIGN checklist has been applied.

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|---|---|---|---|---|---|
| **Medalia2000** | Ten 25-minute sessions, sessions, twice weekly for 5 weeks.<br>Allocation: "subjects were randomly assigned into one of three groups" (Problem-Solving Remediation, Memory Remediation, and Control).<br>Blinding: one investigator scored all pre-tests but remained blind to group assignment until treatment started. Post-tests independently rated by second investigator blind to group assignment.<br>Setting: inpatients, New York City. | N=60*. Diagnosis: schizophrenia (DSM-IV Axis I). History: ages 18-55, no diagnosed brain disease, IQ>70, scores above 16th percentile on Comprehension test of WAIS-R-CT and the Immediate Recall subtest of WMS-LM-I. | 1. Memory Remediation Group: employed a software package developed "to increase memory skills and develop strategies for remembering." Verbal praise and encouragement offered to subjects as they completed tasks. N=18*.<br>2. Problem- solving group: subjects were trained to perform sequential procedures and guided in problem-solving process required to solve problems presented in a software package. N=18.*<br>3. Control Group: subjects participated in "routine unit activities (for example, arts and crafts) or centralised services (for example, leisure time). N=18*. | Dropout.<br>Memory (Wechsler Memory Scale-Revised: Logical Memory, California Verbal Learning Test - Immediate Free Recall List A).<br>Unable to use: Wechsler Adult Intelligence Scale-Revised, Comprehension test (WAIS-R-CT - no data). Independent Living Scale - Problem Solving subscale (ILS-PS - no SD). | *6 subjects dropped out - 2 in each group, leaving 18 participants per group who completed the study. Reasons for dropping out: "included withdrawal of consent, decompensa-tion, and discharge." |

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|---|---|---|---|---|---|
| **Wykes1999** | Allocation: random - no further details.<br>Blinding: raters blind to group assignment.<br>Setting: community psychiatric clinics, South London. | N=33. Diagnosis: schizophrenia (DSM-IV).<br>History: evidence of cognitive difficulties, no evidence of organic brain disease, no plans to change medication during treatment.<br>Sex: 25 M, 8 F.<br>Age: mean ~ 38 years. | 1. Neurocognitive remediation (CR) - CR as set out in Delahunty and Morice's (1993) manual. "In each session, a variety of tasks were presented to practice each of the component processes in complex planning or problem solving".<br>2. Intensive Occupational Therapy (IOT) - including "relaxation, assertiveness training, life diary, comprehension of social information, and role playing."<br>Both "1-hour daily sessions over 40 days" for 3 to 5 days per week. | Mental state (BPRS, PSE).<br>Dropout.<br>Cognitive flexibility (Verbal Fluency, Hayling, Trails, WCST, Response inhibition, Stroop).<br>Planning (Tower of London, Modified 6 Elements).<br>Memory (Digit Span, Sentence Span, Visual Span, Dual Span).<br>Criterion-based measures (number of people who improved on more than 50% of the tests in a domain, number of people who achieved sustained improvement). | Jadad score = 1.<br>Used intention to treat analysis. |

**References of included studies (previous guideline)**

**Benedict 1994**

Benedict RHB, Harris AE, Markow T, McCormick JA, Nuechterlein KH, Asarnow RF. (1994) Effects of attention training on information processing in schizophrenia. *Schizophrenia Bulletin*; 20:537-46.

**Hadas-Lidor 2001**

Hadas-Lidor N, Katz N, Tyano S, Weizman A. (2001) Effectiveness of dynamic cognitive intervention in rehabilitation of clients with schizophrenia. *Clinical Rehabilitation*;15:349-59.

**Medalia 1998**

Medalia A, Aluma M, Tryon W, Merriam AE. (1998) Effectiveness of attention training in schizophrenia. *Schizophrenia Bulletin*; 24:147-52.

**Medalia 2000**

Bark,N.; Revheim,N.; Huq,F.; Khalderov,V.; Ganz,Z.W.; Medalia,A. (2003) The impact of cognitive remediation on psychiatric symptoms of schizophrenia. *Schizophrenia Research* 63: 229 - 235.

*Medalia A, Revheim N, Casey M. (2000) Remediation of memory disorders in schizophrenia. *Psychological Medicine*; 30:1451-1459.

Medalia A, Revheim N, Casey M. (2001) The remediation of problem-solving skills in schizophrenia. *Schizophrenia Bulletin*; 27:259-267.

**Wykes 1999**

Reeder,C.; Newton,E.; Frangou,S.; Wykes,T. (2004) Which executive skills should we target to affect social functioning and symptom change? A study of a cognitive remediation therapy program. *Schizophrenia Bulletin* 30(1): 87 - 100.

*Wykes T, Reeder C, Corner J, Williams C, Everitt B. (1999) The effects of neurocognitive remediation on executive processing in patients with schizophrenia. *Schizophrenia Bulletin*; 25:292-307.

Wykes,T.; Reeder,C.; Williams,C.; Corner,J.; Rice,C.; Everitt,B. (2003) Are the effects of cognitive remediation therapy (CRT) durable? Results from an exploratory trial in schizophrenia. *Schizophrenia Research* 61: 163 - 174.

**Characteristics of excluded studies (previous guideline)**

| Study | Reason for exclusion |
|---|---|
| **Adams1981** | Allocation: case study, not randomised. |
| **Ahmed1994** | Allocation: case series, not randomised. |
| **Bellack1990** | Allocation: allocated sequentially, not randomly.<br>Participants: people with schizophrenia.<br>Interventions: cognitive rehabilitation versus contingent reinforcement and noncontingent reinforcement, no placebo. |
| **Benedict1989** | Allocation: "randomly assigned" - no further details.<br>Participants: 20 people with schizophrenia (DSM-III), mean age ~30 years (SD 5.6) taking mean of 709mg chlorpromazine per day.<br>Interventions: cognitive rehabilitation (computerised attention-training tasks - progression through task hierarchy dependent on improved performance. 11 tasks - "speed of information processing & vigilance"; 14 tasks - "skills in memory, concept formation & problem solving") versus attention placebo (same tasks & attention as experimental group, but no progression criteria, equal time spent on each task) versus no treatment control. Duration of cognitive rehabilitation & attention placebo: 25 X 30 minute sessions.<br>Outcomes: reaction time (+/- auditory distraction), specific reaction time tasks (total = 120 trials) - no usable data. |
| **Brenner1994** | Allocation: not randomised, describes Integrated Psychological Therapy. |

| | |
|---|---|
| **Brown1993** | Allocation: randomised - no further description.<br>Participants: 29 people with "chronic" schizophrenia (DSM-IIIR), mean age ~ 50 years, mean length of stay 7 years.<br>Interventions: Cognitive rehabilitation (Attention Process Training - "a hierarchical, multilevel treatment program designed to remediate attention deficits in brain-injured persons . . . primarily consisting of paper-and-pencil and auditory stimuli/motor response tasks" versus control group ("traditional one-to-one task-oriented occupational therapy program aimed at improving cognitive skills through task completion"). Duration of both interventions: 3 X 60 minute sessions per week for 12 weeks<br>Outcomes: Digit span subscale of WAIS, visual span subscale of the revised memory scale, digit symbol subscale of WAIS, trail making subtests A & B of the Halstead Reitan Neurological Battery, Bay Area Functional Performance Evaluation (BaFPE). Unusual treatment of data from two groups - "[because] neither treatment modality was more effective than the other" . . . . "statistical analysis was done on the combined score" of the two treatment groups. |
| **Corrigan1995** | Allocation: randomised.<br>Participants: people with schizophrenia and schizoaffective disorder.<br>Interventions: two forms of cognitive rehabilitation, no control group. |
| **Delahunty1993** | Allocation: case studies, not randomised. |
| **Fine1994** | Allocation: case study, not randomised. |
| **Finnell1997** | Allocation: not randomised. |
| **Garety1994** | Allocation: not randomised. |
| **Goldberg1994** | Allocation: not randomised, case study. |
| **Granholm1992** | Allocation: not randomised, review. |
| **Jaeger1992a** | Allocation: unclear, "controlled trial" of cognitive rehabilitation aborted because participants "found the program too demanding". |
| **Kern1994** | Allocation: not randomised, review. |
| **Konen1991** | Allocation: not randomised, review. |
| **Michel1998** | Allocation: not randomised, case control. |
| **Morice1996** | Allocation: unclear.<br>Participants: people with schizophrenia<br>Interventions: three different groups, all cognitive rehabilitation and mixed with other interventions. |
| **Nisbet1996** | Allocation: non-randomised controlled study. |
| **Perris1992** | Allocation: not randomised, descriptive paper. |
| **Reed1992** | Allocation: not randomised, case series. |
| **Spaulding1986** | Allocation: not randomised, case series. |
| **Spaulding1993a** | Allocation: not randomised, case series. |

| | |
|---|---|
| **Spaulding1993b** | Allocation: unclear.<br>Participants: those with schizophrenia.<br>Interventions: problem solving training versus a perception training, not cognitive rehabilitation. |
| **Spaulding1994** | Allocation: not randomised, case study. |
| **Spaulding1999** | Allocation: matched randomisation.<br>Participants: people with schizophrenia, schizoaffective disorder, psychosis NOS, bipolar disorder, major depression, OCD, organic personality disorder, personality disorder NOS.<br>Intervention: integrated psychological therapy subprograms versus supportive therapy.<br>Outcomes: measures of social competence, cognitive functioning, clinical status.<br>Analysis: no useable data. |
| **Summerfelt1991** | Allocation: randomised, two period crossover design.<br>Participants: people with schizophrenia and schizoaffective disorder.<br>Intervention: two types of cognitive rehabilitation, with and without monetary reward, no placebo group. |
| **Tryssenaar1994** | Allocation: not randomised, case study. |
| **Trzepacz1991** | Allocation: not randomised, case study. |
| **Velligan1996** | Allocation: non-randomised controlled study. |
| **Vollema1995** | Allocation: randomised - no further details.<br>Participants: 34 people with schizophrenia (DSM-III-R), mean age ~32 (SD ~8), mean number hospitalisations ~3 (SD 2), mean duration of illness ~32 months (SD 43), mean time in hospital since last admission ~ 14 months (SD 20), negative symptoms mean PANSS subscale ~17 (SD 7), > 20 perseverative errors on WCST, mean 260mg chlorpromazine per day.<br>Interventions: cognitive rehabilitation (instruction on WCST - involved 6 measurement (M) occasions; on M3 received instruction "on sorting rules . . . and on the occurrence of shifting sets" before being administered WCST - therefore, intervention = 1 session of instructions) versus cognitive rehabilitation (instruction on WCST and monetary incentive - involved 6 M occasions: on M3 received instruction "on sorting rules . . . and on the occurrence of shifting sets" before being administered WCST and 25 cents for each correct response - therefore, intervention = 1 session of instructions & monetary incentive) versus control (tested on WCST under standard conditions on 6 occasions).<br>Outcomes: WCST - number of categories completed and number of perseverative errors immediately following intervention, 10 minutes and 14 days post intervention. Monetary incentive and instruction - "less effective than instruction alone" but no usable data. |
| **Wexler1997** | Allocation: randomised.<br>Participants: people with schizophrenia.<br>Interventions: two types of cognitive rehabilitation, no placebo group. |
| **Young1995** | Allocation: randomised.<br>Participants: people with chronic schizophrenia<br>Interventions: two forms of cognitive rehabilitation, no placebo control. |

**References of excluded studies (previous guideline)**

**Adams1981**

Adams HE, Malatesta V, Brantley PJ, Turkat ID. (1981) Modification of cognitive processes: a case study of schizophrenia. *Journal of Consulting and Clinical Psychology*;49:460-4.

**Ahmed1994**

Ahmed M, Goldman JA. (1994) Cognitive rehabilitation of adults with severe and persistent mental illness: a group model. *Community Mental Health Journal*; 30:385-93.

**Bellack1990**

Bellack AS, Mueser KT, Morrison RL, Tierney A, Podell K. (1990) Remediation of cognitive deficits in schizophrenia. *American Journal of Psychiatry*; 147:1650-5.

**Benedict1989**

Benedict RHB, Harris AE. (1989) Remediation of attention deficits in chronic schizophrenic patients: a preliminary study. *British Journal of Clinical Psychology*; 28:187-8.

**Brenner1994**

Brenner HD. (1989) The treatment of basic psychological dysfunctions from a systemic point of view. *British Journal of Psychiatry*; 155 (Supplement 5):74-83.

Brenner HD, Boker W, Hodel B, Wyss H. (1989) Cognitive treatment of basic pervasive dysfunctions in schizophrenia. In: Schulz SC, Tamminga CA, editor(s). *Schizophrenia: Scientific Progress*, pp. 358-367. New York: Oxford University Press.

Brenner HD, Hodel B, Genner R, Roder V, Corrigan P. (1992) Biological and cognitive vulnerability factors in schizophrenia: implications for treatment. *British Journal of Psychiatry*; 161(Supplement 18):154-63.

Brenner HD, Hodel B, Roder V, Corrigan P. (1992) Treatment of cognitive dysfunctions and behavioral deficits in schizophrenia. *Schizophrenia Bulletin*; 18:21-6.

Brenner HD, Stramke WG, Mewes F, Liese F, Seeger G. (1980) Erfahrungen mit einem spezifischen therapieprogramm zum training kognitiver and kommunikativer fähigkeiten in der rehabilitation chronisch schizophrener patienten. *Der Nervenarzt*; 51:106-12.

**Brown1993**

Brown C, Harwood K, Hays C, Heckman J, Short JE. (1993) Effectiveness of cognitive rehabilitation for improving attention in patients with schizophrenia. *Occupational Therapy Journal of Research*; 13:71-86.

**Corrigan1995**

Corrigan PW, Hirschbeck JN, Wolfe M. (1995) Memory and vigilance training to improve social perception in schizophrenia. *Schizophrenia Research*; 17:257-65.

**Delahunty1993**

Delahunty A, Morice R, Frost B. (1993) Specific cognitive flexibility rehabilitation in schizophrenia. *Psychological Medicine*; 23:221-7.

**Fine1994**

Fine SB. (1994) Reframing rehabilitation: putting skill acquisition and the mental health system into proper perspective. In: Spaulding WD, ed. *Cognitive Technology in Psychiatric Rehabilitation*. Lincoln, NE: University of Nebraska Press.

**Finnell1997**

Finnell A, Card J, Menditto A. (1997) A comparison of appropriate behavior scores of residents with chronic schizophrenia participating in therapeutic recreation services and vocational rehabilitation services. *Therapeutic Recreation Journal*; (First Quarter):10-21.

**Garety1994**

Garety PA, Kuipers L, Fowler D, Chamberlain F, Dunn G. (1994) Cognitive behavioural therapy for drug-resistant psychosis. *British Journal of Medical Psychology*; 67:259-71.

**Goldberg1994**

Goldberg J. (1994) Cognitive retraining in a community psychiatric rehabilitation program. In: Spaulding WD. *Cognitive Technology in Psychiatric Rehabilitation*. Lincoln, NE: University of Nebraska Press, 1994.

**Granholm1992**

Granholm E. (1992) Processing resource limitations in schizophrenia: implications for predicting medication response and planning attentional training. In: Margolin DI, ed. *Cognitive Neuropsychology in Clinical Practice.* pp. 43–69. New York: Oxford University Press.

**Jaeger 1992a**

Jaeger J, Douglas E. (1992) Neuropsychiatric rehabilitation for persistent mental illness. *Psychiatric Quarterly*; 63:71-94.

**Kern1994**

Kern RS, Green MF. (1994) Cognitive prerequisites of skill acquisition in schizophrenia: Bridging micro- and macro-levels of processing. In: Spaulding WD, ed. *Cognitive Technology in Psychiatric Rehabilitation*. Lincoln, NE: University of Nebraska Press.

**Konen1991**

Konen A, Neis L, Hodel B, Brenner HD. (1993) A propos des thérapies cognitive-comportementales de la schizophrénie. Le programme intégratif de thérapies psychologiques (IPT). *L'Encéphale*; XIX:47-55.

**Michel1998**

Michel L, Danion J-M, Grange D, Sander G. (1998) Cognitive skill learning and schizophrenia: implications for cognitive rehabilitation. *Neuropsychology*; 12:590-9.

**Morice1996**

Morice R, Delahunty A. (1996) Treatment strategies for the remediation of neurocognitive dysfunction in schizophrenia. In: Pantelis C, Nelson HE, Barnes TRE, eds. *Schizophrenia: a Neurological Perspective*. New York: John Wiley.

**Nisbet1996**

Nisbet H, Siegert R, Hunt M, Fairley N. (1996) Improving schizophrenic in-patients' Wisconsin card-sorting performance. *British Journal of Clinical Psychology*; 35:631-3.

**Perris1992**

Perris C. (1992) A cognitive-behavioral treatment program for patients with a schizophrenic disorder. *New Directions for Mental Health Services*; 53:21-32.

**Reed1992**

Reed D, Sullivan, ME, Penn DL, Stuve P, Spaulding WD. (1992) Assessment and treatment of cognitive impairments. *New Directions for Mental Health Services;* 53:7-19.

**Spaulding1986**

Spaulding WD, Storms L, Goodrich V, Sullivan M. (1986) Applications of experimental psychopathology in psychiatric rehabilitation. *Schizophrenia Bulletin*; 12:560-77.

**Spaulding1993a**

Spaulding WD (1993). Spontaneous and induced changes in cognition during psychiatric rehabilitation. In: Cromwell RL, Snyder CR, eds. *Schizophrenia: Origins, Processes, Treatment, and Outcome*. New York: Oxford University Press.

**Spaulding1993b**

Spaulding WD (1993). Spontaneous and induced changes in cognition during psychiatric rehabilitation. In: Cromwell RL, Snyder CR, eds. *Schizophrenia: Origins, Processes, Treatment, and Outcome*. New York: Oxford University Press.

**Spaulding1994**

Spaulding WD, Sullivan M, Weiler M, Reed D, Richardson C, Storzbach D. (1994) Changing cognitive functioning in rehabilitation of schizophrenia. *Acta Psychiatrica Scandinavica*; 90(Supplement 384):116-24.

**Spaulding1999**

Spaulding WD, Reed D, Sullivan M, Richardson C, Weiler M. (1999) Effects of cognitive treatment in psychiatric rehabilitation. *Schizophrenia Bulletin*; 25(4):657-676.

**Summerfelt1991**

Summerfelt AT, Alphs LD. (1991) Reduction of perseverative errors in patients with schizophrenia using monetary feedback. *Journal of Abnormal Psychology;* 100:613-6.

**Tryssenaar1994**

Tryssenaar J, Goldberg J. (1994) Improving attention in a person with schizophrenia. *Canadian Journal of Occupational Therapy*; 61:198-205.

**Trzepacz1991**

Trzepacz P, Starratt C. (1991) In: Tamminga CA, Schultz SC, eds. *Schizophrenia Research*, vol. 1 of *Advances in Neuropsychiatry and Psychopharmacology*. New York: Raven Press.

**Velligan1996**

Velligan DI, Mahurin RK, True JE, Lefton RS, Flores CV. (1996) Preliminary evaluation of cognitive adaptation training to compensate for cognitive deficits in schizophrenia. *Psychiatric Services*; 47:415-7.

**Vollema1995**

Vollema MG, Geurtsen GJ, Augustinus JP, van Voorst JP. (1995) Durable improvements in Wisconsin Card Sorting Test performance in schizophrenic patients. *Schizophrenia Research*; 16:209-15.

**Wexler1997**

Wexler BE, Hawkins KA, Rounsaville B, Anderson M, Sernyak MJ, Green MF. (1997) Normal neurocognitive performance after extended practice in patients with schizophrenia. *Schizophrenia Research*; 26:173-80.

**Young1995**

Young DA, Freyslinger MG. (1995) Scaffolded instruction and the remediation of Wisconsin Card Sorting Test deficits in chronic schizophrenia. *Schizophrenia Research*; 16:199-207.

**Characteristics of included studies (update)**

| **Study ID** | **BELLUCCI2002** |
|---|---|
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 8 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - US |
| | **Number of people screened, excluded & reasons:** Not mentioned |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 47% |
| | **Diagnosis:** Other schizophrenia related [%] Schizoaffective disorder - 53% |
| | **Diagnostic tool:** Primary diagnoses made by treating psychiatrists using a structured clinical interview |

**Inclusion criteria:**
- attending a day treatment programme
- primary diagnosis of schizoaffective disorder or schizophrenia judged to have been present for >=6 months

**Exclusion criteria:**
- age 60+
-those judged to be floridly psychotic (i.e. expressing hallucinations, and/or prominent thought disorder)

**Total sample size:** No. randomised 34

**Gender:** % female 52.9%

**Age:** Mean 42.0

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
- Mean years since first hospitalisation =16.6
- Mean years since first contact with the programme provider = 4.9.

**Baseline stats:**
[CACR / control]
SANS summary: 13.7(3.6) / 13.1(3.8)
SES: 26.5(4.7) / 29.6(4.3)
MMSE: 28.1(1.5) / 25.7(4.1)

**Notes about participants:** Mean GAF = 49.0
Subjects received on average 3.1 psychiatric medications, most commonly atypical antipsychotics (n=27), SSRI antidepressants (n=14), mood stabilisers (n=14), medication to control EPS (n=11), other antipsychotics (n=10) and other antidepressants (n=8)

**Interventions** **Intervention - group 1.:** CACR, 2 1/2 hour session for 8 weeks, n=17

**Intervention - group 2.:** Waiting list control: n=17

**Notes about the interventions:**
Day treatment programme (TAU)
All participants were attending a day treatment programme, which offered medication management, psychiatric evaluation, case management services and therapeutic groups (e.g. psychoeducation, social skills, prevocational training.)

CACR
In addition to the day treatment programme, the participants also received 2 half-hour sessions of CARC for 8 weeks. The CACR training employed Captain's Log Software. The programme had 5 modules, each containing 3-8 cognitive training tasks in attention and concentration,

memory, visuospatial and visuomotor skills and conceptualisation. Trainers provided consistent reinforcement and encouragement without presenting specific performance feedback, using a standard set of acceptable verbalisations.

Waiting-list
Participants assigned to the waiting list control group received only the day programme (TAU)

**Outcomes** **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state SANS; SES

**Cognitive functioning:** Average score/change in cognitive functioning TMT-A; TMT-B; WMS-III; MMSE

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**BURDA1994**

**General info** **Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method** **Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Blindness:** No mention

**Duration:** No. weeks of treatment - 8

**Raters:** Not stated to be independent of treatment

| | |
|---|---|
| | **Design:** Single-centre - Inpatient psychiatric ward in VA medical centre, US |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** Other method Research diagnostic criteria |
| | **Inclusion criteria:**<br>- Chronic inpatient |
| | **Exclusion criteria:**<br>- not reported |
| | **Total sample size:** No. randomised 69 |
| | **Gender:** % female 3% |
| | **Age:** Mean 47 |
| | **Ethnicity:** 12% African American<br>88% Caucasian or Hispanic |
| | **Setting:** Inpatient |
| | **Baseline stats:** Not reported |
| **Interventions** | **Intervention - group 1.:** CRT, 3 x 30 minute sessions over 8 weeks; N = 40 |
| | **Intervention - group 2.:** Control; N = 29 |
| | **Notes about the interventions:**<br>CRT<br>Variety of exercises including attention, memory, visuospatial skills, visuomotor skills and conceptualisation.<br><br>Control<br>Did not participate in any way with computer.<br><br>All participants took part in regular ward including medication. |
| **Outcomes** | **Cognitive functioning:** Average score/change in cognitive functioning – end of treatment only |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| | |
|---|---|
| **Study ID** | **EACK2007** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 52 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Multi-centre - Several different clinics in and around Pittsburgh |
| | **Number of people screened, excluded & reasons:** 43 were recruited, but only 38 completed the treatment (2 participants moved away, 2 withdrew consent and 1 did not meet eligibility criteria upon further review) |
| | **Notes about study methods:** Randomisation procedure not reported. |
| **Participants** | **Diagnosis:** Other schizophrenia related [%] schizoaffective disorder = 26% |
| | **Diagnosis:** Schizophrenia [% of sample] 74% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- diagnosed within the past 8 years.<br>- have an IQ >=80<br>- not be misusing substances during the past 2 months. |

**Total sample size:** No. randomised 38

**Gender:** % female 32%

**Age:** Mean 26.14(6.54)

**Age:** Range 17-43

**Ethnicity:** Caucasian = 68%
African American = 16%

**Setting:** Inpatient

**Setting:** Outpatient

**History:** Participants had been ill for an average of 3.75(2.80) years. All had completed high school, half had attended some collage, and nine were currently employed

**Baseline stats:** Not reported - (only difference from baseline reported)

**Notes about participants:** No further details provided

**Interventions** **Intervention - group 1.:** CET, 60 hours of computer training, n=18

**Intervention - group 2.:** EST; n=20

**Notes about the interventions:**
CET
-participants complete approx 60h of computer training in attention, memory, and problem-solving, and participate in a newly revised 45 session weekly socio-cognitive group that focuses on learning how to take the perspective of others, read non-verbal cues, manage emotions and appraise the social context.

EST
-consists of components from the basic and intermediate phases of Personal Therapy, which focuses on stress reduction strategies and psychoeducation.

Full details of both methods have been described in other papers

**Outcomes** **Cognitive functioning:** Average score/change in cognitive functioning - Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT)

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** +

| | |
|---|---|
| **Study ID** | **HOGARTY2004** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - all participants met the criteria for minimum treatment exposure and were included in the ITT analyses. However paper is not specific about this criteria. |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 52 |
| | **Duration:** Length of follow-up - 1 year |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - US |
| | **Number of people screened, excluded & reasons:** 132 patients were initially enrolled (12 had initially been excluded because of mental insufficiency or organicity). 8 participants withdrew consent before treatment exposure and three were judged to be ineligible by reason of mental insufficiency (IQ<80). |
| | **Notes about study methods:** Patients were randomised by the project statistician. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 70% (56% Paranoid Schizophrenia, 14% Other Schizophrenia.) |
| | **Diagnosis:** Other schizophrenia related [%] 30% schizoaffective disorder |
| | **Diagnostic tool:** Other DSM |
| | **Diagnostic tool:** DSM-IV |

**Inclusion criteria:**
- Fluent in English
- aged 18-60 years
- treated with a Food and Drug Administration-approved antipsychotic medication
- free of any serious alcohol or drug abuse in the preceding 6 months
- IQ >=80
- Had to meet the criteria for cognitive disability (associated with 1 of 3 dysfunctional cognitive styles: impoverished, disorganised, rigid.)

**Total sample size:** No. randomised 121

**Total sample size:** ITT population 121

**Gender:** % female 41%

**Age:** Mean 37.3(8.9)

**Ethnicity:** White - 89%
African American - 11%

**Setting:** Outpatient

**History:** Length of psychotic illness, mean years = 15.7(9.3)
Previous hospitalisations, mean n=5.96(5.97)
Cumulative hospitalisation, mean months = 13.9(4.5)
Time since last worked median years = 4
Estimated WAIS mean - 97.2(11.5)

**Baseline stats:** Scores on the BPRS were not recorded as the measure failed retest reliability because of low variance.

**Notes about participants:** At baseline, 33.5% of patients received clozapine, 28.9% received an atypical antipsychotic medication (mostly risperidone or olanzapine), and 35.5% received a conventional neuroleptic, typically at the minimum effective dose.

**Interventions** **Intervention - group 1.:** CET, approx 75 hours of software training and 56 group sessions); n=67

**Intervention - group 2.:** EST, weekly in phase 1 and biweekly in phase 2; N=54

**Notes about the interventions:**
CET
CET attempts to facilitate the attainment of adult social cognitive milestones, such as perspective taking and social cognitive appraisal. CET is a small-group approach that combines approx 75 hours of progressive software training exercises in attention, memory, and problem solving with 1.5 hours per week of social cognitive group exercises (approx 56 sessions).
-Software exercises required the patients to work in pairs, offer mutual support and encouragement, respond to online Socratic coaching, and use the cueing and fading of prompts until the principles underlying test performance were mastered.
- The participants were divided into 11 CET social cognitive groups. Group sessions typically contained a homework review, a

psychoeducation topic, an exercise by a patient or pair, feedback from other patients and coaches, and a new homework assignment based on the education topic.

EST
EST included most practice principles of the basic and intermediate phases of the demonstrably effective PT approach. EST encouraged illness self-management through the control of subjective cues of distress that might lead to destabilisation or social dysfunctioning.
-Phase 1 provided psychological and material support, psychoeducation regarding the nature and treatment of schizophrenia, resumption of instrumental tasks, role restructuring and basic skills training in stress avoidance.
-Phase 2 included a personalised education concerning vulnerability to stress, adjustment to disability, identification of early signs of decompensation and stress management strategies.
-EST was intended to be applied weekly in phase 1 and biweekly in phase 2

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Cognitive functioning:** Clinically significant change in cognitive functioning - Clinically meaningful changes to the composite scores were also reported.

**Cognitive functioning:** Average score/change in cognitive functioning Composite scores were created based on the results of a battery of tests including WAIS, WCST, WMS, etc.

-The following composite scores were standardised according to a baseline mean (SD) of 50 (10): Processing speed, neurocognition, cognitive style, social cognition and social adjustment.

-The regressed composite change scores between baseline and 1 and 2 years were the main study outcomes.

**Other:** Employment - lower=better:
GAS
Global work readiness

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **KURTZ2007** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Data from all patients randomly assigned to a condition were included in the analysis, regardless of the degree of participation, with the exception of patients who achieved less than 15 total hours of computer training. |
| | **Blindness:** Single-blind |
| | **Duration:** No. weeks of treatment - 52 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - US |
| | **Number of people screened, excluded & reasons:** 42 patients were randomised.<br><br>Individual measures were missing from 2 patients for spatial episodic memory and processing speed function domains, and individual measures for 9 patients were missing from the executive function / reasoning domain.<br><br>-2 cases patient refused, 3 cases addition of a test to the battery after the onset of the study and 6 cases represented technical loss or administrator error. |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Other schizophrenia related [%] Not reported |
| | **Diagnosis:** Schizophrenia [% of sample] not reported |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- outpatients meeting DSM-IV criteria for schizophrenia or schizoaffective disorder. |
| | **Exclusion criteria:**<br>- auditory or visual impairment |

- evidence of mental retardation, traumatic brain injury with a sustained loss of consciousness, presence or history of any neurologic illness other than schizophrenia
- lack of proficiency in English
-criteria met for concurrent substance abuse or dependence.

**Total sample size:** No. randomised 42

**Total sample size:** ITT population - Unclear

**Gender:** % female 33%

**Age:** Mean 35

**Setting:** Outpatient

**History:**
[CR / CS]
Duration of illness: 11.0(10.4) / 9.8(6.3)
Number of hospitalisations: 4.0(2.5) / 3.9(2.9)
Vocabulary scaled score (WAIS-III): 10.0(3.6) / 11.0(3.2)

**Baseline stats:**
[CR / CS]
Working memory: -0.6(1.1) / -0.2(1.0)
Verbal episodic memory: -1.3(1.0) / -0.9(0.9)
Spatial episodic memory: -2.6(1.1) / -2.1(1.1)
Processing speed: -1.2(0.8) / -1.2(0.7)
Reasoning/ executive function: -0.8(1.1) / -0.6(1.2)

The scores above represent z scores generated for the composite domains derived from a number of neurocognitive tests.

**Notes about participants:**
[CR / CS]
% treated with atypical antipsychotics: 91 / 95

**Interventions** **Intervention - group 1.:** Cognitive remediation (CR), target length 100 hours; n=23

**Intervention - group 2.:** Computer skills training (CS), target length 100 hours; n=19

**Notes about the interventions:** Both the groups trained on computers side-by-side in rooms of 3-4 computers each, supervised and coached by clinicians trained in these procedures who offered positive reinforcement.

CR
CR consisted of a sequence of computerised cognitive exercises designed to improve attention, verbal and non-verbal memory and language

processing through repeated drill-and-practice. Exercises and goals are targeted at a level of difficulty at which all patients are successful. Goals are modified as performance improves. Mean number of hours in training = 67.4(28.7)

CS
The computer-skills component control intervention consisted of a 12-month course of computerised tutorials in general computer literacy and specific skills in using Microsoft Office. Participants in groups received a similar duration of treatment and equivalent interaction with a clinician. Treatment consisted of a sequence of training on general word processing skills, spread-sheet management, internet use and other skills directly applicable to an entry-level office position in the community. Patients did not receive practice on exercises expressly designed to strengthen basic neurocognitive skills. Mean number of hours in training = 70.7(28.2)

**Outcomes** **Cognitive functioning:** Average score/change in cognitive functioning Changes to the z scores for the composite factors: Working memory. verbal episodic memory, spatial episodic memory, processing speed and reasoning/executive function.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**PENADES2006**

**General info** **Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method** **Type of study:** Individual randomised trial

**Type of analysis:** ITT - Missing data from dropouts were replaced by the baseline scores following the "carry forward" method.

**Type of analysis:** LOCF

**Blindness:** Only raters blind

**Duration:** Length of follow-up - 6 months

**Duration:** No. weeks of treatment - 16

**Raters:** Independent of treatment

**Design:** Single-centre - Participants were recruited from the hospital clinic mental health centre which serves part of the Barcelona area

**Number of people screened, excluded & reasons:** 52 patients screened, 12 excluded from the randomised study due to: not meeting inclusion criteria (8) and refusal to participate (4)

**Notes about study methods:** Randomisation was independently conducted by an individual who took no part whatsoever in the implementation of assignments. A random number table was used to generate lots that were drawn for sealed envelopes which assigned patients to CRT to CBT groups.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- age <55
- presence of negative symptoms confirmed by the PANSS
- presence of cognitive impairments confirmed by a battery of neuropsychological tests.

**Exclusion criteria:**
- IQ < 85
- organic cerebral diseases or primary diagnosis of substance misuse, psychiatric comorbidity
- psychotic exacerbation in the previous 6 months, plans to change medication during the treatment phase.

**Total sample size:** No. randomised - 40

**Total sample size:** ITT population - 40

**Gender:** % female 42%

**Age:** Mean 35

**Ethnicity:** not reported

**Setting:** Other - Not stated

**History:** the participants on average had an illness duration of 13 years,

**Baseline stats:** [CRT / CBT / TAU]
PANSS positive: 11.13(3.0) / 11.41(2.6) / 10.85(2.5)
PANSS negative: 19.87(8.1) / 20.47(6.0) / 19.01(7.1)

PANSS psychopathology: 35.69(6.3) / 35.41(7.1) / 35.40(8.7)

**Notes about participants:**
[CRT / CBT / TAU]
Medication (n)
Risperidone: 5 / 10 / 10
Olanzapine: 12 / 8 / 10
Clozapine: 3 / 2 / 0

**Interventions** **Intervention - group 1.:** CRT; n=20

**Intervention - group 2.:** CBT, n=20

**Intervention - group 3.:** TAU, n=20

**Notes about the interventions:**
CRT
This was set out in the Frontal/Executive programme. The programme was implemented on an individual basis, using mainly paper and pencil tasks. An errorless learning approach was adopted in tasks of progressive complexity and the problem was set, as far as was possible, at the subject's own pace. The main instructional technique was scaffolding. The patients received 40 1-hour sessions two or three times a week over 4 months.

CBT
A similar number of CBT hours were conducted on an individual basis following a manualised approach.

TAU
All the patients reported a psychotropic medication visit in the 8 weeks preceding study entry and none reported receiving any type of individual psychotherapy.

Training
Not reported

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS positive, PANSS negative

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - LSP

**Cognitive functioning:** Average score/change in cognitive functioning  comprehensive battery of neuropsychological subtests which of which composite scores were obtained in the following domains: Working memory, psychomotor speed, verbal memory, nonverbal memory, executive function.

| | |
|---|---|
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Adequately addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **SARTORY2005** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 3 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Germany |
| | **Number of people screened, excluded & reasons:** Not mentioned |
| | **Notes about study methods:** randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** ICD-10 |
| | **Total sample size:** No. randomised 42 |
| | **Gender:** % female 33% |

**Age:** Mean 32

**Age:** Range 21-60

**Setting:** Inpatient

**History:**
[Cognitive remediation / TAU control]
Duration of disorder, years: 5.5(4.8) / 6.8(5.5)

**Baseline stats:**
[Cognitive remediation / TAU control]
Verbal IQ: 25.0(7.5) / 22.7(5.3)
Trail B: 122.4(55.4) / 151.0(58.7)
Prose recall immediate: 24.9(6.9) / 23.0(9.3)
Prose recall delayed: 19.4(7.0) / 18.7(8.8)
Word fluency: 67.4(21.4) / 68.7(22.0)
Digit symbol: 39.0(13.2) / 37.7(8.9)

**Interventions** **Intervention - group 1.:** Computerised training programme (CPT), 15 sessions over 3 weeks.; n=21

**Intervention - group 2.:** TAU control; n=21

**Notes about the interventions:**
CPT
Cogpack was used for cognitive remediation. The programme consists of a series of 30 computer tasks tapping different functional areas at varying levels of difficulty. Tasks are designed to train: attention and concentration; verbal, spatial and numerical ability; and memory or fast reaction time. Training sessions took place in small group (up to 6), with an attendant present at all times to introduce patients to the use of computers and to assist them whenever they needed help.

TAU
While patients of the treatment group received cognitive remediation, the control group attended occupational therapy.

**Outcomes** **Cognitive functioning:** Average score/change in cognitive functioning - Verbal IQ; TMT-B; Prose recall (delayed and immediate); word fluency; digit symbol

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% 100% completed study

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| | |
|---|---|
| **Study ID** | **SILVERSTEIN2005** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 6 weeks individual therapy + 16 sessions of CREP |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - US |
| | **Number of people screened, excluded & reasons:** 40 patients were enrolled, 3 were discharged during the APT phase and 6 refused to participate in the CREP group. |
| | **Notes about study methods:** Based on the APT questionnaires, patients demonstrating the greatest impairment were matched as closely as possible, and then each patient from each pair was randomly assigned to a group. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:** all participants were patients on the Second Chance Programme and were considered treatment refractory |
| | **Total sample size:** No. randomised - 40 randomised (analysis conducted on 31 completers) |
| | **Gender:** % female 14% |
| | **Age:** Mean 39 |
| | **Age:** Range 18-55 |

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:** - Mean length of stay in state hospital prior to entry to Second Chance Programme = 7.1years.
- All patients were without history of neurological disorders, mental retardation, or head injury

**Baseline stats:**
[IBR+CR / IBR]
Shipley Institute of Living Scale Vocab: 73.29(9.1) / 73.77(10.57)
PANSS negative: 13.81(6.64) / 15.18(2.21)
PANSS positive: 11.31(5.25) / 12.72(3.88)

**Notes about participants:** - All patients were medicated, with atypical antipsychotics and considered to be symptomatic but symptomatically stable.

**Interventions** **Intervention - group 1.:** Intensive behavioural rehabilitation + Cognitive rehabilitation (IBR+CR): 6 sessions of attention process training followed by 16 sessions of an IBR (CREP); n=18

**Intervention - group 2.:** IBR control: 6 weeks TAU followed by 16 CREP sessions; n=13

**Notes about the interventions:**
CREP
CREP is a form of Intensive Behavioural Rehabilitation (IBR). The CREP group is a manualised 16-session group that uses the standardised format. Each session covers a different topic related to successful maintenance of community tenure after hospital discharge (for example, recognition of medication side effects, avoidance of substance misuse). The topics are taught using learning activities, including verbal instruction, videotape presentations, role-plays, problem-solving exercises, and homework assignments. CREP sessions were conducted by the first six authors on a pre-determined rotation basis.

IBR+CR
-In addition to CREP, the participants received 6 weeks of individual sessions of APT. The APT focussed on sustained attention and consisted of 27 exercises presented in order of increasing difficulty. These exercises were in the following formats: attention tapes; number sequencing; paragraph listening and mental arithmetic.
-Attention-shaping was added to the standard CREP as part of the CR intervention. Beginning with the third CREP session, each participant was instructed that to receive their participation token they would have to meet an individualised in-class attentiveness gaol. The goal consisted of two parts: 1) the subtarget was a duration goal (for example, 2 minutes); 2) the class goal specified the number of subtargets (for example, 2 minutes 2 times). Participants were also systematically prompted for attentive and inattentive behaviour.

IBR control.
-This group received the same number of hours treatment but participated in additional groups instead of APT. After 6 weeks of TAU they began a CREP module which followed the standard format, without the use of attention shaping.

-Participants did not receive any attention tokens during the CREP module but instead received tokens for participation (for example, making at least one contribution, not demonstrating clear evidence of inattentiveness). Systematic prompts relating to attentive or inattentive behaviour were not used.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS - T2 has been used as this represents the end of CRT treatment. (CRT vs TAU)

**Cognitive functioning:** Average score/change in cognitive functioning - APT questionnaire; mean duration of attentiveness; MMLT; CVLT; DSDT; SAT

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Poorly addressed

**1.3 An adequate concealment method is used.:** Poorly addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**SPAULDING1999**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Blindness:** No mention

**Duration:** No. weeks of treatment - 36

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre - Rehabilitation unit, US

**Number of people screened, excluded & reasons:** 101 people were screened and recruited for the study, 11 withdraw from the study, 10 of whom withdraw prior to pretreatment assessment

**Notes about study methods:** Participants were recruited in cohorts of 8 to 12 subjects at each 6-month cycle. Participants in the cohort were matched and then assigned to either treatment or control. Where a cohort contained an odd number of participants, the unmatched individual was randomly assigned to either treatment condition.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 87%

**Diagnosis:** Other [%] 13% other including bipolar disorder and personality disorder

**Diagnostic tool:** Other DSM

**Inclusion criteria:** Criteria for admission into the rehabilitation unit included:
- Aged 18+
- History of treatment failure in all other available settings
- Not responding to inpatient treatment sufficiently to allow for discharge
- Primary diagnosis of an Axis 1 disorder
- IQ >=70

**Exclusion criteria:**
- Primary diagnosis of mental retardation or substance misuse
- Dangerous behaviour requiring high security setting

**Total sample size:** No. randomised - 101

**Total sample size:** ITT population - 91

**Gender:** % female 39%

**Age:** Mean 36

**Ethnicity:**
[CRT / supportive therapy]
Race, n
Caucasian: 43 / 37
Black: 5 / 4
Hispanic: 1 / 0
Native American: 0 / 1

**Setting:** Inpatient

**History:**
[CRT / ST]
Age at 1st hospitalisation: 23.7(7.2) / 24.0(7.9)

**Baseline stats:**
[CRT / ST]
PANSS pos: 1.51(1.57) / 1.46(1.59)
PANSS neg: 1.38(1.35) / 1.15(1.33)

**Notes about participants:**
[CRT / ST]
CPZ equivalent (mg/day): 1495.43(1762.20) / 1742.94(1961.20)

**Interventions** **Intervention - group 1.:** cognitive remediation, 6-month treatment; N = 48

**Intervention - group 2.:** Supportive therapy, 6 months; N = 42

**Notes about the interventions:**
Cognitive remediation
Cognitive component of integrated psychological therapy. The group based therapy aims to "re-establish basic neurocognitive functions". The programme consisted of structured group activities which demanded different cognitive abilities and operations. The role of the therapist was to introduce the activity and guide the participant and evaluation of the responses by the patients. There was some flexibility in the programme with repetition of specific activities when the patient faced particular difficulties or cognitive deficits.

Supportive therapy
Based on a supportive therapy manual designed to control for non-specific aspects of the cognitive intervention.

All participants were also included in the units standard regimen (Community Transition Program). The comprehensive package included pharmacotherapy, social skills training , education and training in self-management and behaviour modification.

**Outcomes** **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS (positive, general and negative subscales)

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - AIPSS, UCLAS skills assessment modules

**Cognitive functioning:** Average score/change in cognitive functioning - Included cognitive data at end of treatment. Did not report cognitive variables at follow up.

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| | |
|---|---|
| **Study ID** | **TWAMLEY2008** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer - 11 participants dropped out of the CRT group whereas only 3 dropped out of standard care. All analyses are presented for completers only, no information including baseline stats are given regarding the drop-outs other than they did not differ from completers |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 12 |
| | **Duration:** Length of follow-up - 3 months |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre, US |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 47.5% |
| | **Diagnosis:** Other schizophrenia related [%] 47.5% |
| | **Diagnosis:** Other [%] Other primary psychosis - 5% |
| | **Inclusion criteria:**<br>- Diagnosis of primary psychotic disorder |

- aged 21+
- English speaking

**Exclusion criteria:**
- Dementia or other neurological conditions
- loss of consciousness >30 minutes
- alcohol and or substance misuse or dependence n the last month

**Total sample size:** No. randomised 52

**Total sample size:** ITT population Data reported for 38 completers

**Gender:** % female 34%

**Age:** Mean 48

**Ethnicity:** Caucasian - 65.8%
Black - 13.2%
Latino/Hispanic - 13.2%
Asian - 5.3%
Other - 2.6%

**Setting:** Other Setting not stated

**History:**
[CRT / SC]
Mean duration of illness, yrs: 19.6(14.2) / 27.5(10.4)

**Baseline stats:**
[CRT / SC]
PANSS positive: 17.9(7.3) / 17.0(6.5)
PANSS negative: 14.1(6.6) / 14.3(5.3)

**Notes about participants:**
[CRT / SC]
Mean premorbid IQ: 105.2(10.7) / 108.7(9.6)
76.3% SGAs only
7.9% both SGAs and FGAs
7.9% FGAs only
7.9% no antipsychotic medication

**Interventions** **Intervention - group 1.:** CRT, 12 x2 hour weekly group sessions; N = 25

**Intervention - group 2.:** TAU; N = 27

**Notes about the interventions:**
Cognitive training
The programme emphasised teaching and practising compensatory and environmental strategies in the following domains: prospective memory, attention and vigilance, learning and memory and executive functioning. The compensatory strategies were both cognitive/internal and behavioural/external and included techniques such as use of acronyms and writing down information respectively. The goal of the training and homework assignments was to help clients develop habits to help with real-world cognitive functioning.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS positive and negative subscales

**Quality of Life:** Average score/change in quality of life QOLI - global satisfaction

**Cognitive functioning:** Average score/change in cognitive functioning - Various cognitive tests aimed at investigating the following cognitive skills: Memory, attention/ vigilance, verbal learning and memory, executive functioning, processing speed, working memory, language and visual learning and memory

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed - Larger drop out from the intervention group post randomisation and prior to treatment compared to the SC group

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed Larger number of drop out from the intervention group compared to the SC group

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**VANDERGAAG2002**

**General info**

**Funding source:** Not mentioned

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Blindness:** No mention

**Duration:** No. weeks of treatment - 22 sessions conducted over approx 12 weeks.

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre

**Number of people screened, excluded & reasons:** No details provided

**Notes about study methods:** Closed envelopes with lots were used to randomly assign patients to groups.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** Other DSM

**Exclusion criteria:**
-history of neurological disorder, mental retardation or other developmental disorder
-history of substance misuse

**Total sample size:** No. randomised 42

**Gender:** % female 36%

**Age:** Mean 30

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[Experimental Group / Control]
Duration of illness, years: 9.9(5.8) / 9.6(8.1)

**Baseline stats:**
[Experimental / control]
Emotion matching: 45.3(6.3) / 44.4(6.2)
Emotion labelling: 18.0(4.9) / 18.8(3.3)
CPT: 2.7(1.1) / 3.1(1.0)
TMT-A: 49.7(27.6) / 47.1(17.5)
TMT-B: 143.4(77.0) / 133.6(1400.6)
WAIS digit symbol: 36.1(10.0) / 38.1(10.2)
WAIS picture: 9.9(5.1) / 11.1(4.3)

**Notes about participants:**
[Experimental / control]

Neuroleptic dose:
Haloperidol equivalents: 13.3(12.2) / 11.8(8.0)

- patients had been stabilised on antipsychotic medication for 2-3 months and were capable of participating in a 20-minute, pre-study skills training session.

**Interventions** **Intervention - group 1.:** Experimental group, cognitive training programme over 12 weeks; n=21

**Intervention - group 2.:** Control, leisure activities for 12 weeks; n=21

**Notes about the interventions:**
Cognitive training programme:
Progressed from training on perception of simple, basic stimuli to more complex stimuli, to training on reasoning skills, and finally to emotion perception and apprehension of social situations. Four strategies were embedded within the exercises: self-instruction, memory enhancement, inductive reasoning, and compensatory training procedures.
-The training was conducted in 45 exercises over a total of 22 sessions. Each patient was trained individually in 20-minute sessions. Between-session homework assignments were given so that subjects could practice the training exercises outside the laboratory setting.

Control group
Engaged in leisure activities for the same amount of time that the experimental group spent in training. The two instructors involved in the training session also participated in the leisure activities. These typically included playing board games and other similar activities.

Both groups were maintained on their initial type and dose of antipsychotic medication throughout.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Cognitive functioning:** Average score/change in cognitive functioning Cognitive battery including: Emotion matching; Emotion labelling; CPT; SPAN; TMT-A; TMT-B; RAVLT; Rey-Osterreith Complex figures; WAIS digit symbol substitution; WISC (mazes); Word fluency; WAIS picture arrangement.

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was**

**completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| **Study ID** | **VELLIGAN2000** |
|---|---|
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** LOCF |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre, US |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 84% |
| | **Diagnosis:** Other schizophrenia related [%] 16% schizoaffective disorder |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia or schizoaffective disorder<br>- Aged 18-33<br>- No history of seizure disorder, head trauma, organic brain disorder or mental retardation<br>- History of compliance to medication and clinic visits<br>- No history of drug or alcohol misuse within past 3 months<br>- Discharge destination within 70 miles of hospital |
| | **Total sample size:** ITT population - 45 |
| | **Total sample size:** No. randomised - 45 |

**Gender:** % female 25%

**Age:** Mean 37

**Ethnicity:** 48% - Mexican American
37% - Anglo American
15% - African American, Asian or mixed ethnicity

**Setting:** Outpatient - Participants were recruited on discharge from an inpatient unit following an acute exacerbation

**History:**
[CRT / Control / TAU]
Age of illness onset: 22.36(4.67) / 22.50(6.05) / 22.17(3.30)
Length of index hospitalisation, months: 7.33(15.29) / 7.08(12.98) / 5.33(1.58)

**Baseline stats:**
[CRT / Control / TAU]
GAF: 43.18(2.22) / 38.93(9.39) / 42.53(11.91)
Negative symptoms: 13.83(2.22) / 15.04(3.75) / 14.41(3.17)
Positive symptoms: 2.53(1.36) / 2.55(0.81) / 2.83(1.32)

**Notes about participants:**
[CRT / Control / TAU]
Taking SGAs, n(%): 10(66.7) / 9(60.0) / 14(93.3)

**Interventions**

**Intervention - group 1.:** Cognitive adaption training - CRT, weekly sessions for 9 months; N = 15

**Intervention - group 2.:** Control, weekly sessions for 9 months; N = 15

**Intervention - group 3.:** TAU; N = 15

**Notes about the interventions:**
CRT
Manual-driven series of compensatory strategies based on neuropsychological, behavioural and occupational therapy principles. The CAT treatment plans are based on two dimensions: 1) level of apathy versus disinhibition and 2) level of impairment in executive functions. Examples of treatment plans include providing checklists for tasks, cues prompting the initiation of tasks and posters, etc. The general plans are adapted for individual strengths and limitations in verbal/visual attention, memory, and motor coordination.

Control
Designed to account for the nonspecific therapist effects. Participants were seen on the same schedule as the CRT group and were given adaptations to their environment that were unrelated to cognitive functioning.

| | |
|---|---|
| | TAU<br>The follow-up only group did not receive any additional interventions besides standard care. All groups received TAU which consisted of standard medication follow ups. |
| **Outcomes** | **Global state & service outcomes (e.g. CGI):** Relapse - Defined as rehospitalisation during the study or exacerbation of positive symptoms, defined as an increase of 2 points or more to a score of >=4 on at least 2 of the 4 BPRS items comprising the positive subscale. |
| | **Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAF |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state BPRS positive and negative subscales |
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Multnomah Community Ability Scale |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **VELLIGAN2002** |
| | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Independent of treatment |

**Design:** Single-centre

**Number of people screened, excluded & reasons:** 113 patients approached for participation; 68 refused to participate in the study.

**Notes about study methods:** Randomisation was based on a computer-generated sequence made by an independent researcher. The randomisation sequence was concealed from all other research personnel.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 69%

**Diagnosis:** Other schizophrenia related [%] 31%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- Diagnosis of schizophrenia or schizoaffective disorder.
- age 18-55
- no history of seizure disorder, head trauma, mental disorder secondary to a general medical or neurological condition, or mental retardation
- willingness to comply with antipsychotic medication and evidence of regular attendance at clinic visits
- evidence of stable residence for the preceding 3 months.

**Total sample size:** No. randomised - 45

**Gender:** % female 35%

**Age:** Mean 39.64(7.82)

**Ethnicity:** Mexican-American - 44%
Anglo-American - 44%
Remainder of participants were African-American, Asian-American or of mixed ethnicity

**Setting:** Outpatient

**History:**
[CAT / Control / follow-up only]
Age of onset: 21.50(6.65) / 19.46(6.55) / 21.00(3.79)
% meeting criteria for current substance abuse or dependence (n): 13.33(2) / 13.33(2) / 13.33(2)

**Baseline stats:**
[CAT / Control / Follow-up only]

SOFAS: 34.53(17.36) / 39.67(12.57) / 39.07(14.55)
MCAS: 60.27(7.43) / 58.93(7.00) / 58.86(9.00)
QoL: 50.53(14.57) / 53.20(14.98) / 51.20(12.54)
BPRS positive: 2.62(1.07) / 3.32(1.26) / 3.25(1.14)
NSA: 72.47(15.66) / 70.40(13.37) / 68.53(11.93)

CVLT: 34.57(11.34) / 28.88(11.37) / 36.13(17.18)
TMT-A: 74.28(39.21) / 73.71(39.21) / 91.53(74.19)
TMT-B: 159.36(91.68) / 159.14(82.44) / 183.47(145.39)
Verbal fluency: 25.78(7.07) / 22.64(12.54) / 28.40(13.71)
WCST: 10.70(10.39) / 10.64(11.50) / 10.67(12.27)
Digit Span: 10.71(3.27) / 8.79(3.09) / 10.13(4.05)
CPT: 18.86(13.32) / 16.93(14.70) / 11.33(10.83)

**Notes about participants:**
[CAT / Control / Follow-up only]
% on atypical antipsychotics: 86.67 / 66.67 / 73.33

**Interventions** **Intervention - group 1.:** Cognitive Adaptation Training (CAT); weekly visit for 9 months; n=15

**Intervention - group 2.:** Control, weekly visits for 9 months; n=15

**Intervention - group 3.:** Follow-up only; n=15

**Notes about the interventions:**
CAT
Manual-driven series of compensatory strategies based on neuropsychological, behavioural and occupational therapy principles. The CAT treatment plans are based on two dimensions: 1) level of apathy versus disinhibition and 2) level of impairment in executive functions. Examples of treatment plans include providing checklists for tasks, cues prompting the initiation of tasks and posters, etc. The general plans are adapted for individual strengths and limitations in verbal/visual attention, memory, and motor coordination. Interventions are explained, maintained and altered as necessary by 30-minute weekly visits from CAT trainers.

Control
Control participants are seen for home visits on the same schedules as CAT members and were given adaptations for their environment that were unrelated to cognitive adaptive functions (for example, posters, plants etc).

Follow-up only
These participants were assessed on the same schedule as the other two groups but did not receive any treatment in addition to TAU.

**Outcomes** **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state BPRS; NSA - only F-value for between group comparisons reported

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SOFAS, MCAS - only F-value for between group comparisons reported

**General and psychosocial functioning (e.g. SFS):** Clinically significant response in general functioning - Examined the proportion of patients who improved using both 10 and 20 points as an indicator of clinical significance.

| | |
|---|---|
| | **Quality of Life:** Average score/change in quality of life QOL- only F-value for between group comparisons reported |
| | **Cognitive functioning:** Average score/change in cognitive functioning - CVLT; TMT-A; TMT-B; Verbal fluency; WCST; Digit span; CPT |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Well covered |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?: ++** |

| | |
|---|---|
| **Study ID** | **VELLIGAN2008** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - It is unclear from the paper whether ITT has been used, as the paper reports the number of participants with baseline and at least one follow-up assessment. However the paper also reports the numbers followed up at each assessment and does not state which of the two figures were used. |
| | **Blindness:** Only raters blind - Efforts were made to maintain the blindness of the rater. Participants and collaterals were asked not to divulge information about any visits or refer to any items they may have received during the study. If the blind was broken, alternative raters blind to group assignment completed the assessments. |
| | **Duration:** No. weeks of treatment - 104 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre, US |

**Number of people screened, excluded & reasons:** 140 of the 230 patients approached consented, of these 19 dropped out prior to pre-randomisation baseline assessments for the following reasons (n), decided not to participate (11), participating in other studies (5), hospitalised (1), could not be located (1), had seizure disorder (1). A further participant dropped out during baseline and prior to randomisation,

**Notes about study methods:** Randomisation procedure not reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] % not reported

**Diagnosis:** Other schizophrenia related [%] % not reported

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- DSM-IV diagnosis of schizophrenia or schizoaffective disorder
- aged 18-60
- treated with an SGA other than clozapine
- no hospitalisations within past 3 months
- stable living environment >=3 months

**Exclusion criteria:**
- substance misuse interfered with study participation
- documented history of significant head trauma, seizure disorder, neurological disorder or mental retardation
- currently being seen by ACT team
- history of violence in past year
- SOFAs >80

**Total sample size:** ITT population - 113 had at least a baseline and follow-up assessment although it is unclear whether the paper used these for the results as only F and t-values.

**Total sample size:** No. randomised 120

**Gender:** % female 50%

**Age:** Mean 41

**Ethnicity:**
[CAT / GES / TAU]
% non-Hispanic white: 47.22 / 34.21 / 35.90
% Hispanic: 41.67 / 42.11 / 35.90

**Setting:** Outpatient

**History:** Not reported

**Baseline stats:**
[CAT / GES / TAU]

BPRS psychosis factor: 2.8(1.2) / 2.7(1.4) / 2.8(1.4)

**Interventions** **Intervention - group 1.:** CAT, 9 months of weekly home visits followed by 15 monthly visits; N = 36

**Intervention - group 2.:** GES, Once monthly call for 24 months; N = 38

**Intervention - group 3.:** TAU

**Notes about the interventions:**
TAU
All interventions were on top of TAU which consisted of standard case management and antipsychotic medication.

CAT
Cognitive adaptation training - manualised approach of compensatory strategies based upon neuropsychological, behavioural and occupational therapy. CAT plans are customised to the individual's apathy, disinhibition and level of cognitive impairment. The CAT approach may also use supports such as alarm clocks in combination with specific strategies.

GES
General environmental support - manual driven series of environmental supports offered to patients at their regular clinic visits. The GES package was designed using the supports that were most frequently used and descried as helpful by CAT patients in previous studies. Supports include things such as watches, bus pass, alarm clocks.

**Outcomes** **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - MACS used for assessment of negative symptoms - BPRS used during assessment but data not reported as no significant differences across groups or time points.

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Only t-values reported for SOFAs

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed- Although only the raters were blind, this study has been given an adequately addressed rating as there was an effort to maintain blinding throughout the 24 month assessment period.

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Poorly addressed - Only reports usable data for significant differences and not for BPRS

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not

reported adequately

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** +

| | |
|---|---|
| **Study ID** | **VELLIGAN2008B** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Included participants with baseline and >= 1 post-baseline follow up |
| | **Blindness:** Only raters blind - Participants were requested not to talk about any of part of the therapy to the raters. If the blind was broken with one rater, a new rater conducted the remaining evaluations |
| | **Duration:** No. weeks of treatment 36 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre – 3 clinics and participants discharged from inpatient units, US |
| | **Number of people screened, excluded & reasons:** 240 people approached, 156 consented, of these 51 did not participate due to various reasons. Most frequent reasons for non-participation included: rehospitalisation, homelessness, withdrawal of consent, unable to complete assessments and demonstrating aggressive behaviour |
| | **Notes about study methods:** Randomisation was stratified by recruitment site (hospital vs. community clinic), gender and age |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] % not reported |
| | **Diagnosis:** Other schizophrenia related [%] % with schizoaffective disorder not reported |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia or schizoaffective disorder<br>- Aged 18-60<br>- Treated with an oral antipsychotic and continuing medication and follow-up at the Centre for Care Services<br>- Primary responsibility for taking own medication<br>- Stable residence<br>- Able to understand and complete rating scales and neuropsychological tests |
| | **Exclusion criteria:**<br>- On clozapine or depot medication |

- History of significant head trauma, seizure disorder or mental retardation
- History of substance abuse or dependence in last month
- History of violence in past 6 months

**Total sample size:** ITT population - 95

**Total sample size:** No. randomised - 105

**Gender:** % female 43%

**Age:** Mean 39

**Ethnicity:** Hispanic - 37%
Anglo American - 37%
African American - 21%
Other or mixed ethnicity - 5%

**Setting:** Outpatient

**History:** No details reported

**Baseline stats:**
[CAT / Pharm-CAT / TAU]
BPRS psychosis factor: 2.5(1.34) / 2.6(1.47) / 2.7(2.34)

**Notes about participants:**
[CAT / Pharm-CAT / TAU]
Baseline medication
% Risperidone: 38.2 / 21.9 / 41.4
% Olanzapine: 41.2 / 46.9 / 34.5
% Other: 20.6 / 31.2 / 24.1

**Interventions** **Intervention - group 1.:** CAT, weekly 30-45 minute sessions for 9 months; N = 37

**Intervention - group 2.:** Pharm-CAT, weekly 30-45 minute sessions for 9 months; N = 36

**Intervention - group 3.:** TAU; N = 32

**Notes about the interventions:**
CAT
Manual-driven series of compensatory strategies based on neuropsychological, behavioural and occupational therapy principles. The CAT treatment plans are based on two dimensions: 1) level of apathy versus disinhibition and 2) level of impairment in executive functions. Examples of treatment plans include providing checklists for tasks, cues prompting the initiation of tasks and posters etc. The general plans are adapted for individual strengths and limitations in verbal/visual attention, memory, and motor coordination.
Interventions are explained, maintained and altered as necessary by 30-minute weekly visits from CAT trainers.

Pharm-CAT
Subset of full CAT that focuses solely on medication and appointment adherence. Strategies include prompts to take medication, pill boxes etc.

TAU
All the above were in addition to TAU which consisted of medication and follow-up

CAT and Pharm-CAT were provided by therapists with bachelor's or master's degrees in psychology or related fields trained to use a combination of didactic and in vivo strategies. Fidelity checks were used to ensure that the therapists were adhering to the model.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Relapse - Developed an index for relapses in remitted and partially remitted patients. A relapse defined as a score on any of the four psychosis items increased by a minimum of 2 points to a score of 5 or higher, if the patient was suicidal, rehospitalised or unable to care for themselves without constant supervision.

Data was not usable for relapse as paper collapses across both CAT conditions

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Only significant P-values provided for SOFAs

**Non-adherence to study medication:** Non-adherence - Only significant p-vales provided for adherence measures

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed- Although only rater blind, additional effort was taken to ensure the blinding remained throughout the study and follow up period

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Poorly addressed- Only presents p-values for significant differences between groups. Data for non-significant differences is not usable

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **VOLLEMA1995** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 2 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Multi-centre - Two psychiatric hospitals, the Netherlands |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** Other DSM |
| | **Inclusion criteria:**<br>- DSM-III-R diagnosis of schizophrenia |
| | **Exclusion criteria:**<br>- History of neurological illness<br>- Major drug and alcohol abuse<br>- Serious personality disorders<br>- IQ<70 |
| | **Total sample size:** No. randomised 34 |
| | **Gender:** % female 29% |
| | **Age:** Mean 32 |
| | **Ethnicity:** Not reported |
| | **Setting:** Inpatient |
| | **History:**<br>Average number of rehospitalisations - 2.8 |

Duration of illness (months) - 32

**Baseline stats:** Not reported

**Interventions** **Intervention - group 1.:** CRT - sorting rules, 6 sessions; N = 12

**Intervention - group 2.:** CRT group 2 , sorting rules plus contingency management; N = 12

**Intervention - group 3.:** Standard care; N = 10

**Notes about the interventions:**
The trial contained 6 testing sessions. Participants in the standard care group only received this testing without any instruction in the tasks. Both CRT groups received training in the sorting instructions to improve their WCST performance. One of the CRT groups also received contingency management to reward them for correct responses whilst undergoing the WCST training.

**Outcomes** **Cognitive functioning:** Average score/change in cognitive functioning - Cognitive measures at end of treatment only

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**WYKES2007**

**General info** **Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method** **Type of study:** Individual randomised trial

**Type of analysis:** ITT - Participants were analysed in the treatment groups to which they were randomised irrespective of whether they

adhered to their treatment.

**Blindness:** Single-blind

**Duration:** Length of follow-up - 3 months

**Duration:** No. weeks of treatment - approx 12 weeks (40 sessions, with an average of 3 per week)

**Raters:** Independent of treatment- Symptom and quality of life assessments were assessed by an independent rater but self report assessments were collected by a research assistant who was not blind to treatment allocation.

**Design:** Multi-centre - Participants were recruited from those in contact with mental health services in South London usually while they were inpatients.

**Number of people screened, excluded & reasons:** 66 patients were referred. 16 did not meet clinical criteria clinical criteria, 6 did not provide consent and 4 did not meet clinical criteria cognitive criteria

**Notes about study methods:** Participants were randomised to group by an independent trial statistician. Block randomisation was used with CRT and control treatment being assigned randomly to 4 patients each within blocks of 8

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- Diagnosis of schizophrenia with an onset prior to the age of 19 and a duration of illness <3 years.
-Cognitive difficulties in cognitive flexibility, and/or memory.
-Difficulties in social functioning
-stable dose and type of medication, for >=1 month prior to inclusion.

**Total sample size:** No. randomised - 40

**Total sample size:** ITT population - 40

**Gender:** % female 35%

**Age:** Mean 18.2(2.5)

**Age:** Range 14-22

**Ethnicity:** No details reported

**Setting:** Outpatient

**Setting:** Inpatient

**History:** Time since first contact with psychiatric services (months) on average was 12(0-36)

**Baseline stats:**
[CRT / TAU]
BPRS total: 37.2(9.6) / 37.8(8.4)

Social behavioural problems: 12.8(9.1) / 14.4(9.1)
QoL: 23.8(12.2) / 23.9(9.8)
Rosenberg SES: 32.1(5.4) / 34.5(7.3)
WCST no. of categories: 3.6(2.2) / 3.3(1.8)
WAIS-R Digit Span: 11.8(3.0) / 12.2(3.6)
Modified 6 elements test: 4.1(1.7) / 4.2(1.8)

**Notes about participants:**
CRT / TAU]
Medication (n/%)
Atypical: 14(67) / 17(89)
Typical: 6(29) / 2(11)
None: 0(0) / 1(5)
Full scale IQ: 85.3(10.9) / 85.3(14.6)

**Interventions**

**Intervention - group 1.:** CRT, 40 hourly sessions, n=21

**Intervention - group 2.:** TAU control; n=19

**Notes about the interventions:**
CRT
Individual cognitive remediation therapy delivered over 40 sessions with an average of 3 sessions per week. In each session, a variety of tasks were presented to practice the component processes in remembering, complex planning and problem solving. At first, information processing strategies or means to organise behaviour are incorporated into the tasks. The three steps of this process are: 1) therapist demonstrates the information processing overtly, 2) patient uses such methods overtly and 3) patient uses methods covertly.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS; SES

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SBS

**Quality of Life:** Average score/change in quality of life - QoL

**Cognitive functioning:** Clinically significant change in cognitive functioning % of participants attaining a normal score on cognitive tests.

**Cognitive functioning:** Average score/change in cognitive functioning Digit Span (WAIS-III); WCST; Planning (modified 6 elements test);

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** ++

| | |
|---|---|
| **Study ID** | **WYKES2007A** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Participants were analysed in the treatment group to which they were randomised irrespective of whether they adhered to their treatment. |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 40 sessions over approx. 12 weeks |
| | **Duration:** Length of follow-up - 6 months |
| | **Duration:** Range (for each group) - 0-40 sessions |
| | **Duration:** Mean duration (for each group) - 36.9 sessions |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre participants were recruited from local community mental health centres in the South London and Maudsley NHS Trust |
| | **Number of people screened, excluded & reasons:**<br>254 referred<br>110 refused consent<br>52 failed initial eligibility<br>7 failed cognitive screening. |
| | **Notes about study methods:** Participants were randomly allocated by an independent statistician using a concealed randomisation method. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- Been in contact with services for >=1 years
-Aged17+
-Diagnosis of schizophrenia and evidence of both social functioning and thinking difficulties.

**Total sample size:** No. randomised 85

**Total sample size:** ITT population - Not clear

**Gender:** % female 27%

**Age:** Mean 36

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** Approx 50% had been in touch with the psychiatric services for at least 10 years.

**Baseline stats:**
[CRT / control]
Memory (digit Span): 14.2(3.9) / 15.1(3.9)
WCST: 2.4(1.5) / 2.2(1.3)
Planning (BADS): 11.7(4.6) / 12.7(5.1)
PANSS total: 62.9(16.4) / 56.9(14.7)
SES: 17.3(4.4) / 16.7(4.2)
SBS: 11.6(8.5) / 13.7(11.2)

**Notes about participants:**
[CRT / control]
Atypical medication, n
Clozapine: 16 / 12
Olanzapine: 8 / 12
Risperidone: 7 / 2
Amisulpride: 1 / 2
Quetiapine: 2 / 1
Typical medication, Mean dose, mg CPZ equivalent: 368 / 300

**Interventions** **Intervention - group 1.:** CRT, 40 sessions, n=43

**Intervention - group 2.:** Control, n=42

**Notes about the interventions:**

CRT
In addition to TAU, the treatment group underwent CRT which consisted of 40 face-to-face sessions, each involving a number of pencil and paper tasks that provide practice in a variety of cognitive skills. CRT is based on 3 general principles: 1) teaching new efficient information processing, 2) individualised therapy and 3) aiding the transfer of cognitive gains into the real world. The programme consists of 3 modules: cognitive flexibility, working memory and planning.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state, PANSS; SES
Paper notes that the level of symptoms appears to be greater in the therapy group at baseline. This variable was included as a covariate in all the models considered, however only unadjusted end point means have been reported.

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SBS

**Cognitive functioning:** Average score/change in cognitive functioning - Digit Span, WCST; BADS

**Cognitive functioning:** Clinically significant change in cognitive functioning - For the cognitive measures NNT for a clinically significant change was calculated.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

**References of included studies (update)**

**BELLUCCI2002**

Bellucci,D.M.; Glaberman,K.; Haslam,N. (2003) Computer-assisted cognitive rehabilitation reduces negative symptoms in the severely mentally ill. *Schizophrenia Research* 59: 225 - 232.

**BURDA1994**

Burda, P.C., Starjey, T.W, Dominguez, F., Vera, V. (1994) Computer-assisted cognitive rehabilitation of chronic psychiatric inpatients. *Computers in Human Behaviour* 10: 359-368.

**EACK2007**

Eack,S.M.; Hogarty,G.E.; Greenwald,D.P.; Hogarty,S.S.; Keshavan,M.S. (2007) Cognitive enhancement therapy improves emotional intelligence in early course schizophrenia: Preliminary effects. *Schizophrenia Research* 89(1-3): 308-311.

**HOGARTY2004**

Hogarty,G.E.; Flesher,S.; Ulrich,R.; Carter,M.; Greenwald,D.; Pogue-Geile,M.; Kechavan,M.; Cooley,S.; DiBarry,A.L.; Garrett,A.; Parepally,H.; Zoretich,R. (2004) Cognitive enhancement therapy for schizophrenia: effects of a 2-year randomized trial on cognition and behavior. *Archives of General Psychiatry* 61(9): 866 - 876.

**KURTZ2007**

Kurtz,M.M.; Seltzer,J.C.; Shagan,D.S.; Thime,W.R.; Wexler,B.E. (2007) Computer-assisted cognitive remediation in schizophrenia: What is the active ingredient? *Schizophrenia Research* 89(1-3): 251-260.

**PENADES2006**

Penades,R.; Catalan,R.; Salamero,M.; Boget,T.; Puig,O.; Guarch,J.; Gasto,C. (2006) Cognitive remediation therapy for outpatients with chronic schizophrenia: a controlled and randomized study. *Schizophrenia Research*. 87(1-3): 323 - 331.

**SARTORY2005**

Sartory,G.; Zorn,C.; Groetzinger,G.; Windgassen,K. (2005) Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. *Schizophrenia Research* 75: 219 - 223.

**SILVERSTEIN2005**

Silverstein,S.M.; Hatashita-Wong,M.; Solak,B.A.; Uhlhaas,P.; Landa,Y.; Wilkniss,S.M.; Goicochea,C.; Carpiniello,K.; Schenkel,L.S.; Savitz,A.; Smith,T.E. (2005) Effectiveness of a two-phase cognitive rehabilitation intervention for severely impaired schizophrenia patients. *Psychological Medicine* 35(6): 829 - 837.

**SPAULDING1999**

Spaulding, W.D., Reed, D., Sullivan, M., Richardson, C. & Weiler, M. (1999) Effects of cognitive treatment in psychiatric rehabilitation. *Schizophrenia Bulletin* 25: 657-676.

**TWAMLEY2008**

Twamley,E.W.; Savla,G.N.; Zurhellen,C.H.; Heaton,R.K.; Jeste,D.V. (2008) Development and pilot testing of a novel compensatory cognitive training intervention for people with psychosis. *American Journal of Psychiatric Rehabilitation*. 11(2): 144-163.

**VANDERGAAG2002**

Van der Gaag M.; Kern,R.S.; van den Bosch,R.J.; Liberman,R.P. (2002) A controlled trial of cognitive remediation in schizophrenia. *Schizophrenia Bulletin* 28: 167 - 176.

**VELLIGAN2000**

Velligan, D.I., Bow-Thomas, C.C., Huntzinger, C., Ritch, J., Ledbetter, N., Prihoda, T.J. & Miller, A.L. (2000) Randomized controlled trial of the use of compensatory strategies to enhance adaptive functioning in outpatients with schizophrenia. *American Journal of Psychiatry* 157: 1317-1323.

**VELLIGAN2002**

Velligan,D.I.; Prihoda,T.J.; Ritch,J.L.; Maples,N.; Bow-Thomas,C.C.; Dassori,A. (2002) A randomized single-blind pilot study of compensatory strategies in schizophrenia outpatients. *Schizophrenia Bulletin28*(2): 283 - 292.

**VELLIGAN2008**

Velligan,DI; Diamond,PM; Maples,NJ; Mintz,J.; Li,X.; Glahn,DC; Miller,AL (2008) Comparing the efficacy of interventions that use environmental supports to improve outcomes in patients with schizophrenia. *Schizophrenia Research* 102(1-3): 319.

**VELLIGAN2008B**

Velligan,DI; Diamond,PM; Mintz,J; Maples,N; Li,X; Zeber,J; Ereshefsky,L; Lam,Y; WingF; Castillo,D; Miller,AL (2008) The use of individually tailored environmental supports to improve medication adherence and outcomes in schizophrenia. *Schizophrenia Bulletin* 34(3): 493.

**VOLLEMA1995**

Vollema MG, Geurtsen GJ, van Voorst AJP. (1995) Durable improvements in Wisconsin Card Sorting Test performance in schizophrenic patients. *Schizophrenia Research* 16: 209-215.

**WYKES2007**

Wykes, T., Newton, E., Landau, S., et al. (2007) Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: An exploratory randomized controlled trial. *Schizophrenia Research*. 94(1-3): 221-230.

**WYKES2007A**

Wykes,T.; Reeder,C.; Landau,S.; Everitt,B.; Knapp,M.; Patel,A.; Romeo,R. (2007) Cognitive remediation therapy in schizophrenia: randomised controlled trial. *British Journal of Psychiatry*. 190: 421 - 427.

Reeder,C; Smedley,N; Butt,K; Bogner,D; Wykes,T (2006) Cognitive Predictors of Social Functioning Improvements Following Cognitive Remediation for Schizophrenia. *Schizophrenia Bulletin* 32(Suppl1): S123 - S131.

**Characteristics of excluded studies (update)**

**BELL2001**

**Reason for exclusion:** CRT + vocational employment services - outside scope

**BELL2003[BELL2001]**

**Reason for exclusion:** Primary paper excluded:
CRT + vocational employment services - outside scope

**BELL2005[BELL2001]**

**Reason for exclusion:** Primary paper excluded:
CRT + vocational employment services - outside scope

**BELL2007[BELL2001]**

**Reason for exclusion:** Primary papers excluded

**BELL2008[BELL2001]**

**Reason for exclusion:** Primary paper excluded
CRT + vocational employment services - outside scope

**Bellack2001**

**Reason for exclusion:** Does not meet intervention definition

**GREIG2007**

**Reason for exclusion:** CRT + vocational employment services - outside scope

**Lewis 2003**

**Reason for exclusion:** - participants were not randomised. A method of minimisation was used instead.

**LINDENMAYER2008**

**Reason for exclusion –** CRT + vocational employment service – outside scope

**LOPEZ-LUENGO2003**

**Reason for exclusion:** - 15/39 participants excluded from all analyses. The paper does not explicitly state whether this occurred before or after randomisation. It appears from the follow-up paper that these exclusions were post-randomisation as reasons for exclusion include relapse, drop-out, change of address etc.
- cannot use just drop out as paper did not report the numbers randomised into each group before these 15 participants were excluded

**LOPEZ-LUENGO2005[LOPEZ-LUENGO2003]**

**Reason for exclusion:** - 15/39 participants excluded from all analyses. The paper does not explicitly state whether this occurred before or after randomisation. It appears from the follow-up paper that these exclusions were post-randomisation as reasons for exclusion include relapse, drop-out, change of address, etc.
- cannot use just drop out as paper did not report the numbers randomised into each group before these 15 participants were excluded

**MCGURK2005A**

**Reason for exclusion:** CRT + vocational employment services - outside scope

**MCGURK2007[MCGURK2005]**

**Reason for exclusion:** Primary paper excluded
CRT + vocational employment services - outside scope

**MCGURK2008**

**Reason for exclusion:** No relevant comparison

**MORITZ2007**

**Reason for exclusion:** Does not fit definition of CRT - focuses on meta-cognition and not basic cognitive processes
No relevant comparison

**Tompkins1995**

**Reason for exclusion:** Does not meet intervention definition

**UELAND2004**

**Reason for exclusion:** Early onset schizophrenia (<18 years old) - outside scope

**UELAND2005[UELAND2004]**

**Reason for exclusion:** Primary paper excluded
Early onset schizophrenia (<18 years old) - outside scope

**VAUTH2005**

**Reason for exclusion:** CRT + vocational employment services - outside scope

**References of excluded studies (included in previous guideline, but excluded from update)**

Bellack, AS, Weinhardt, LS, Gold, JM, Gearon, JS. (2001) Generalization of training effects in schizophrenia. *Schizophrenia Research*; 48 (2-3):255-262.

Tompkins LM, Goldman RS, Axelrod BN. (1995) Modifiability of neuropsychological dysfunction in schizophrenia. *Biological Psychiatry*; 38:105-11

**References of excluded studies (update)**

Bell M.D.; Bryson G.J.; Greig T.C.; Fiszdon J.M.; Wexler B.E. (2005) Neurocognitive enhancement therapy with work therapy: Productivity outcomes at 6- and 12-month follow-ups. *Journal of Rehabilitation Research and Development* 42/6(829-838):

Bell, M.; Bryson, G.; Greig, T.; Corcoran, C.; Wexler, B.E. (2001) Neurocognitive Enhancement Therapy with Work Therapy. *Archives of General Psychiatry* 58: 763 - 768.

Bell,M.; Bryson,G.; Wexler,B.E. (2003) Cognitive remediation of working memory deficits: durability of training effects in severely impaired and less severely impaired schizophrenia. *Acta Psychiatrica Scandinavica* 108(2): 101 - 109.

Bell,M.; Fiszdon,J.; Greig,T.; Wexler,B.; Bryson,G. (2007) Neurocognitive enhancement therapy with work therapy in schizophrenia: 6-month follow-up of neuropsychological performance. *Journal of Rehabilitation Research and Development.* 44(5): 761 - 770.

Bell,M.; Zito,W.; Greig,T.; Wexler,B.E. (2008) Neurocognitive enhancement therapy and competitive employment in schizophrenia: Effects on clients with poor community functioning. *American Journal of Psychiatric Rehabilitation*. 11(2): 109-122.

Greig TC, Zito W, Wexler BE, Fiszdon J, Bell MD. (2007) Improved cognitive function in schizophrenia after one year of cognitive training and vocational services. *Schizophrenia Research*. 96(1-3):156-61.

Lewis,L.; Unkefer,E.P.; O'Neal,S.K.; Crith,C.J.; Fultz,J. (2003) Cognitive rehabilitation with patients having persistent, severe psychiatric disabilities. *Psychiatric Rehabilitation Journal*. 26: 325 - 331.

Lindenmayer, J.P., McGurk, S.R., Museser, Khan, A., Wance, D., Hoffman, D., Wolfe, R & Xie, H. (2008) A randomized controlled trial of cognitive remediation among inpatients with persistent mental illness. *Psychiatric Services* 59(3): 241 - 247.

Lopez-Luengo,B.; Vazquez,C. (2003) Effects of Attention Process Training on cognitive functioning of schizophrenic patients. *Psychiatry Research* 119(1-2): 41 - 53.

Lopez-Luengo,B.; Vazquez,C. (2005) Effects of a neuropsychological rehabilitation programme on schizophrenic patients' subjective perception of improvement. *Neuropsychological Rehabilitation* 15(5): 605 - 618.

McGurk,S.R.; Mueser,K.T. (2008) Response to cognitive rehabilitation in older versus younger persons with severe mental illness. *American Journal of Psychiatric Rehabilitation*. 11(1): 90-105.

McGurk,S.R.; Mueser,K.T.; Feldman,K.; Wolfe,R.; Pascaris,A. (2007) Cognitive training for supported employment: 2-3 year outcomes of a randomized controlled trial. *The American Journal of Psychiatry* 164: 437 - 441.

McGurk,SR; Mueser,KT; Pascaris,A (2005A) Cognitive training and supported employment for persons with severe mental illness: one-year results from a randomized controlled trial. *Schizophrenia Bulletin* 31(4): 898-909.

Moritz,S.; Woodward,T.S. (2007) Metacognitive training for schizophrenia patients (MCT): A pilot study on feasibility, treatment adherence, and subjective efficacy. *German Journal of Psychiatry*. 10(3): 69-78.

Ueland, T. & Rund, B.R. (2004) A controlled randomized treatment study: the effects of a cognitive remediation program on adolescents with early onset psychosis. *Acta Psychiatrica Scandinavica* 109: 70-74.

Ueland, T. & Rund, B.R. (2005) Cognitive remediation for adolescents with early onset psychosis: a 1-year follow-up study. *Acta Psychiatrica Scandinavica*. 111: 193-201.

Vauth, R.; Corrigan, P.W.; Clauss, M.; Dietl, M.; Dreher-Rudolph, M.; Stieglitz, R.-D.; Vater Rainer Research Group of Cognitive-Behavioral Intervention for Schizophrenia (2005) Cognitive strategies versus self-management skills as adjunct to vocational rehabilitation. *Schizophrenia Bulletin* 31(1): 55-66.

## Counselling and supportive therapy

| Previous guideline review | 1. Review type<br>2. No. of studies<br>3. No. randomised | Interventions | Outcomes reported in review |
|---|---|---|---|
| Pilling S, Garety P, Michelson D, Whittington C.<br><br>Counselling and Supportive Therapy for schizophrenia.<br><br>(New systematic review produced for schizophrenia guideline) | 1. Systematic review of RCTs.<br>2. 14 (8 RCTs from existing reviews of other interventions, 3 new RCTs also used in other reviews, 3 new RCTs not used in other reviews).<br>3. 1143. | 1. Counselling or supportive therapy was a discrete psychological intervention where: the intervention is facilitative, non-directive and/or relationship focused, with the content largely determined by the patient; and the intervention does not fulfil the criteria for any other psychological intervention.<br>2. Other active interventions.<br>3. Standard care was defined as the normal level of psychiatric care provided in the area where the trial was carried out. | Leaving the study early.<br>Death.<br>Relapse.<br>Readmission.<br>Mental state: Continuous measures.<br>Mental state: Criterion-based. |
| **Update** | **Follow up to existing studies:** 4 papers providing follow-up data to existing RCTs.<br>**New studies:** 6 RCTs.<br>**Existing studies excluded from update:** 2 RCTs: Levine1998; Turkington2000. | | **Notes:**<br>Definition updated |

**Characteristics of included studies (previous guideline)**

| Study | Methods | Participants | Interventions | Outcomes | Notes |
|---|---|---|---|---|---|
| **Donlon1973** | Allocation: patients matched and then "randomly placed" into one of two groups. Blinding: none. Duration/frequency: 18 weeks, nine biweekly sessions, each lasting 90 minutes. Actual supportive therapy content of group sessions lasted ~30 minutes. Actual supportive therapy content in individual sessions lasted ~10-20 minutes. | Outpatients. Diagnosis: "chronic schizophrenia or chronic paranoid schizophrenia." N=24. Age: mean 33, range 19-51. 11 M 13 F. History: all patients were "treatment refractory" and shared "marked anxiety in interpersonal relationships and a tendency to be aloof, suspicious, and noncommunicative." Mean duration of lifetime hospitalisation 3.2 years, range 2 months-18 years. | 1. Group supportive therapy: structured group meetings, intended to allay interpersonal anxiety "with a nonthreatening milieu of acceptance and emotional support and to provide nurturance through warmth and refreshments." N=12*.<br><br>2. Individual supportive therapy: intended to provide a "nonthreatening, accepting, supportive therapeutic relationship with freedom from the stress of group membership and to provide nurturance." N=12*. | Leaving the study early. No. of admissions.<br><br>Unable to use: Socialisation (no data). Cost (no SD). | *Does not report actual numbers in each group - N=12 is an assumption based on method of randomisation. |
| **Eckman1992** | Allocation: "randomly assigned." Blinding: attempts were made to blind raters, but some patients revealed information about their allocation | Inpatients/outpatients. Diagnosis: schizophrenia (DSM-III-R). N=41. Mean age: ~40. Sex: all M. History: mean duration of illness (months) skills training group 171.50 (SD 110.16), supportive psychotherapy group 165.24 (SD 86.21); Mean age at onset 26.10 | 1. Group psychotherapy: subjects engaged in an insight-oriented and supportive group process, and provided with education about schizophrenia as an illness and the importance of adhering to medication. Medication and symptom management were discussed, but no structured curriculum was followed and no formal behavioural techniques were used. "The group could | Leaving the study early.<br><br>Unable to use: BPRS (no usable data) Skill attainment (no usable data). | |

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| | during rating sessions. Duration/frequency: 18 months, twice weekly 90-minute sessions for first 6 months, weekly sessions thereafter. | (SD 7.07), supportive psychotherapy group 24.76 (SD 4.92); mean no. hospitalizations 3.75 (SD 2.27), supportive psychotherapy group 4.00 (SD 1.61). | best be described as aiming for individual and personal goals encouraged through exploratory and supportive leadership." N=21.<br><br>2. Modular skills training: based on two modules from the UCLA Social and Independent Living Skills Program with highly prescribed curricula for teaching medication and symptom self-management. N=20. | | |

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| **Falloon1981** | Allocation: 'randomized procedure' - no further details.<br>Blinding: clinical exacerbations not blind, target symptoms, compliance with medication, BPRS, PSE blind. Hopkins Symptom Checklist, self rating.<br>Duration: 9 months treatment, 2 years follow up.<br>Frequency: 1 hour per week/3 months, 1 hour per 2 weeks/6 months, 1 hour per month/15 months. | Diagnosis: schizophrenia (DSM-III, PSE).<br>N = 39.<br>Age: range 18-41 years, mean 25.8.<br>History: stabilised after relapse, English speakers, mean previous admissions ~3, mean duration ill ~ 4 years, high EE (CFI). | 1. Home family therapy: patient + family, 24-hour support, clinic-based therapist, crisis intervention / home visits as needed, weekly 3/12, fortnightly 6/12. N=20.<br>2. Supportive management: outpatient clinic-based individual supportive psychotherapy. N=19. | 1. Relapse.<br>2. Hospital admission.<br>3. Leaving the study early.<br>4. Drug compliance.<br>5. Unemployed.<br>6. Residential care.<br>7. Imprisonment.<br>8. Social impairment.<br>9. Ability to cope.<br><br>Unable to use:<br>1. Mental state ("7 point scale" no further details).<br>2. Duration of exacerbation (no SD).<br>3. Duration unstable (no SD).<br>4. Family functioning (SBAS, no usable data).<br>5. Family knowledge (no data).<br>6. Patient functioning (no usable data).<br>7. Patient coping (SAS-SR, no usable data).<br>8. Time in employment (no SD).<br>9. Costs (no SD). | |
| **Haddock1998** | Allocation: "randomly allocated."<br>Blinding: raters blind. Duration: 5 weeks or until | Inpatients<br>Diagnosis: schizophrenia or schizoaffective (DSM-IV). N=21.<br>Age: ~29.<br>Sex: 19 M 2 F.<br>History: 1st treatment for | 1. CBT: manual-based. 4 treatment stages: i) engagement and assessment of mental state and symptoms to allow cognitive-behavioural analysis of how symptoms might relate to cognitions, behaviour and coping strategies. Stress-vulnerability model | Leaving the study early.<br>Number of days in hospital.<br>Relapse.<br>BPRS. | Pilot study to Lewis 2002. |

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| | patient discharged if this period was shorter, booster sessions at 1, 2, 3,4 months post-discharge. 2 year follow-up. Frequency: mean no. CBT sessions 10.2 (SD 5.1), 1.67 booster sessions. Mean no. SC sessions 9.1 (SD=4.36), 0.91 booster sessions. | schizophrenia less than 5 years ago, currently admitted to acute ward for onset or relapse of psychotic symptoms. | used to link biological and psychological mechanisms; ii) prioritised problem list developed collaboratively with patient. Problems assessed for trigger situations and cognitions; iii) & iv) intervention and monitoring.<br><br>2. Supportive counselling (SC): manual-based – no further description.<br><br>3. Routine care. | Unable to use:<br>1. No. of days to 1st readmission (no SD).<br>2. No. of days to relapse (no SD).<br>3. PSYRATS scale (no data). | |

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| **Herz2000** | Allocation: randomisation using computer-generated cards stored in sealed envelopes.<br>Blinding: raters blind. Duration: 18 months. | Outpatients.<br>Diagnosis: schizophrenia or schizoaffective disorder (DSM-II-R). N=82.<br>Age: ~30.<br>Sex: 53 M, 29 F.<br>History: mean no. previous admissions - Programme for relapse prevention (PRP) group 2.27 (1.29), Supportive therapy group 2.64 (1.28). At least 1 hospitalisation in past 3 years, and 2 or more lifetime admissions. | 1. Programme for relapse prevention (PRP = multimodal intervention):<br>i) education for patients and family; ii) active monitoring of symptoms; iii) clinical intervention when prodromal symptoms detected;<br>iv) 1-hour weekly supportive group therapy emphasising coping skills, or 30-45 minute individual supportive therapy sessions if patients refused group treatment;<br>v) 90-minute multi-family psychoeducation, biweekly for 1st 6 months, monthly thereafter.<br><br>2. Individual supportive therapy and medication management: biweekly for 15-30 minutes. | Leaving the study early.<br>Relapse.<br>Readmission.<br>Noncompliance with medication.<br><br>Unable to use:<br>1. Early Signs Questionnaire, PANSS, GAS (no SDs reported). | |
| **Hogarty1997** | Allocation: random assignment - two concurrent trials (with/without families).<br>Blinding: none.<br>Duration: 3 years.<br>Frequency: weekly for personal therapy, with less contact in year 3 for those who completed treatment objectives; biweekly for supportive therapy in all years. | Outpatients.<br>Diagnosis: schizophrenia or schizoaffective disorder (DSM-IV). N=101.<br>Age: with family mean 28.6 (SD 7.5), living independently of family mean 33.0 (SD 7.6).<br>Sex: with family 56 M 41 F, living independently of family 24 M 30 F.<br>History: mean duration of illness living with family 6.2 years (SD 6.5), living independently of family 10.2 (SD 8.2). | 1. Personal therapy: focus on "modifying model of person," environmental and emotional monitoring - internal coping strategies. N=48.<br><br>2. Supportive therapy: active listening, correct empathy, appropriate reassurance, reinforcement of patient health-promoting initiatives, and reliance on the therapist for advocacy and problem solving in times of crisis. N=53. | Leaving the study early<br>Relapse.<br><br>Unable to use:<br>1. Social adjustment (no usable data).<br>2. Mental state (no usable data).<br>3. Family rating (no usable data). | Therapists: Masters level psychiatric nurse, clinical specialists and doctoral level clinical psychologists.<br>Supervision: fidelity to therapy was facilitated by explicit treatment manuals as well as by weekly individual and peer-group supervision provided by two senior (doctoral |

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| | | | | | level) clinical supervisors and/or the principal investigator and by treatment process ratings that identified the practice principles used and the goals achieved.<br>CBT type: coping, stress-vulnerability/ problem solving. |

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|---|---|---|---|---|---|
| **Kemp1996** | Allocation: randomised using tables of random numbers.<br>Blinding: none.<br>Duration: 2-3 weeks (4-6 sessions in total). 18 months follow-up.<br>Frequency: 20-60 minutes twice a week. | Inpatients.<br>Diagnosis: 43 schizophrenia (DSM-III-R), remaining sample mood disorders.<br>N=74.<br>Age: CBT group mean 34 (SD 10.6), control group mean 37 (SD 11.9).<br>Sex: 39 M 35 F.<br>History: mean duration of illness CBT group 8.5 years (SD 6.3), control group 10.7 years (SD 9.6). | 1. CBT + standard care: compliance therapy - reviewing history of illness, discussing the benefits and drawbacks of drug treatment, the stigma of drugs, the discrepancy between patient's action and beliefs. N=39.<br>2. Supportive counselling: therapists listening to patients' concerns but declined to discuss treatment. N=35. | 1. Death<br>2. Leaving the study early.<br>3. Relapse.<br>4. BPRS.<br>5. Global Assessment of Functioning scale (GAF).<br>5. Extended Schedule for Assessment of Insight.<br>6. Drug Attitudes Inventory.<br>7. Attitudes to Medication Questionnaire.<br><br>Unable to use:<br>1. Medication compliance (not a peer-reviewed published scale).<br>2. Attitudes to treatment questionnaire (not a peer-reviewed published scale). | Therapists: research psychiatrist & clinical psychologist. Both trained in CBT and attended a workshop on motivational interviews.<br>Supervision: therapists received regular supervision.<br>CBT type: compliance therapy. |
| **Levine1998** | Allocation: randomised.<br>Blinding: none.<br>Duration: 6 weeks, 4 week follow-up. | Diagnosis: paranoid schizophrenia.<br>History: ill > 5 years, not comorbid substance misuse, nor chronic physical condition or orthodox religious conviction.<br>N=12.<br>Age: range 20-45 years. | 1. CBT: "cognitive-dissonance group therapy" – "group devoted to the various possibilities of understanding life events," alternative explanations for delusional explanations generated in homework assignments, reviewed in groups, six weekly 50 minute sessions + standard care. N=6.<br>2. Supportive therapy: group based, "focused on difficulties that patients faced in coping with everyday life," six weekly sessions + standard care. N=6. | Mental state: PANSS scores at follow-up - positive, negative, general, thought disturbance and total scores.<br>Leaving the study early.<br>Unable to use:<br>PANSS scores at end of treatment (SDs not provided) | Therapists: authors, "previously trained in inducing cognitive dissonance in paranoid patients." |

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| **Lewis2002** | Allocation: "independent, concealed randomisation of individuals with minimisation." Stratification according to 1st or 2nd admission, inpatient or day patient, M or F, 1st episodes further stratified for duration of symptoms of more or less than 6 months. Blinding: "all outcome assessments were made blind to treatment allocation." Duration/frequency: 15-20 hours within 5-week treatment envelope, plus booster sessions at a further 2 weeks, and 1, 2, 3 months. | Inpatients (N=264) and day patients (N=45). Diagnosis: schizophrenia, schizophreniform, schizoaffective, or delusional disorder (DSM-IV). N=309. Age: median 27.4. Sex: 216 M, 93 F. History: all patients either 1st episode (N=257) or 2nd episode (N=52) admissions, positive psychotic symptoms for 4 weeks or more, moderate or severe score (4 or more) on PANSS target item for delusions or hallucinations. | 1. CBT: manual-based. 4 treatment stages: i) engagement and assessment of mental state and symptoms to allow cognitive-behavioural analysis of how symptoms might relate to cognitions, behaviour and coping strategies. Stress-vulnerability model used to link biological and psychological mechanisms; ii) prioritised problem list developed collaboratively with patient. Problems assessed for trigger situations and cognitions; iii) & iv) intervention and monitoring. 2. Supportive counselling (SC): manual-based – no further description. 3. Routine care. | Leaving the study early. Death. PANSS (Positive and Negative Syndrome Scale): total and positive scale scores. Delusions Scale (DS). Auditory Hallucinations Scale (AHS). | |
| **Marder1996** | Allocation: random. Blinding: none Duration: 2 years. | Outpatients. Diagnosis: schizophrenia (DSM-III-R). N=80. Age: treatment group mean 38.5 (SD 9.0), control group mean 37.9 (SD 8.6). | 1. Social skills training: 90 minute sessions, twice weekly, for first 6 months, then weekly, to compensate for schizophrenic symptoms and cognitive deficits, using cognitive restructuring principles, repeated behavioural rehearsal, video modelling, | 1. Leaving the study early. 2. Relapse/readmission. 3. SAS (social adjustment). | Therapists: therapy administered by one or two leaders who were doctoral and master's level psychologists, an |

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| | | Sex: all males.<br>History: mean duration of illness - treatment group mean 12.5 years (SD 8.9), control group mean 13.4 years (SD 9.0), mean age at onset of illness - treatment group mean 25.5 (SD 5.7), control group mean 24.4 years (SD 4.8). | social reinforcement, homework. N=43.<br>2. Supportive group psychotherapy: encouraging patients to set personal goals and harness group dynamics, explore problems and obstacles. N=37. | Unable to use:<br>1. Exacerbation in symptoms (no usable data). | occupational therapist, and a social science technician. Therapist for control condition was a doctoral-level psychologist. |

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| **Sensky2000** | Allocation: "simple randomization applied independently" for two sets of patients, one from London and another from the north of England. Blinding: "assessors were independent of the randomization procedure and remained blind to each patient's assigned group throughout the study." Duration: 9 months. Frequency: number and length of sessions "were flexible to accommodate the needs of individual patients, but the initial aim was to offer each patient at least 45 minutes of therapy each week. After this phase, which could last up to 2 months, the session frequency could be reduced." | Outpatients.<br>Diagnosis: schizophrenia (ICD-10 RDC & DSM-IV). N=90.<br>Age: mean 39 (CT), 40 (BF).<br>Sex: 53 M 37 M.<br>History: mean duration of illness 14 years, mean number of previous admissions 14. | 1. CBT: began by examining the antecedents of emergence of psychotic disorder, developing a normalising rationale, generating shared case formulation. Thereafter, coping strategies for positive symptoms developed. Finally, interventions for negative symptoms attempted "using paced activity scheduling and diary recording of mastery and pleasure." N=46.<br><br>2. Befriending: designed to provide patients with approximately the same amount of therapist contact as CBT group, with sessions spaced at similar intervals. Intervention was empathic and nondirective. "Psychotic or affective symptoms were not directly tackled in any way." Sessions focused on neutral topics (for example, hobbies, sports, current affairs). N=44. | 1. Leaving the study early.<br>2. CPRS endpoint.<br>3. SANS endpoint.<br>4. MADRS endpoint.<br>5. Clinical improvement (50% cut off) on CPRS, MADRS, and SANS.<br><br>Unable to use:<br>1. Patient satisfaction (no usable data). | Therapists: two experienced psychiatric nurses. Supervision: therapists provided with regular supervision. Interviews were audiotaped for supervision and for quality control. |
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| **Stanton1984 (Gunderson 1984 in psycho-analysis ET)** | Allocation: random, no further details.<br>Blinding: unclear.<br>Duration: 2 years, had to stay in therapy for 6 months to be eligible to go onto 2 year follow-up. | Setting: all hospitalised initially, then in community.<br>Diagnosis: schizophrenia, DSM II & III, diagnosis confirmed three times.<br>Age: 18-35 years.<br>N=164 (almost 2000 screened).<br>Sex: not mentioned.<br>Inclusion criteria: minimal prior treatment, no drug or alcohol problems, no organic illnesses, able to function outside of hospital for 4 consecutive months in some major role without medication in the previous2 years. | 1. Insight-oriented psychotherapy: N=88*.<br><br>2. Reality-adaptive, supportive psychotherapy: "generally focused on problems in the current living situation of the client… intended to identify problems that could be solved or that could be expected to recur in the future so that more effective coping strategies could be mapped out." Techniques included support, reassurance, limits, clarification. N=76*. | 1. Global impression (rehospitalised, unable to take household responsibilities, unable to have key relationship, not self supporting).<br>2. Leaving the study early.<br><br>Unable to use:<br>1. Cognition (no SD).<br>2. Ego functioning (no SD).<br>3. Signs and symptoms of illness (no SD).<br>4. Use of medication (no SD).<br>5. Hospitalisation (no SD). | *Gunderson reports randomising 95 people. In earlier report of same study (Stanton 1984) 164 people were said to have been randomised. For the 69 dropouts there are no other available data other than leaving the study early. There are only usable data of 95 people staying in therapy beyond 6 months. |
| **Tarrier1998** | Allocation: random allocation, stratified sample technique.<br>Blinding: blinded raters.<br>Duration: 10 weeks<br>Frequency: 20 sessions altogether, 1 hour twice a week. | Outpatients.<br>Diagnosis: schizophrenia, schizoaffective psychosis, delusional disorder (DSM III R).<br>N=87.<br>Age: mean 39 (SD 11).<br>Sex: 69 M 18F.<br>History: median duration of illness 11 years, persistent positive symptoms. | 1. CBT: coping strategy enhancement, training in problem solving, strategies to reduce relapse + standard care. N=33.<br>2. Supportive counselling: emotional support, unconditional regard, general counselling + standard care. N=26.<br>3. Standard care. N=28. | 1. Leaving the study early.<br>2. Relapse.<br>3. Mental state: important improvement (BPRS).<br>Unable to use: 1. BPRS change scores (SD not reported). 2. Positive and negative symptom severity (SD not reported). | Therapists: 3 were experienced clinical psychologists.<br>Supervision: the therapists met on a regular basis to discuss cases. Sessions were taped.<br>CBT type: coping/problem solving. |
| **Turkington** | Allocation: random, but in 2:1 ratio (CBT | Patients were seen in a variety of settings - home, hostels, day | 1. CBT: "inductive questioning identified faulty cognitions" and a shared explanation | 1. Leaving the study early. | Therapist: general psychiatrist. |

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| **2000** | group: control group). Blinding: assessors, families, and treatment team blind to randomisation. Duration: 2 months. Frequency: 6 sessions, 20-40 minutes in length. Three sessions were in first 2 weeks, then frequency was decreased, "to finish 6-8 weeks after the commencement of therapy." | hospitals, as inpatients in hospital. Diagnosis: schizophrenia (ICD-10). N=19. Age: CBT group mean 37.4, befriending group mean 44.2. Gender ratio (M:F): 7:5 (CBT group), 2:4 (befriending group). Mean length of illness (years): 9.2 (CBT group), 13.0 (befriending group). Mean length of hospitalisation (years): 11.3 (CBT group), 14.3 (befriending group). | of the onset and maintenance of symptoms was developed. Alternative explanations of delusional beliefs were explored. N=13.<br><br>2. Befriending: "provided with regular contact with a general psychiatrist, in addition to normal management by their treatment team." N=6. | 2. Comprehensive Psychopathological Rating Scale (CPRS).<br><br>Unable to use: (SD not given):<br>1. Montgomery-Asberg Depression Rating Scale (MADRS).<br>2. Time spent in hospital (6 months after commencement of treatment). | Pilot study to Sensky 2000. |

**References of included studies (previous guideline)**

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**Turkington 2000**

*Turkington D, Kingdon D. (2000) Cognitive-behavioural techniques for general psychiatrists in the management of patients with psychoses. *British Journal of Psychiatry*; 177:101-106.

**Characteristics of included studies (update)**

| **Study ID** | **JACKSON2007** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Analyses were performed on all 62 participants and follow-up interviews were conducted where possible, regardless of whether they had withdrawn.<br><br>Ten multiply imputed (MI) datasets were generated to deal with missing responses |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - Up to 14 weeks maximum |
| | **Duration:** Length of follow-up - 1 year |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Early Psychosis Prevention Centre (EPPIC), Melbourne, Australia |
| | **Number of people screened, excluded & reasons:** 427 people screened, of whom 111 were excluded due to ineligibility, a further 126 people referred within the time-frame could not be approached e.g. no response to telephone calls/ letters, DNA at appointments. Therefore 190 people were approached for inclusion into the study. Of these 128 refused to participate. |
| | **Notes about study methods:** Randomisation was stratified according to affective and non-affective psychotic diagnosis to ensure equal distribution across therapists and treatment conditions. The randomisation process was conducted by an independent statistician. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 13% |
| | **Diagnosis:** Other schizophrenia related [%] schizophreniform - 40%<br>schizoaffective - 11% |
| | **Diagnosis:** Other [%] bipolar / depressive - 21% |

Delusional / psychotic (NOS) - 15%

**Diagnostic tool:** DSM-IV

**Exclusion criteria:**
- inability to speak English
- intellectual disability (IQ<70)
- psychosis due to a medical condition
- change to non-psychotic diagnosis
- left the EPPIC catchment area
- treatment from a private psychiatrist/ psychologist
- participating in a first-episode mania trial
- exhibiting violent behaviour or being incarcerated

**Total sample size:** No. randomised - 62

**Total sample size:** ITT population - 53 at end of treatment, 55 at follow-up

**Gender:** % female 27%

**Age:** Range EPPIC age range = 15-25

**Age:** Mean 22

**Ethnicity:** Not reported

**Setting:** Other EPPIC - a comprehensive treatment service which included an inpatient unit, an outpatient case management system, family work, accommodation, prolonged recovery programmes and tailored group programmes.

**History:**
[ACE / befriending]
Mean age of onset of psychosis: 21.58(3.49) / 21.67(4.20)
Median length of psychosis (untreated) in days: 83 / 107
Number of in-patient hospitalisation: 12 / 14

**Baseline stats:**
[ACE / Befriending]
Positive symptoms (psychotic subscale of BPRS): 11.68(4.17) / 12.29(4.50)
Negative symptoms (SANS): 22.55(11.66) / 25.55(14.86)
SOFAS: 52.10(11.77) / 51.84(7.09)

**Notes about participants:**
[ACE / Befriending]
Mean neuroleptic dosage in CPZ equivalent: 224(112) / 297(136)
Number who received ECT: 4 / 1

**Interventions** **Intervention - group 1.:** ACE (Active Cognitive Therapy for Early Psychosis), Maximum of 20 sessions of therapy over 14 weeks; n=31

**Intervention - group 2.:** Befriending; n=31

**Notes about the interventions:**
ACE
-ACE manual based on adapted CBT approach.
-Involves the assessment of presenting psychotic and non-psychotic symptoms followed by the formulation of the relationship between these complaints and the participant's life history. Problems are prioritised according to a flowchart that directed the ACE therapy.

Befriending
-based on befriending therapy
-aimed to control for time in therapy, participant expectations and positive experiences of therapy.
-consisted of talking about neutral topics that interested the participant or engaging in activities such as board games, walking or playing sport. The therapist's primary goal was to keep the participant engaged for the full duration of the session and to keep the conversation or activity as close to a neutral chat as possible.

Training
The therapists received 3 months of training in the treatments and were supervised throughout the trial.

**Outcomes** **Death:** Suicide

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Global state & service outcomes (e.g. CGI):** Days in hospital

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - Positive symptoms - measured using the psychotic subscale of the BPRS, SANS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SOFAS

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was**

**completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| **Study ID** | **PATTERSON2006** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer subset of the ITT group who, in addition to completing both a baseline and follow-up assessment, attended at least 25% of all group sessions. |
| | **Type of analysis:** ITT - consisted of participants who attended at least one session of their assigned intervention and completed both a baseline and follow-up assessment. |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 24 weeks |
| | **Duration:** Length of follow-up - 6 months |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - 25 Board and Care facilities in San Diego County, US |
| | **Number of people screened, excluded & reasons:** 465 patients were screened and 219 excluded. Reasons for exclusion include: failure to meet inclusion criteria (n=144), refused to participate (n=67), other (n=8) |
| | **Notes about study methods:** Once at least five consent forms had been received from a particular B&C centre, all participating patients from that B&C were randomised. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 80.5% |
| | **Diagnosis:** Other schizophrenia related [%] schizoaffective disorder - 19.5% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- aged >40 years<br>- patients with longstanding psychotic disorders<br>- patients with a DSM-IV chart diagnosis of schizophrenia or schizoaffective disorder |

**Exclusion criteria:**
- DSM-IV diagnosis of dementia
- serious suicide risk
- could not complete the assessment battery
- participating in any other psychosocial intervention or drug research at the time of study intake

**Total sample size:** No. randomised - 240

**Total sample size:** ITT population - 195

**Gender:** % female 35%

**Age:** Mean - 51

**Ethnicity:** Caucasian - 53%
Hispanic - 25%
African-American - 13.5%
Asian-American - 4%
Native American - 3%
Other - 1.5%

**Setting:** Other - Board and Care facilities

**History:**
[FAST intervention / AC]
Duration of illness, years: 11.6(2.8) / 11.7(2.6)

**Baseline stats:**
[FAST intervention / AC]
UPSA total: 60.3(2.4) / 64.9(2.5)
SSPA: 24.9(0.9) / 27.9(0.9)
MMAA: 14.9(1.1) / 14.8(1.2)
PANSS total: 59.9(2.5) / 62.8(2.7)
HAM-D: 9.9(0.9) / 9.8(0.9)
QWB: 53.9(1.5) / 56.3(1.5)

**Notes about participants:**
[FAST intervention / AC]
Daily neuroleptic dose, mg: 476.5(635.4) / 438.7(472.1)

**Interventions** **Intervention - group 1.:** FAST intervention, 24 weekly sessions of 120 minutes; N=124

**Intervention - group 2.:** Attention Control (AC), 24 weekly 120 minute sessions; n=116

**Notes about the interventions:**

Functional Adaptation Skills Training (FAST)
Based on Liberman et al's Social and Independent Living Programme, a manualised social-cognitive theory-based behavioural intervention was created. The intervention focused on improving six areas of everyday functioning: medication management, social skills, communication skills, organisation and planning, transportation, and financial management. FAST consisted of 24 weekly, 120-minute group sessions.

Attention Control (AC)
Individuals received their medication as usual and participated in 24 weekly, 120-minute group sessions that provided a supportive environment for addressing personal problems.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS; HAM-D

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - UPSA; SSPA

**Quality of Life:** Average score/change in quality of life - QWB

**Other:** MMAA

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not reported adequately

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed

**2.1 How well was the study done to minimise bias?:** +

**Study ID**

**PINTO1999**

**General info**

**Funding source:** Not mentioned

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Blindness:** No mention

**Duration:** No. weeks of treatment - 36

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre - Naples, Italy

**Number of people screened, excluded & reasons:** Not reported

**Notes about study methods:** Randomisation procedure not reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- DSM-IV diagnosis of schizophrenia
- No evidence of current substance misuse or organic pathology
- Treatment-refractory schizophrenia as documented by >=2 previous neuroleptic drug trials of at least 6 weeks at a dose of >600mg chlorpromazine equivalent

**Total sample size:** No. randomised - 41

**Total sample size:** ITT population - 37 completers

**Gender:** % female 31%

**Age:** Mean - 34

**Ethnicity:** Not reported

**Setting:** Outpatient

**Setting:** Inpatient

**History:**
[CBT+SST / Supportive therapy]
Illness duration, years: 9.2(3.3) / 8.2(2.9)
Hospital admissions: 11.6(7.9) / 11.7(6.6)

**Baseline stats:**
[CBT+SST / Supportive therapy]
BPRS: 83.1(21.7) / 81.7(20.6)

**Notes about participants:**

All participants were on Clozapine
[CBT+SST / supportive therapy]
Clozapine dose, mg: 552.6(129.6) / 547.2(109.1)

**Interventions** **Intervention - group 1.:** CBT+SST, 6 months; N = 20

**Intervention - group 2.:** Supportive therapy, 6 months; N=21

**Notes about the interventions:**
CBT+SST
The CBT intervention focused on improving clients' abilities to manage their current psychotic symptoms and was based on the manual by Fowler et al. Skills training methods were used to improve social behaviours including self-case, medication self-management, social conversation, interpersonal problem solving, self-directed recreation, family communication and management of personal resources. Both the CBT and SST components involved rehearsal, positive reinforcement, in vivo exercises and homework assignments.

Supportive therapy
Individual supportive therapy sessions included basic psychoeducation about the nature and treatment of schizophrenia, active listening, empathy and reassurance, reinforcement of the clients; health-promoting initiatives, help in managing a crisis and advocacy of the clients' needs.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS, SANS, SAPS

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| Study ID | ROHRICHT2006 |
|---|---|
| General info | **Funding source:** Non-industry support<br>**Funding source:** Pharmaceutical industry<br>**Published or unpublished data?:** Published |
| Method | **Type of study:** Individual randomised trial<br>**Type of analysis:** ITT - Participants were included in the analysis if they provided a post-therapy assessment regardless of their participation in the interventions.<br>**Blindness:** Only raters blind - All screening, baseline and outcomes assessments were made by an experienced psychiatrist blind to treatment allocation. Patients were requested not to reveal any details of the treatment during post-therapy and follow-up assessments in an attempt to maintain rater blinding.<br>**Duration:** Length of follow-up - 4 months<br>**Duration:** No. weeks of treatment - 10<br>**Raters:** Independent of treatment<br>**Design:** Single-centre - East London, UK<br>**Number of people screened, excluded & reasons:** 67 participants were referred for possible inclusion, 22 were excluded due to: not meeting the inclusion criteria (n=22) and withdrawal from the assessment (10). In total 45 were randomised<br>**Notes about study methods:** Eligible patients were randomly allocated to one of the treatment conditions following the opening of a sealed envelope by the project co-ordinator, who had no involvement in data collection or assessments. |
| Participants | **Diagnosis:** Schizophrenia [% of sample] 100%<br>**Diagnostic tool:** DSM-IV<br>**Inclusion criteria:**<br>- age 20–55 years<br>- an established diagnosis of schizophrenia according to DSM-IV, with >=2 acute psychotic symptoms;<br>- currently an outpatient with time since last inpatient treatment >than 1 month;<br>- suffering from persistent symptoms of schizophrenia for >=6 months with a high degree of negative symptoms at baseline, i.e. PANSS negative score >=20 and/or one of the Anergia items ('emotional withdrawal', 'motor retardation' or 'blunted affect') >=6<br>- stable medication prior to entering the study.<br>**Exclusion criteria:**<br>- evidence of organic brain disease<br>- severe or chronic physical illness<br>- substance misuse as primary diagnosis. |

**Total sample size:** ITT population - 42

**Total sample size:** No. randomised - 45

**Gender:** % female 50%

**Age:** Mean 38

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
[Body-orientated psychological therapy / Supportive counselling]
Duration of illness, year: 12.1(10.5) / 10.8(7.3)
No. of previous hospitalisations: 3.7(2.8) / 4.4(3.8)

**Baseline stats:**
[BPT / SC]
PANSS total: 79.0(13.9) / 76.3(21.1)

**Notes about participants:**
[BPT / SC]
Chlorpromazine equivalent: 497.9(289.1) / 440.5(324.8)

**Interventions**

**Intervention - group 1.:** BPT, 20 sessions of 60-90 minutes over 120 weeks; n=24

**Intervention - group 2.:** SC, 20 sessions of 60-90 minutes over 120 weeks; n=21

**Notes about the interventions:**
TAU
Both BPT and SC were in additional to TAU provided by community psychiatrists. Treatment plans were not substantially altered during the trial period. In both treatment conditions, group size was limited to a maximum of 8.

BPT
The treatment manual used in the intervention was defined by the first author and aimed to integrate different techniques into a clinically focused and syndrome specific method. The protocol manual was designed to achieve the following aims
1) overcome communication barriers through introduction of non-verbal techniques
2) refocus cognitive and emotional awareness towards the body
3) stimulate activity and emotional responsiveness
4) promote exploration of self-potentials focusing on body strength and capability, experiencing the body as a source of creativity, reliability, pleasure and self-expression
5) modify dysfunctional self-perceptions
6) to address common psychopathological features.

SC
The therapist focused on individual differences and corresponding problem-solving strategies regarding the core negative symptoms.

Training
A part-time dance movement therapist conducted BPT. Two nurse therapists, also with previous training and experience in providing psychological therapies for schizophrenia patients, delivered SC. All therapists had many years' experience of working with patients with schizophrenia and attended specific training sessions before the trial. Each received three supervision sessions to ensure adherence to the given treatment manual (on the basis of written records of each session).

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state PANSS - primary outcome focused on the negative PANSS subscale

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state no. with symptom reduction >=20%

**Adverse events:** Average score/change in specific adverse effects SAS

**Satisfaction with treatment:** Service user satisfaction Client's Assessment of Treatment Scale; Helping Alliance Scale

**Quality of Life:** Average score/change in quality of life - Manchester Short Assessment of Quality of Life (MANSA)

**Other:** Medication change, number of treatment sessions attended

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed - special attention was paid to ensuring the blindness of the rater.

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| Study ID | SHIN2002 |
|---|---|
| General info | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| Method | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 10 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - US |
| | **Number of people screened, excluded & reasons:** participants were recruited from a pool of 110 Korean patients with chronic mental illness.<br>-65 patients met diagnostic criteria for study entry.<br>-48 consented to participate. |
| | **Notes about study methods:** Randomisation procedure not reported |
| Participants | **Diagnosis:** Schizophrenia [% of sample] not reported |
| | **Diagnosis:** Other schizophrenia related [%] % with schizoaffective disorder and schizophreniform disorder not reported |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- Any patient with a diagnosis of schizophrenia, schizoaffective disorder, or schizophreniform disorder |
| | **Total sample size:** No. randomised - 48 |
| | **Gender:** % female 58% |
| | **Age:** Mean - 37 |
| | **Age:** Range - 22-53 |
| | **Ethnicity:** all participants were Korean-American |
| | **Setting:** Outpatient |
| | **History:**<br>[Experimental group / control group]<br>Number of hospitalisations: 2.71(1.76) / 1.21(1.18)<br>Time since last hospitalisation, months: 7.17(6.43) / 12.67(19.30) |

**Baseline stats:**
[Experimental / Control]
BPRS total: 91.88(9.76) / 91.83(6.70)
Stigma-Devaluation Scale: 18.54(2.40) / 20.21(2.43)
Family Crisis Oriented Personal Evaluation Scale
total: 80.92(8.22) / 81.02(6.88)

**Notes about participants:**
[Experimental / Control]
Years in US: 14.25(3.00) / 15.08(4.38)
Living arrangement, n(%):
Living away from family: 7(29.2) / 4(16.7)
Living with family: 17(70.8) / 20(83.3)

**Interventions** **Intervention - group 1.:** Experimental group - psychoeducational group; n=24

**Intervention - group 2.:** Control; n=24

**Notes about the interventions:**
TAU - Control
The control group received 10 Individual supportive therapy sessions, each 45 minutes in duration. All of the sessions were conducted in Korean

Psychoeducation
In addition to TAU at the clinic (individual supportive therapy), treatment included 10 weekly psychoeducational group sessions each 90 minutes long. Each session included a variety of educational techniques designed to enhance the participants' learning and to maintain their attention. The curriculum included modules on definitions of illness, medications and side effects, relapse prevention, crisis and illness management, stigma, communication and stress management skills, self-help, and community resources. In addition traditional disease concepts were integrated.

To reinforce the interventions, parallel sessions, also conducted in Korean, were offered to family members of all participants.

**Outcomes** **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS

**Other:** Stigma-Devaluation Scale; Family Crisis Oriented Personal Evaluation Scale.

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not reported adequately

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| **Study ID** | **VALMAGGIA2005** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All randomised participants, excluding 4 patients whose data were lost by assessor |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 6 months |
| | **Duration:** No. weeks of treatment - 22 weeks |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Various mental health hospitals across the Netherlands and one in Belgium |
| | **Number of people screened, excluded & reasons:** 66 assessed for eligibility: 2 did not meet inclusion criteria, 2 refused consent; 62 randomised |
| | **Notes about study methods:** For the randomisation procedure, the project coordinator had two baskets: a 'treatment' basket which contained sealed envelopes with lots for each of the two treatment conditions and a 'used' basket where the drawn lots could be placed. To ensure the anonymity of the participants, each individual was given a code, and the coordinator used a form to communicate the results of the random assignment to the local therapist. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |

**Inclusion criteria:**
- Age 18–70 years;
- DSM-IV diagnosis of schizophrenia
- Residual delusions or auditory hallucinations experienced for at least 3 months
- A stable medication regimen (last medication change more than 6 weeks prior to recruitment).
- A confirmed resistance to psychopharmacological treatment was established according to the following conventional criteria: symptoms unresponsive to at least two different antipsychotic compounds including an atypical antipsychotic, taken for enough time and in an acceptable dosage, as advised in the prescription guidelines (Kane et al, 1988).

**Exclusion criteria:** To exclude patients experiencing predominantly symptoms from the disorganisation dimension, the following exclusion criteria were also applied:
- Conceptual disorganisation;
- Stereotypic thinking;
- Disorientation, measured by the Positive and Negative Syndrome Scale (PANSS; Kay et al, 1987), items P254, N753 and G1052;
- Drug or alcohol addiction as a primary diagnosis (patients using drugs or alcohol below the level of this criterion were included);
- Mental retardation (premorbid IQ580);
- Organic conditions;
- CBT given for persistent psychotic symptoms in the past.

**Total sample size:** No. randomised 62

**Total sample size:** ITT population 58; 4 of 62 had data lost by assessor

**Gender:** % female 29%

**Age:** Range - 18-70

**Age:** Mean - 35.5 (10.8)

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:** Years of positive symptoms: 10.7 (7.5)
Years since diagnosis: 9 (7)

**Baseline stats:**
[CBT / Supportive counselling]
PANSS General: 33.81 (9.73) / 33.47 (7.03)
PSYRATS Auditory Hallucination (cognitive): 5.63 (5.34) / 7.83 (4.86)
PSYRATS Delusion (cognitive): 9.14 (4.64) / 7.09 (5.47)

**Notes about participants:** Participants had tried five different antipsychotics on average (if the same medication was taken twice, it was counted as one). All patients had taken at least one atypical antipsychotic and more than 2/3 had taken clozapine (Table 1). All patients were

taking antipsychotic medication during the trial, and the majority were on atypical antipsychotic regimens. Nine patients were using a typical compound during the trial because they had been given depot medication. The medication regimens were kept stable during the study. Three patients experienced a relapse and their medication had to be changed; these patients were considered to have withdrawn from the study.

**Interventions** **Intervention - group 1.:** CBT: 16 sessions in 22 weeks; n=36

**Intervention - group 2.:** Supportive counselling: 16 sessions in 22 weeks; n=26

**Notes about the interventions:**
CBT
A comprehensive treatment manual was written (by the first three authors) and the participating therapists were trained in using this protocol. CBT consisted of four phases: engagement, establishing links between thoughts, emotions and behaviour, reducing symptoms and associated distress, and relapse prevention.

Supportive counselling
The supportive counselling protocol was a conventional method previously used. The therapist shows non-critical acceptance, warmth, genuineness and empathy.

Training
A comprehensive treatment manual was written (by the first three authors) and the participating therapists were trained in using this protocol.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Relapse

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state Relapse defined as >10 increase on PANSS positive symptom subscale with the deterioration in symptoms lasting >3 days

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state PANSS, PSYRATS

**Other:** Included number needed to treat

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

**References of included studies (update)**

Bateman,K.; Hansen,L.; Turkington,D.; Kingdon,D. (2007) Cognitive behavioral therapy reduces suicidal ideation in schizophrenia: results from a randomized controlled trial. *Suicide & Life-Threatening Behavior*.37(3): 284 - 290.

Jackson, H.J., McGorry, P.D., Killackey, E., Bendall, S., Allott, K., Dudgeon, P., Gleeson, J., Johnson, T., Harrigan, S. (2007) Acute-phase and 1-year follow-up results of a randomised controlled trial of CBT versus Befriending for first-episode psychosis: the ACE project. *Psychological Medicine*; 38(5):725-35.

Patterson,T.L.; Mausbach,B.T.; McKibbin,C.; Goldman,S.; Bucardo,J.; Jeste,D.V. (2006) Functional adaptation skills training (FAST): a randomized trial of a psychosocial intervention for middle-aged and older patients with chronic psychotic disorders. *Schizophrenia Research* 86(1-3): 291 - 299.

Pinto, A., La Pia, S., Mennella, R., Giorgio, D. & DeSimone, L. (1999) Cognitive-behavioural therapy and clozapine for clients with treatment-refractory schizophrenia. *Psychiatric Services* 50(7): 901-904.

Rohricht, F., Priebe, S. (2006) Effect of body-oriented psychological therapy on negative symptoms in schizophrenia: a randomised controlled trial. *Psychological Medicine* 36: 669-678.

Shin,S.K.; Lukens,E.P. (2002) Effects of psychoeducation for Korean Americans with chronic mental illness. *Psychiatric Services*; 53(9): 1125 - 1131.

Tarrier,N.; Haddock,G.; Lewis,S.; Drake,R.; Gregg,L.; SoCRATES,TrialGroup (2006) Suicide behaviour over 18 months in recent onset schizophrenic patients: the effects of CBT. *Schizophrenia Research* 83(1): 15 - 27.

Tarrier,N.; Lewis,S.; Haddock,G.; Bentall,R.; Drake,R.; Kinderman,P.; Kingdon,D.; Siddle,R.; Everitt,J.; Leadley,K.; Benn,A.; Grazebrook,K.; Haley,C.; Akhtar,S.; Davies,L.; Palmer,S.; Dunn,G. (2004) Cognitive-behavioural therapy in first-episode and early schizophrenia. 18-month follow-up of a randomised controlled trial. *British Journal of Psychiatry* 184: 231 - 239.

Turkington, D., Sensky, T., Scott, J., Barnes, T.R.E., Nur, U., Siddle, R., Hammond, K., Samarasekara, N., Kingdon, D. (2007) A randomised controlled trial of cognitive-behaviour therapy for persistent symptoms in schizophrenia: A five-year follow-up. *Schizophrenia Research* 98: 1-7.

Valmaggia,L.R.; van-der Gaag M.; Tarrier,N.; Pijnenborg,M.; Slooff,C.J. (2005) Cognitive-behavioural therapy for refractory psychotic symptoms of schizophrenia resistant to atypical antipsychotic medication. Randomised controlled trial. *British Journal of Psychiatry* 186: 324 - 330.

**Characteristics of excluded studies (update)**

**DURHAM2003**

**Reason for exclusion:** Does not meet definition for counselling and supportive therapy

**GIGANTESCO2006**

**Reason for exclusion:** - Outside scope: rehabilitation service, does meet criteria for any other psychological intervention

**MAK2007**

**Reason for exclusion:** Does not meet definition for counselling & supportive therapy

**MCCAY2006**

**Reason for exclusion:** Non RCT

**SCHMID2007**

**Reason for exclusion:** Non-RCT

**References of excluded studies (update)**

Durham,R.C.; Guthrie,M.; Morton,R.V.; Reid,D.A.; Treliving,L.R.; Fowler,D.; Macdonald,R.R. (2003) Tayside-Fife clinical trial of cognitive-behavioural therapy for medication-resistant psychotic symptoms. Results to 3-month follow-up. *British Journal of Psychiatry* 182: 303 - 311.

Gigantesco,A.; Vittorielli,M.; Pioli,R.; Falloon,I.R.; Rossi,G.; Morosini,P. (2006) The VADO approach in psychiatric rehabilitation: A randomized controlled trial. *Psychiatric Services* 57(12): 1778 - 1783.

Mak,G.K.L.; Li,F.W.S.; Lee,P.W.H. (2007) A pilot study on psychological interventions with Chinese young adults with schizophrenia. *Hong Kong Journal of Psychiatry*. 17(1): 17-23.

McCay,E.; Beanlands,H.; Leszcz,M.; Goering,P.; Seeman,M.V.; Ryan,K.; Johnston,N.; Vishnevsky,T. (2006) A group intervention to promote healthy self-concepts and guide recovery in first episode schizophrenia: a pilot study. *Psychiatric Rehabilitation Journal*. 30(2): 105 - 111.

Schmid,G.B.; Wanderer,S. (2007) Phantasy therapy: Statistical evaluation of a new approach to group psychotherapy for stationary and ambulatory psychotic patients. *Forschende Komplementarmedizin*.14(4): 216-223.

## Family intervention

| Previous guideline review | 1. Review type<br>2. Funding<br>3. Period covered<br>4. Data analysis<br>5. No. of studies<br>6. No. participants randomised | Interventions | Reported Outcomes |
|---|---|---|---|
| Pilling S, Bebbington P, Kuipers E, Garety P, Geddes J, Orbach G, and Morgan C.<br><br>Psychological treatments in schizophrenia: I. Meta-analysis of family intervention and cognitive behaviour therapy.<br><br>*Psychological Medicine*, 2002, 32, 763-782. | 1. Systematic review of RCTs.<br>2. Intramural sources of support to the review: University College London. Extramural sources of support to the review: Department of Health, UK.<br>3. Database origin to 1999.<br>4. Meta-analysis of Odds Ratio and standardised mean difference.<br>5. 16 (18 including 2 new trials).<br>6. 1316 (1458 including new trials). | 1. To be classed as Family Intervention, an intervention had to include family sessions with a specific supportive and treatment function, and a minimum of one of the following treatment components: psycho-educational intervention; problem solving/crisis management work; intervention with the identified patient. In addition, interventions were required to be at least 6 weeks long.<br>2. Standard care.<br>3. Other active treatments. | 1. Death by suicide.<br>2. Mental State I: Relapse.<br>3. Mental State II: Readmission.<br>4. Compliance I: With treatment.<br>5. Compliance II: With medication.<br>6. Family outcomes. |
| **Update** | **Existing studies reclassified:** 1 RCT (Posner1992) was reclassified as Psychoeducation; two previous RCTs were classified as having family intervention as part of a multimodal treatment (Herz2000 and Lukoff1986).<br>**Follow up to existing studies:** 5 papers provided follow-up data to existing RCTs: Dyck 2000 (4 papers); Barrowclough 1999 (1 paper).<br>**New studies:** 19 RCTs. | | **Notes:**<br>Definition updated |

**Characteristics of included studies (previous guideline)**

| Study | N | Intervention | Patient participa-tion | Duration and frequency | Comparison groups | Measures analysed in this report |
|---|---|---|---|---|---|---|
| **Barrowclough 1999** | 79 | Needs-based cognitive-behavioural family intervention combined with general family support. | Included. | 10-20 sessions. | General family support and standard care. | Relapse, hospital admission, social functioning (Social Functioning Scale - SFS), global adjustment (Global Assessment Scale - GAS). |
| **Bloch1995** | 63 | Family counselling education, coping training. | Excluded. | 6 weekly sessions. | Single session discussion and educational audiotape and booklet. | Hospital admission, dropout. |
| **Dyck2000** | 63 | Multiple-family group intervention (superimposed on standard care): coping and illness management skills were developed through an educational videotape, lectures, and written guidelines. Ongoing support and formal clinical problem solving was provided in biweekly multiple-family groups. | Excluded for some sessions. | 3 weekly single family sessions (excluding participants), followed by multi-family educational workshop (excluding participants). Subsequently, multiple-family group (including participants) met biweekly for the next 11 months. | Standard care: medication management and case management. Some participants also received rehabilitative services, including a work-ordered day programme, a social programme on evenings and weekends, and a supported employment programme. | Symptom severity (Modified Scale for the Assessment of Negative Symptoms - MSANS) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Buchkremer1995** | 99 | Therapeutic relative groups: psychoeducational training, problem solving and relatives self-help groups. | Excluded. | 1 hour per fortnight/2 years. | Standard care. | Death, relapse, hospital admission, unemployment. |
| **Falloon1981** | 39 | Home family therapy, 24-hour support, clinic-based crisis intervention and home visits. | Included. | 1 hour per week/3 months, 1 hour per 2 weeks/6 months, 1 hour per month/15 months. | Supportive management: out-patient clinic-based individual supportive psychotherapy. | Relapse, hospital admission, dropout, drug compliance, unemployment, social impairment. |
| **Glynn1992** | 41 | Behavioural family therapy. | Included. | Mean 21 per sessions per year/1 year. | Customary care. | Relapse, hospital admission, unemployment, dropout. |
| **Goldstein1978** | 104 | Crisis-oriented family therapy. | Included. | 1 session per week/6 weeks<br>6 month follow-up. | Standard care. | Relapse, dropout. |
| **Hogarty1997** | 77 | Survival skills training and reintegration within the home and community. | Excluded for some sessions. | ½ hour fortnightly in year 1.<br>1 per 2-4 weeks for next 2 year | Supportive therapy: active listening, correct empathy, appropriate reassurance. | Relapse, dropout. |
| **Leff1982** | 24 | Educational sessions, relatives' group, home-based family sessions. | Included. | Mean 5.6 hours over 9 months, 15 month follow-up. | Standard care (neuroleptic drugs). | Death, relapse, medication compliance. |
| **Leff1989** | 23 | Family therapy in the home with the participant and two psychoeducation lectures. | Included. | 1 hour per 2 weeks/9 months, and then 1 per month for 15 months. | Relatives' group and two psychoeducation lectures. | Relapse, dropout, EE, social and occupational activities. |
| **McFarlane1995a** | 172 | Multiple (six) family groups. | Excluded for some sessions. | Fortnightly for 2 years. | Single family treatment. | Relapse, hospital admission, dropout, unemployment. |

| | | | | | | |
|---|---|---|---|---|---|---|
| **McFarlane1995b** | 46 | Multiple family treatment. | Excluded for some sessions. | 1 every 2 weeks (1st 2 years), 1 every month (next 2 years). | Single family treatment. | Relapse, dropout. |
| **Posner1992** | 55 | Psychoeducational support group program. | Excluded. | 1½ hours per week for 8 weeks, follow-up 10 months. | Standard care. | Death, hospital admission, dropout. |
| **Schooler 1997** | 313 | Applied family management and monthly family group. | Included. | 1½ hours per week for 13 weeks, per fortnight for 13 weeks, monthly thereafter. | Supportive family management: monthly multi-family group meetings. | Hospital admission, medication compliance, dropout. |
| **Tarrier1988** | 83 | Enactive programme: active participation of families in psychoeducation and stress management programme. | Included. | 13 sessions over 9 months, 7 years follow-up. | Standard care. | Death, relapse, dropout, EE. |
| **Vaughan1992** | 36 | Counselling sessions for family and home exercises. | Excluded. | 1 hour per week for 10 weeks. | Standard care. | Death, relapse, hospital admission, medication compliance, dropout. |
| **Xiong1994** | 63 | Family educational supportive sessions and monthly family group meetings. | Included. | 45 minutes per 2-3 weeks/9 months, 1 per 4 weeks/15 months + 90 minute monthly group. | Standard care. | Death, relapse, hospital admission, family burden. |
| **Zhang1994** | 78 | Educative and family group sessions, additional follow-up as needed. | Included. | 1 session every 3 months for 18 months | Outpatient department follow-up and medication. | Relapse, hospital admission, medication compliance. |

**References of included studies (previous guideline)**

**Barrowclough 1999 {published data only}**

Barrowclough C, Tarrier N, Lewis S et al. (1999) Randomised controlled effectiveness trial of a needs-based psychosocial intervention service for carers of people with schizophrenia. *British Journal of Psychiatry*; 174:505-511.

Sellwood W, Barrowclough C, Tarrier N, Quinn J, Mainwaring J, Lewis S. (2001) Needs-based cognitive-behavioural family intervention for carers of patients suffering from schizophrenia: 12 month follow-up. *Acta Psychiatrica Scandinavica*; 104:346-355.

Sellwood, W., Wittkowski, A., Tarrier, N., Barrowclough, C. (2007) Needs-based cognitive behavioural family intervention for patients suffering from schizophrenia: 5-year follow-up of a randomised controlled effectiveness trial. *Acta Psychiatrica Scandinavica* 116: 447-452.

**Bloch 1995 {published data only}**

Bloch S, Szmukler GI, Herrman H, Benson A, Colussa S. (1995) Counseling caregivers of relatives with schizophrenia: themes, interventions, and caveats. *Family Process*; 34:413-25.

Szmukler GI, Herrman H, Colusa S, Benson A, Bloch S. (1996) A controlled trial of a counselling intervention for caregivers of relatives with schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*; 31:149-55.

**Buchkremer 1995 {published data only}**

Buchkremer G, Schulze Monking H, Holle R, Hornung WP. (1995) The impact of therapeutic relatives' groups on the course of illness of schizophrenic patients. *European Psychiatry*; 10:17-27.

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**Characteristics of included studies (update)**

| **Study ID** | **BRADLEY2006** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 52 |
| | **Duration:** Length of follow-up - 18 months |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Melbourne, Australia |
| | **Number of people screened, excluded & reasons:** Service users were recruited from outpatient continuing care settings. Of the 73 who met inclusion criteria and who were invited by their case managers, 59 service user-caregiver pairs agreed to participate in the study. |
| | **Notes about study methods:** Randomisation: staff member drew names from a canister and, without looking at the names, assigned them to experimental and control groups. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] No mention |
| | **Diagnosis:** Other schizophrenia related [%] No mention |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia, schizoaffective disorder, or schizophreniform disorder<br>- Aged between 18 and 55 years<br>- >=10 hours contact with family members each week |
| | **Total sample size:** No. randomised - 59 |
| | **Total sample size:** ITT population - 50 analysed (excluding those who refused consent or dropped out during study) |
| | **Gender:** % female 70% |

**Age:** Mean - 34

**Ethnicity:** 58% English speaking caregiver-consumer pairs
42% Vietnamese caregiver-consumer pairs

**Setting:** Outpatient

**History:** Had been hospitalised in past 24 months: 42%
Mean hospitalisations in past 12 months: Multi-family groups 0.60 (1.5) / Control 0.29 (0.86)

**Baseline stats:**
[Multi-family groups / Control]
BPRS total: 50.84(11.89) / 46.00(9.44)

**Notes about participants:**
Medication (Multi-family groups / Control)
SGAs: 68% / 88%
FGAs only: 20% / 16%

48% of participants were Vietnamese speaking and used English interpreters

**Interventions** **Intervention - group 1.:** Multi-family groups; n=25

**Intervention - group 2.:** Case management (control); n=25

**Notes about the interventions:**
Case management (control)
Control condition consisted of regular appointments with a case manager and doctor to assess mental health and to provide medication and individual psychosocial rehabilitation on the basis of consumers' needs. Appointment frequency was every 2 to 3 weeks on average, and the sessions lasted from 30 minutes to 1 hour. Family contact was provided on an individual basis as required for all participants in the control and treatment groups. Family contact consisted of phone or direct contact and focused on providing psychoeducation, monitoring the consumer's mental state, and giving general support.

Multi-family groups
In addition to case management, service users and carers were provided up to three single-family joining sessions and then invited to attend two half-day multiple-family psychoeducation sessions. The family psychoeducation sessions provided information about schizophrenia using a previously published approach. The sessions gave family members the opportunity for informal social networking. Topics included the nature of the illness, treatment approaches (medication and psychosocial), consumer and family needs, common family reactions to illness, common problems that servicer users and families face, and guidelines about what the family can do to help. Each group of six or seven service user-carer pairs was then invited to participate in a multi-family group with two trained group leaders; groups met every other week for 12 months.

Training
Staff training was initially provided by a 3-day national workshop conducted by William McFarlane that outlined the multiple-family group method. Each of the groups had two therapists - a primary therapist and a support cofacilitator. Group leaders used a standardised treatment manual which was the critical tool in directing the structure and content of the sessions to maintain consistency of the therapeutic approach. Regular supervision was provided to all group leaders by the lead primary therapist. She was a senior psychologist and family therapist who was highly familiar with the McFarlane model. Additional external consultation was provided by a therapist at a specialist family therapy service.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes**

**Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** defined as the symptoms after a period of remission of such symptoms, persisting continuously for a minimum of 7 days and requiring intensive community treatment or hospital admission: rate and number of episodes

**Global state & service outcomes (e.g. CGI):** Time to relapse, time to rehospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS, SANS

**Satisfaction with treatment:** Carer satisfaction- Family Burden Scale

**Quality of Life:** Average score/change in quality of life - QOL

**Other:** In employment for 12 months
Note more participants were employed in the control group (9) at entry compared with the treatment group (1)

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Poorly addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| | |
|---|---|
| **Study ID** | **BRESSI2008** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer - All participants completed the intervention |
| | **Blindness:** Single-blind |
| | **Duration:** Length of follow-up - 12 months |
| | **Duration:** No. weeks of treatment - 52 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Milan, Italy |
| | **Number of people screened, excluded & reasons:** 124 participants were screened for inclusion with 54 meeting the inclusion criteria. 40 participants gave their informed consent to participate in the study and 14 refused consent. |
| | **Notes about study methods:** Participants were matched by clinical and demographic characteristics and randomised into two blocks of 20, then randomly assigned to one of two conditions. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] % not reported |
| | **Diagnosis:** Other schizophrenia related [%] % not reported |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- Inpatients<br>- Diagnosis of schizophrenia or schizophrenic spectrum disorder<br>- patients were required to take an SGA regardless of any other medication prescribed<br>- 18-65 years old<br>- Living/ lived with the family of origin for >=6 months and had face-to-face contact >=35 hours per week with relatives |
| | **Exclusion criteria:**<br>- Presence of an organic disorder underlying the psychiatric condition<br>- IQ <75 |
| | **Total sample size:** No. randomised 40 |
| | **Total sample size:** ITT population 40 |

**Gender:** % female 25%

**Age:** Range 19-46

**Age:** Mean 29

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[FI / control]
Length of illness, months: 101.0(68.5) / 103.6(97.1)
Number of hospital admissions: 1.5 / 2.0

**Baseline stats:** Not reported

**Interventions** **Intervention - group 1.:** Family Intervention (Systemic FI), Engagement phase + 12 1.5 hour sessions; N =20

**Intervention - group 2.:** Standard Care; N = 20

**Notes about the interventions:** Family Intervention
The intervention was systemic in nature and provided in addition to standard care. In the initial phase of SFT, relatives and patients attended psychoeducational sessions to enhance their knowledge with regards to the most prominent aspects of the illness, including symptoms, signs of relapse, medication compliance. The rest of the intervention was based on the Milan approach in which the treatment group is behind a one-way mirror while the interviewer is a neutral, dispassionate, information gatherer whose primary source of information is the family's response to circular questioning. The intervention consisted of reframing of the family problems, positively connoting the family process and recommending either no change or cautioning not to change too quickly. Other interventions included systemic questioning alone, assigning tasks to monitor behaviour, prescribing rituals or gathering additional information.

Standard care
Consisted of drug treatment and interviews with a psychiatrist (number varied with a min 1 per month). The patients were not given any individual or group psychotherapeutic or rehabilitative treatment.

Training and supervision
Sessions were conducted by a team of 2 female therapists (psychologists) qualified at the Milan school of family therapy after a standard 4-year training programme. One of the therapists was lecturer at the Milan School.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes** **Global state & service outcomes (e.g. CGI):** Outpatient Service Utilisation

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Global state & service outcomes (e.g. CGI):** Relapse - Defined using Brown and Birley (1968) criteria as a transition from nonschizophrenic

state to a schizophrenic state, with the appearance of specific symptoms evaluated on a standardised scale, or the marked exacerbation of a symptom already present.

**Non-adherence to study medication:** Non-adherence Compliance to medication - Also reported good clinical compliance

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

**Study ID**

**CARRA2007**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT - All patients randomised to the study were included in the analysis at both 12 and 24 months.
All relatives entered the statistical analysis with burden outcomes at 12 months but dropouts were excluded at 24 months.

**Blindness:** Single-blind

**Duration:** No. weeks of treatment - 104

**Raters:** Independent of treatment

**Design:** Single-centre - Study was carried out in a non-profit, family advocacy and support agency, The Association for Research on Schizophrenia (ARS) in Lombardy, Italy.

**Number of people screened, excluded & reasons:** Participants were selected from those who had been referred to the ARS between 1995 -

2000 (n=320). 205 met the inclusion criteria. In total 101 relatives agreed to participate, gave informed consent and completed the assigned treatment.

**Notes about study methods:** Participants were intentionally allocated in unequal numbers to IG, IG+SG and TAU groups with a randomisation ratio 2:1:1. Participants were randomised using a random number table to enter the IG and IG+SG groups. A further group of relatives on the ARS waiting list were randomly allocated to the TAU group.

Both relatives and clinicians in the IG groups were blind to successive participation in the SG.

Allocation concealment was ensured by the external involvement of a statistician who was not involved in enrolling participants and was responsible for the method of sequence generation.

**Participants** **Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
Relatives:
- living with someone suffering from schizophrenia and had not attended family groups or other support services before
- patient was clinically stable (having had no psychiatric hospitalisation or any relapse for 6 months prior to study entry) and was not receiving any psychosocial or rehabilitative treatment other than standard care;
- patient did not have a primary diagnosis of alcohol or drug dependence or organic disease.

Community based service managers were asked to check the following criteria:
- patients' DSM-IV diagnoses of schizophrenia
- GAS score >= 30
- compliance with standard care, with a specifically designed 3-point scale defining non-compliance as a rating of 3 (refusal of every proposed treatment)
- consistency of prescribed pharmacological treatment,

**Total sample size:** No. randomised - 101

**Total sample size:** ITT population - 101

**Gender:** % female 28%

**Age:** Mean Patients - 30

**Ethnicity:** not reported

**Setting:** Outpatient

**History:**
[IG / IG+SG / TAU]

Onset age: 21.1(7.7) / 18.7(4.2) / 19.9(6.4)
Duration of illness, years: 9.6(8.1) / 11.3(7.6) / 10.3(9.2)
Previous hospitalisations: 2.7(3.0) / 4.8(8.0) / 3.0(4.3)

**Baseline stats:**
[IG / IG+SG / TAU]
Patients:
ordinarily employed, n(%): 12(24) / 3(12) / 6(24)

Relatives:
high EE, n(%): 19(38) / 10(38) / 10(40)
high warmth, n(%): 14(28) / 3(12) / 1(4)

**Notes about participants:** All but 3 patients were receiving standard doses of antipsychotics (300-1000 mg chlorpromazine equivalents)

**Interventions** **Intervention - group 1.:** IG, weekly meetings for 24 sessions; n = 50

**Intervention - group 2.:** IG +SG, addition SG weekly meetings for 48 sessions over 2 years; n=26

**Intervention - group 3.:** TAU; n=25

**Notes about the interventions:**
TAU
All patients received standard care, which entailed key worker's management and consistent pharmacological interventions.

Both family programmes involved only one relative from each patient’s family.

IG
- weekly meetings composed of 16–18 relatives for 24 sessions (1.75 hours per session) using an informative approach. Contents and goals are mainly derived from the model of relatives groups but were preliminary in-home individual family sessions.
-Curricula include: aetiology, positive symptoms, negative symptoms, mood disorders, problem behaviours, medical and psychiatric treatment, denial and non-compliance, interpersonal and social issues, relationship with family, education, independence and dependence, resources and benefits. Educational tools include lectures, videos and leaflets.

Support group (SG)
- comprises weekly meetings for 48 sessions (1.5 hours per session) over 2 years with a support group (SG), made up of 8– 9 relatives who have previously attended the IG and consisted of two stages that roughly correspond to the phases of the group.
-The first phase involves training on communication and coping skills, stress identification and management, and multiple family group-based problem solving, derived from the psychoeducational multiple family group approach
- The second phase emphasizes mutual support and consists of deliberate efforts to mould the group into a social network that can persist for

| | |
|---|---|
| | an extended period and satisfy family needs for social contact, support, and ongoing monitoring.<br>Training<br>Both the IG and SG programmes were co-led by two specifically trained psychiatrists not involved in patients' community standard care. |
| | **Family/carer involvement:** Only family/carer involved |
| **Outcomes** | **Global state & service outcomes (e.g. CGI):** Relapse - GAS score < 30 - 12 months (24 month data not added as it was unclear if these data included relapses in the first 12 months or were new cases) |
| | **Global state & service outcomes (e.g. CGI):** Re-hospitalisation 12 months (24 month data not added as it was unclear if these data included hospitalisations in the first 12 months or were new cases) |
| | **Other:** Psychosocial functioning: unemployment - 12 months<br>Family outcomes: subjective and objective burden - 12 months<br>(24 month data not added as it was unclear if these data included participants in the first 12 months or were new cases) |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Well covered |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **CHENG2005** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |

**Blindness:** No mention

**Duration:** No. weeks of treatment - 10

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre - China

**Notes about study methods:** Randomised by the researcher by drawing lots

**Participants**

**Diagnosis:** Other [%] - All participants were family members of clients who had been diagnosed with schizophrenia

**Inclusion criteria:**
Patients:
- DSM-IV schizophrenia diagnosis
- Age >=18
- Diagnosed within 1 year with no more than two periods of hospitalisation

Carers:
- Family member who cared for (>=4 hour per day) and lived with a person with schizophrenia
- Age >=18
- Could understand and read Cantonese
- Had not received psychoeducational group therapy from other healthcare agencies

**Exclusion criteria:** Patient:
- Had history of other mental disorders

Carers:
- Providing care to another family member with a chronic physical or mental illness

**Total sample size:** No. randomised - 64

**Gender:** % female 62.5% of carers were female

**Setting:** Outpatient - Community mental hospital in Hong Kong

**Baseline stats:**
[Experimental Group / Control Group]
FBIS: 18.78 / 17.03
SES: 20.81 / 25.16
SSQ-6: 23.09 / 25.53

**Notes about participants:**
Carer's relationship with client n, (%)
Spouse: 14 (21.9)

Parent: 29 (45.3)
Grandparent: 10 (15.6)
Sibling: 3 (4.7)
Friend: 2 (3.1)
Child: 6 (9.4)

**Interventions** **Intervention - group 1.:** Experimental - psychoeducation programme; n=32

**Intervention - group 2.:** Control; n=32

**Notes about the interventions:**
Control:
Routine care including medical and nursing care, information giving about mental and physical conditions of the patient, treatment plan and effects of medications, individual counselling by nurses and social workers, and referrals to financial aid and social welfare services.

Psychoeducation/ experimental group
In addition to routine care, participants took part in a psychoeducation programme consisting of 10 weekly 2-hour sessions. It focused on knowledge and treatment of the illness, management of symptoms and medication, dealing with crisis, mental health services, communication and problem- solving skills, and stress-coping skills.

**Outcomes** **Other:** Outcomes for patients were not reported.
The following outcomes for the carers were included: FBIS: SES; SSQ-6

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Poorly addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| Study ID | CHIEN 2004A |
|---|---|
| General info | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| Method | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All randomised participants |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 12 |
| | **Duration:** Length of follow-up - 3 months |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - two major outpatient clinics in Hong-Kong |
| | **Number of people screened, excluded & reasons:** 500 eligible identified: 52 (from power calculations) randomly selected and approached, 4 withdrew before baseline assessment; 48 randomised |
| | **Notes about study methods:** Randomisation procedure not reported |
| Participants | **Diagnosis:** Schizophrenia [% of sample] 100 |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>Carers' criteria:<br>- Lived with and cared for one relative with a primary diagnosis of schizophrenia according to DSM-IV<br>- Relative with schizophrenia experienced no comorbidity of other mental illness during recruitment to the study and who had been diagnosed with schizophrenia for no more than 3 years<br>- Aged 18 years or above and could understand and read the Chinese language<br>- Free from any psychiatric disorder themselves |
| | **Exclusion criteria:** - Cared for more than one family member with mental or chronic physical illness<br>- Were the primary carer for less than 3 months. |
| | **Total sample size:** No. randomised - 48 |
| | **Total sample size:** ITT population - 48 |
| | **Gender:** % female (Patients) 50% |
| | **Age:** Mean (Patients) Experimental: 39.9 (6.1) / Control: 36.3 (5.5) |
| | **Ethnicity:** Not reported |
| | **Setting:** Outpatient |

**History:** ~2 years of illness

**Baseline stats:** Patients in both groups were assessed as having a stable or improved mental condition during three months prior to the start of the intervention

**Notes about participants:** Medication: Mostly conventional antipsychotics, such as chlorpromazine and haloperidol (88% in experimental group and 85% in control group), with more than 70% of them taking medium doses of these drugs (haloperidol equivalent mean values)

**Interventions** **Intervention - group 1.:** Mutual support group: 12 x 2 hour sessions; n=24

**Intervention - group 2.:** TAU for 3 months; n=24

**Notes about the interventions:**
Mutual support groups
The protocol specified that the facilitator and peer leader should follow six principles of group-work practice identified in the literature as successful in strengthening a mutual support group. These were: (1) sharing personal data (disclosing information with trust), (2) fostering dialectical processes (letting members think about ideas and alternatives to solve problems), (3) encouraging discussion of taboo areas (sharing of secret and internal psychological conflicts), (4) fostering a sense of being all-in-the-same boat (feeling in similar situation and working against a common plight), (5) encouraging mutual support (reciprocal giving and receiving help and support among members), and (6) providing opportunities of individual problem solving (helping individual members to deal with unique troubles).

TAU
Usual care comprised outpatient clinics with: (1) medical consultation with a psychiatrist who provided the family with information about the illness, treatment plan and effects of medications; (2) advice on financial aid and social welfare services by medical social workers; and (3) advice, possible referral to mental health services, and education seminars on schizophrenia care organised monthly by registered psychiatric nurses.

All patients received TAU.

Training
The principal researcher (WTC), an experienced psychiatric nurse and group worker, acted as the group facilitator and assisted and encouraged the development of the group, being most active during the first two sessions. A peer leader elected by the group participants, agreed to co-ordinate and planned the group sessions in collaboration with the facilitator. Fidelity of the facilitator and peer-group leader to the protocol was assured by review of the audiotape of each group session by the research team and feedback. In addition, the facilitator received bi-weekly supervision from other members of the research team at which problems of group facilitation were discussed and strategies for the next group session clarified.

**Family/carer involvement:** Only family/carer involved - Not explicitly stated, but throughout the paper only the family caregiver is mentioned as attending the sessions.

**Outcomes** **Global state & service outcomes (e.g. CGI):** Re-hospitalisation - Duration of rehospitalisation

| | |
|---|---|
| | Average number of rehospitalisations per participant |
| | **Satisfaction with treatment:** Carer satisfaction - FBIS, Family Assessement Device (FAD), FSSI |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **CHIEN2004B** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All randomised participants regardless of failure to comply or complete treatment. |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 24 |
| | **Duration:** Length of follow-up - 12 months |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Two regional outpatient clinics in Hong Kong |
| | **Number of people screened, excluded & reasons:** Written consent was obtained from 146 families, of whom 96 (66 percent) were randomly selected and assigned to one of the three study groups: mutual support (N=32), psychoeducation (N=33), and standard care (N=31). The remaining 50 families, who had been informed about the possibility of not being selected for the study, were placed on a waiting list because of |

time and manpower constraints on group formation.

**Notes about study methods:** randomisation procedure not reported

**Participants** **Diagnosis:** Schizophrenia [% of sample] 100

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
Carers:
- Lived with and cared for one relative with a primary DSM-IV diagnosis of schizophrenia, for not more than 5 years
- Patient had no comorbid mental illness or substance misuse
- Age >=18
- Could understand Chinese.

**Exclusion criteria:**
Carers:
- Cared for more than one family member with mental illness
- Had been primary carer for <3 months

**Total sample size:** No. randomised - 96

**Total sample size:** ITT population - 96

**Gender:** % female 35%

**Age:** Range - All at least 20 years of age

**Age:** Mean - 31.7

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** Mean duration of illness: Just over 2 years (6 months to 5 years)

**Baseline stats:**
[mutual support / psychoeducation / standard care]
SLOF: 127.3(16.8) / 125.8(17.3) / 121.2(16.1)
FSSI: 3.6(1.5) / 3.9(1.7) / 3.6(1.2)
PANSS positive: 10.5(3.7) / 10.1(4.1) / 10(3.9)

**Notes about participants:** Medication: More than half of them (17 to 20 in each group) were taking a medium dosage of antipsychotics (haloperidol equivalent mean values of between 8.30±7.02 and 10.34±8.13 mg/day). Two-thirds of the patients (21 to 23 patients, or 66 to 70%) in the three groups were taking oral medication, and one-fifth (six or seven patients, or 19 to 23%) were taking both oral and depot intramuscular medications. Nearly half the patients in the three groups were taking atypical neuroleptics (14 to 16 patients, or 45 to 49%).

**Interventions** **Intervention - group 1.:** Mutual support group: 12x 2 hour bi-weekly sessions; n=32

**Intervention - group 2.:** Psychoeducation: 12x 2 hour bi-weekly sessions; n=33

**Intervention - group 3.:** TAU; n=31

**Notes about the interventions:** Mutual support groups
The mutual support group consisted of peer-led and researcher-facilitated group sessions comprising five stages (engagement, recognition of psychological needs, dealing with needs, adopting new roles, ending) designed to provide information, emotional support, and coping skills for caregiving in stages. Emphasis was given to specific Chinese cultural characteristics and issues, including a strong social stigma associated with mental illness and seeking mental health services, a hierarchical but interdependent family structure, and a strong tendency to expect immediate and practical help. Time was given to individual problem solving and to helping individual family members deal with particular troubles. Post-meeting practice in caring for the mentally ill relative at home was also emphasised and evaluated after each group stage.

Psychoeducation
The content and format of this professionally-led psychoeducation programme. The duration of the education and survival skills sessions was modified to 6 months in accordance with participants' preferences and convenience and given the resource constraint. The purposes of this intervention were to provide information about schizophrenia and its treatment, educate families about the biological basis of schizophrenia, improve illness management, develop social support networks and coping skills, and provide techniques for improving communication, problem solving, and crisis intervention.

TAU
Routine psychiatric outpatient and family services only, consisting of monthly medical consultation and advice, individual nursing advice on community health care services, social welfare and financial services provided by medical social workers, and counselling provided by clinical psychologists if necessary.

Training
In the mutual support group, a peer leader, elected by group members and trained by researchers during a 2-day leadership workshop worked closely with the principal researcher, assisting and encouraging the development of the group stages, as recommended in the literature. For the psychoeducation group, the two clinicians were psychiatric nurses who were selected by the clinics and were experienced in leading group and psychiatric rehabilitation programmes. They were trained by the research team and one family therapist via two 3-day workshops and practice within five family sessions, which were rated and evaluated by the training team. Supervision and progress monitoring of the two programmes included consistent reviews of the audiotape of each session and regular clarification of problems and issues arising from the meetings.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation- Frequency and duration

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS (only positive symptoms reported)

| | |
|---|---|
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SLOF- sub-scale (social functioning) |
| | **Other:** Mental health service needs and use (measured with Family Support Services Index) |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **CHIEN2007** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - No details provided |
| | **Blindness:** Single-blind |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Hong Kong |
| | **Number of people screened, excluded & reasons:** 200 family members screening, 150 agreed to participate. Of these 84 were randomly selected to take part in the study |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
Family members were included if:
- aged 18+
- free from any psychiatric disorder
- lived with and cared for a relative with a primary diagnosis of schizophrenia

**Exclusion criteria:**
Family members were excluded if:
- cared for more than one relative with a chronic mental or physical condition

**Total sample size:** No. randomised - 84

**Total sample size:** ITT population - 84

**Gender:** % female Carers - 67%
Patients - 49%

**Age:** Mean Carers - 41 years
Patients - 29 years

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** Average duration of patients' illness was 3.6year and ranged from 1-7 years

**Baseline stats:**
[FI / Control]
BPRS: 10.5(3.7) / 10.0(3.9)

**Notes about participants:** 57% of patients were taking SGAs

**Interventions** **Intervention - group 1.:** Family Intervention, 18 sessions x 2 hour session; N = 42

**Intervention - group 2.:** Standard Care; N = 42

**Notes about the interventions:**
Family Intervention
In addition to TAU and consisted of 4 stages based upon a manualised approach. These included orientation and engagement, educational workshop, therapeutic family role and strength rebuilding and termination. The programme used culturally sensitive family intervention model. The content of the intervention was based upon the needs assessment of 180 family members of Chinese persons with schizophrenia.

Standard care
Involved routine psychiatric outpatient and family services only.

| | |
|---|---|
| | Training and supervision<br>Group instructor was a registered psychiatric nurse trained in a 3-day workshop held by a family therapist and the researchers. The instructor was provided with information about schizophrenia and the necessary skills to lead a group. The instructor had ongoing supervision throughout the intervention. |
| | **Family/carer involvement:** Both person with schizophrenia and their family/carer |
| **Outcomes** | **Global state & service outcomes (e.g. CGI):** Days in hospital - Duration and number of rehospitalisations |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS |
| | **Other:** Family Assessment Device; Family Burden Interview Schedule; Specific levels of functioning Scale |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **GARETY2008** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT |
| | **Blindness:** Only raters blind |

**Duration:** Length of follow-up - data collected at 12 months (after treatment) and 24 months (end of treatment + 12 months follow-up)

**Duration:** No. weeks of treatment - 36

**Raters:** Independent of treatment

**Design:** Multi-centre - 5 locality mental health services in London and East Anglia: inner city London (2), suburban outer London (1), county town (Norwich) and rural centre (Norfolk)

**Number of people screened, excluded & reasons:** 683 patients meeting inclusion criteria were identified, 382 patients withheld consent. A total of 301 patients provided informed consent, of whom 218 entered pathway 1 (individual pathway) and 83 pathway 2 (carer pathway)

**Notes about study methods:** Randomisation was stratified within each of the centres, and within inpatient or outpatient status at the time of relapse. Randomisation schedules were independently generated by a trial randomisation service in a separate location from all trial centres, using randomised permuted blocks with a block size randomly varying between 2-10 for the individual pathway and 3-9 in the carer pathway.

If patients had no carer they were invited to participate in the individual study. Those who identified a carer, a relative or friend with whom they lived or were in close contact >-10 hours per well, the patient was asked to give informed consent for the carer pathway study. The carers were then approached for their consent. At the trial recruitment midpoint it became apparent that otherwise eligible patients with carers had been excluded from the study because their carer had refused to participate. From this point in cases where patients or carers refused carer participation, participants with carers were offered entry to the individual pathway.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 85.4%

**Diagnosis:** Other schizophrenia related [%] schizoaffective disorder = 13.3%
Delusional disorder = 1.3%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- current clinical diagnosis of non-affective psychosis (F2 in the ICD-10 and DSM-IV)
- aged 18-65
- second subsequent psychotic episode starting <=3 months before they agreed to enter trial
- Rating >=4 for at least one positive symptom on the PANSS

**Exclusion criteria:**
- primary diagnosis of alcohol or substance dependency, organic syndrome or learning disability
- a command of spoken English inadequate for engaging in psychological therapy
- unstable residential arrangements such that the likelihood of being available for the duration of the trail was low.

**Total sample size:** No. randomised - 301

**Total sample size:** ITT population - Primary outcome data at 24 months available for 295 participants

**Gender:** % female 30%

**Age:** Mean - 37

**Ethnicity:** White - 72.3%
Black Caribbean - 7.6%
Black African - 9.2%
Black other - 2.3%
Indian - 1.6%
Other - 7%

**Setting:** Inpatient

**Setting:** Outpatient

**History:**
Non carer pathway:
[TAU / CBT]
Inpatient, n: 78 / 76
Outpatient, n: 34 / 30
Mean length of illness, years: 9.9(8.7) / 10.9(8.1)
Mean no. admissions: 4.4(4.4) / 5.0(5.6)
History of violence:
No: 79 / 66
Yes: 30 / 35
History of suicide or self-harm:
No: 65 / 65
Yes: 42 / 35

Carer Pathway:
[TAU / CBT / FI]
Inpatient, n: 18 / 16 / 16
Outpatient, n: 10 / 11 / 12
Mean length of illness, years: 10.5(8.6) / 10.9(9.7) / 13.3(11.8)
Mean no. admissions: 4.6(5.50 / 3.4(3.2) / 6.5(9.2)
History of violence:
No: 23 / 20 / 21
Yes: 5 / 7 / 7
History of suicide or self-harm:
No: 15 / 16 / 14
Yes: 13 / 11 / 12

**Baseline stats:**
Non-carer pathway:
[TAU / CBT]
PANSS total: 66.26(15.91) / 62.32(13.49)

Carers pathway:
[TAU / CBT / FI]
PANSS total: 64.11(15.28) / 66.89(14.26) / 70.93(13.36)

**Interventions** **Intervention - group 1.:** CBT, 12-20 sessions; non-carers pathway n=106; carer pathway n=27

**Intervention - group 2.:** FI, 12-20 sessions; carer pathway n=28

**Intervention - group 3.:** TAU; non-carers pathway n=112; carer pathway n=28

**Notes about the interventions:**
TAU
Consisted of good standard care, delivered according to national and local service protocols and guidelines, including the prescription of antipsychotic medication. TAU did not preclude the provision of psychological intervention, although in practice this was relatively rare.

CBT
Adaptation of a generic CBT for psychosis manual. It was specifically aimed at targeting key aspects of relapse prevention. The first stage focused on engagement and assessment. A central focus of the work was developing a shared formulation of relapse, including where appropriate a new model of disorder emphasising alternatives to delusional thinking. Therapists then attempted to target the key problems associated with vulnerability to relapse. The last stage involved developing a set of self regulatory strategies to manage relapse.

FI
Followed a manual with an emphasis on improving communication, offering discussion of up-to-date information about psychosis, problem solving, reducing criticism and conflict, improving activity, and emotional processing of grief, loss and anger. Sessions focused on one problem at a time and were aimed at an individual formulation of each family's problem as they defined them. There was a particular focus on relapse prevention.

Training for CBT
Five lead trial therapists, all doctorate level or equivalent clinical psychologists provided therapy to 72% of total treatment cases. A further 37 CBT treatment cases were seen by therapists employed by the local mental health services, these were a mixture of doctoral clinical psychologists and nurses who had received specialist training in CBT. All therapists were required to demonstrate competence in CBT. This was followed by a period of intensive training in workshops with both the expert CBT therapists on the trial and external experts. Lead therapists from each centre met monthly for case discussion and supervision with the expert CBT therapists.

Training for FI
FI involved a lead and co-therapist working together. The five lead therapists for CBT also acted as the lead FI therapists. All lead therapists were required to show in-depth knowledge of evidence-based FI in psychosis and to demonstrate key techniques in role-play. They also attended intensive training from an expert FI therapist. All co-therapists attended FI training workshops or received individual training from a trial lead therapist. The local therapists were a mix of doctorate level clinical psychologists and nurses who had received training in FI. The trial lead therapists were provided with specialist expert monthly supervision throughout the trial, and attended advanced skills workshops by experts. The lead therapists also meet fortnightly for peer supervision and case presentations.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes**

**Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Relapse following full remission: Data reported but not entered because number of people achieving remission was low, therefore data difficult to interpret.

Relapse following partial or full remission:
Relapse ratings were made using a published method employed in a previous RCT. Relapse ratings are based on evidence of the re-emergence of, or significant deterioration in, positive psychotic symptoms of at least moderate degree persisting for at least 2 weeks

**Global state & service outcomes (e.g. CGI):** Remission ratings were made using a published method employed in a previous RCT. Ratings are based on changes in positive psychotic symptoms. Evidence is required of improvement in (for partial remission) or absence of (for full remission) positive psychotic symptoms continuing for at least 4 weeks.

**Global state & service outcomes (e.g. CGI):** Days in hospital

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS total, positive and negative

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Social & Occupational Functioning Assessment Scale and Time Budget

**Quality of Life:** Average score/change in quality of life - EUROQOL:

**Other:** Beck Depression Inventory

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed

**2.1 How well was the study done to minimise bias?:** ++

| **Study ID** | **JENNER2004** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All participants randomised and who gave consent |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - The Netherlands |
| | **Number of people screened, excluded & reasons:** 100 approached, 22 ineligible, 2 more which were excluded after randomisation as one was found to have concealed primary substance misuse and the other was assigned to control but erroneously received experimental treatment. |
| | **Notes about study methods:** Randomisation by minimisation procedure, conducted by independent medical technology unit of the university hospital. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] Paranoid schizophrenia 78% |
| | **Diagnosis:** Other schizophrenia related [%] Schizoaffective 15%<br>Psychosis NOS 7% |
| | **Diagnostic tool:** Other method - SCAN interview |
| | **Inclusion criteria:**<br>- Experiencing auditory hallucinations for >2 years after adequate treatment<br>- Diagnosis of non-affective psychosis, including schizophrenia, schizoaffective and psychotic disorder NOS<br>- Former use of at least two antipsychotics in adequate doses or period according to Dutch Psychiatric Association guidelines |

- No previous CBT for auditory hallucinations
- No current misuse of psychoactive drugs or alcohol (moderate use of cannabis or alcohol was allowed)
- Estimated IQ >80.

**Total sample size:** No. randomised - 80

**Total sample size:** ITT population - 69

**Gender:** % female 46%

**Age:** Mean 36 (11.2)

**Ethnicity:** No mention

**Setting:** Outpatient

**History:** Duration of hallucinations (years): 12 (10.4)
Lifetime admissions: 3

**Baseline stats:**
[HIT / TAU]
PANSS Total: 60.0 (15.6) / 60.4 (12.5)

**Interventions** **Intervention - group 1.:** HIT; n=37

**Intervention - group 2.:** TAU; n=39

**Notes about the interventions**
HIT (hallucination-focused integrated treatment)
Multimodal intervention focusing on regaining control and command over persistent hallucinations, integrating motivational, behavioural, cognitive, psychoeducational and rehabilitative elements. The approach is a directive style of single family therapy that integrates motivational interventions, training in coping skills, CBT, psychoeducation and operant conditioning regarding medication. Positive outreach crisis intervention was available around the clock. Programme comprised of approx. 20x 1 hour sessions over 9 to 12 months.

TAU (treatment-as-usual)
Routine care delivered by community mental health teams includes psychiatric, social, financial, occupational management, crisis intervention, and day patient care (drop-in centres and rehabilitation activities).

Where possible, contact time was controlled in the two conditions to be similar.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS, PSYRATS, AHCL (Auditory Hallucinations Coping List)

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Social Disabilities Schedule

| | |
|---|---|
| | **Engagement with services (e.g. SES):** Average score/change in engagement with services - Adherence to treatment |
| | **Other:** Use of medications (antipsychotics and adjuncts) |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Well covered |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** ++ |

| | |
|---|---|
| **Study ID** | **KOPELOWICZ2003** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 12 |
| | **Duration:** Length of follow-up - 6 months |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre- Community mental health centre in Los Angeles, US |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedures not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 78% |

**Diagnosis:** Other schizophrenia related [%] Schizoaffective 22%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- Age between 18 and 60 years
- Primary DSM-IV chart diagnosis of schizophrenia or schizoaffective disorder
- At least one episode of treatment in an inpatient facility of at least 1 week's duration in the previous 12 months
- Spanish speaking
- Living with their family.

Patients with other concurrent diagnoses (for example, substance misuse, depression, personality disorder) were not excluded.

**Total sample size:** No. randomised - 92

**Total sample size:** ITT population - 84 completers

**Gender:** % female 33%

**Age:** Mean - 38.4

**Ethnicity:** Mexican-American 60%
Other Central American 32%
Caribbean 9%

**Setting:** Outpatient

**History:**
[Skills-training / TAU]
Age of illness onset: 24.9 (8.8) / 24.2 (12.0)
Lifetime hospitalisations: 3.4 (2.6) / 3.1 (2.8)

**Baseline stats:**
[Skills-training / TAU]
PANSS Positive: 14.0 (5.7) / 12.4 (4.9)
PANSS Negative: 17.8 (5.5) / 17.7 (5.4)
PANSS General: 30.3 (6.4) / 26.3 (5.2)
PANSS Total: 62.1 (13.7) / 56.4 (11.8)

**Notes about participants:** All study participants were prescribed antipsychotic education with few changes in type or dose of medication made during the study protocol. Approximately two-thirds of the subjects in both groups were taking one of the newer generation antipsychotic medications. There was no statistically significant difference between groups on the dose of antipsychotic medication prescribed.

[Skills-training / TAU]

Antipsychotic dose: 316.2 (188.6) / 328.3 (167.5)

**Interventions** **Intervention - group 1.:** Family-assisted skills training: 90-minute sessions for four times per week over 3 months; n=45

**Intervention - group 2.:** TAU; n=47

**Notes about the interventions**

Family-assisted skills training

Aimed to teach patients instrumental, social and problem solving skills with focus on two modules (medication management and symptom management). Included workbooks, videos and other teaching materials. Group sessions involving family members (with role plays etc.) also took place weekly, educating them as coaches for the patient and how to adapt the home environment for assisting the patient's skill use.

TAU

The comparison group, as well as those in the skills training groups, continued to receive treatment as usual, comprising case management by social workers and monthly psychiatric visits (typically 20 minutes once a month) for medication management using a multidisciplinary team approach. Other needs such as housing and employment were also addressed. Finally, if patients experienced an exacerbation of symptoms, contact with the psychiatrist and/or psychiatric nurse increased (either at the Centre or in the "field") until the patient was stabilised, or referred to inpatient treatment.

Training

The disciplines of the skills session trainers included nursing, psychology and social work. Each module included a trainer's manual which specified what was to be said and done to teach a module's skills. To ascertain that the modules were being conducted systematically and correctly, a therapist fidelity evaluation form was used.

**Family/carer involvement:** Both the person with schizophrenia and their family/carer - Patients were involved in skills training groups which met for 90-minute session for four times per week during the 3 months.

Family members of patients were included in weekly "generalisation sessions" aimed at utilising relatives as generalisation agents.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS Positive/Negative/Total

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Independent Living Skills Survey

**Satisfaction with treatment:** Carer satisfaction Family Burden Interview Schedule - no data reported, but authors stated there were no significant differences between groups.

**Quality of Life:** Average score/change in quality of life - Lehman QoL - no data reported, but authors stated there was no significant differences between groups

**Other:** Proportion adhering to medication regimen, Rating of Medication Influences Scale, skills acquisition was measured by the Medication

Management; Skills and Symptom Management skills tests.

Family outcomes: Hope for Future Scale; Five-Minute Speech Sample (FMSS) for expressed emotion - no data reported, but authors state that there were no significant differences between groups.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**LEAVEY2004**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT - Main comparisons were carried out on an ITT basis defined as patients being analysed according to their randomisation status whether or not they actually received the intervention

**Blindness:** Single-blind

**Duration:** No. weeks of treatment - 36 (7 sessions, each one lasting approx 1 hour)

**Duration:** Length of follow-up - Followed up at 4 and 9 months

**Raters:** Independent of treatment

**Design:** Single-centre - UK

**Number of people screened, excluded & reasons:** 198 patients identified as eligible, 92 patients were excluded for the following reasons: refused (n=52), no contact (n=22), moved away (n=11), no carer (n=7)

**Notes about study methods:** Block randomisation design - 8 cards indicating control or intervention were individually placed in envelopes at the administration centre by someone who was neither a researcher nor support worker. A second person with no connection to the study randomly selected an envelope to assign allocation.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] Not mentioned

**Diagnosis:** Other schizophrenia related [%] Not mentioned

**Diagnostic tool:** Other ICD

**Inclusion criteria:** - developed a first episode of psychotic illness within the last 6 months

**Exclusion criteria:** - any organic disorder or learning difficulties.

**Total sample size:** No. randomised - 106

**Total sample size:** ITT population - 106

**Gender:** % female 35.8%

**Age:** Range - No age range or mean details given. Participants were classed as younger (16-25 years) or older (25+). 51.9% were classified as the former.

**Ethnicity:** White UK - 42.5%
Other - 57.5%

**Setting:** Inpatient

**Setting:** Outpatient

**History:**
[Treatment / Control]
Section n(%): 22(38.6) / 21(42.9)
Non-section n(%): 35(61.4) / 28(57.1)

**Baseline stats:**
[Treatment / Control]
Hospitalisation n(%): 40(70) / 29(59)
Carer rated severity of illness n(%): Very serious: 24(42) /20(41)

**Notes about participants:** Details of any concomitant medication not reported.
61% of carers were parents of patients. 53% and 54% of control and treatment patients respectively lived with their carers.

**Interventions**

**Intervention - group 1.:** Brief intervention for families; n=57

**Intervention - group 2.:** Control - Usual psychiatric care; n=49

**Notes about the interventions:** Usual psychiatric care:
Carers received support from the community mental health teams as part of their services to patients. Usual psychiatric care is often informal and ad hoc, in that it follows no set protocol. The professionals in the team are not provided with specific training for support of families.

Brief family intervention:
The family intervention was received in addition to usual psychiatric care. The intervention began within 6 months of first contact with services and was provided over seven sessions, each one lasting approximately an hour, usually in the carer's own home. The sessions were designed to be interactive rather than didactic and covered (a) information gathering from the relative; (b) an educational component on psychotic illness, symptoms and early warning signs, treatment, and help seeking; and (c) coping strategies, problem solving and communication with the patient. The approach taken was essentially psychoeducational, incorporating a problem-solving component. Carers were also provided with an information pack about psychotic illness and addresses and telephone numbers for local and national services and support groups. The support team were bilingual, came from a range of ethnic backgrounds and who held at least a certificate in counselling. We strove to match the worker with the carer on ethnicity.

Blinding:
Researchers were instructed to avoid any discussion with carers about the support they received. Carers were also asked not to discuss care issues with the researchers.

Training
The support team was recruited from a local health services link workers team. The link workers were bilingual, came from a range of ethnic backgrounds and held at least a certificate in counselling. An experienced community mental health nurse and qualified family support trainer gave them training to provide the intervention. The trainer provided a background and theoretical underpinning of each of the components of the project. The support team were provided with supervision throughout.

**Family/carer involvement:** Only family/carer involved- Abstract states, relatives were randomly allocated to receive a brief intervention.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation- Data entered in RevMan

**Satisfaction with treatment:** Carer satisfaction- VSSS-32: data not usable

**Other:** Perceived severity of illness as rated by carer - data not usable
Median time spent by carers looking after patients - data not usable
CSI - data not usable
Living with parents

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| **Study ID** | **LI2005** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Cluster randomised trial - intraclass correlation coefficient (ICC) not reported |
| | **Type of analysis:** Completer |
| | **Blindness:** Open |
| | **Duration:** Length of follow-up - 3 and 9 months |
| | **Duration:** No. weeks of treatment - Length of study not clear - appeared to be tied to duration of hospitalisation.<br>For the education group, total duration of sessions was 8 hours with the patient and 36 hours with the family in the hospital, 2 hours per month for 3 months after discharge for patient and family together |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Beijing, China |
| | **Number of people screened, excluded & reasons:** 101 families recruited and randomised |
| | **Notes about study methods:** Randomisation by ward |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** Other method - CCMD-II-R (Chinese Classification of Mental Disorders) |

**Inclusion criteria:**
- Admitted to hospital for treatment of non-acute schizophrenia
- Age 16–65 years
- Living with a family member at least 3 months prior to the current hospital admission.

**Exclusion criteria:**
- Evidence of learning disability, presence of known organic mental disorder and significant or habitual drug or alcohol use.

**Total sample size:** No. randomised - 101

**Gender:** % female 57%

**Age:** Range
Education / TAU
Age
<=20: 6 (13) / 5 (9)
21-30: 11 (24) / 19 (34)
31-40: 21 (46) / 22 (40)
41-50: 5 (11) / 9 (16)
>=51: 3 (6) / 0 (0)

**Setting:** Inpatient

**Setting:** Outpatient

**History:**
Education / TAU
Hospitalisation times
First time: 26 (57) / 32 (58)
Second time: 12 (26) / 17 (31)
Third or more: 8 (17) / 6 (11) p = 0.6142

Duration of illness, years
<=1: 17 (37) / 18 (33)
>1, <=5: 11 (24) / 20 (36)
>5, <=10: 8 (17) / 8 (14)
>10, <=20: 9 (20) / 8 (14)
>20: 1 (2) / 1 (2) p = 0.3201

**Baseline stats:**
Education / TAU
BPRS: 46.1 (12.5) / 47.1 (10.3)

NOSIE: 168.2 (36.0) / 159.5 (29.6)

**Interventions** **Intervention - group 1.:** Family education; n=46

**Intervention - group 2.:** TAU; n=55

**Notes about the interventions:**
Family education
The programme was designed primarily to educate families and patients about schizophrenia and its treatment, and to teach skills to help patients and families cope more effectively, particularly with the disruptive consequences of the illness. This was delivered on top of usual care.

TAU
The control group received usual standard treatment and care, in which there was no organised education programme, but patients and families could seek information from staff, and educational pamphlets and materials were available in a ward library.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Relapse - defined as rehospitalisation or BPRS >5

**Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAS-Chinese

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS

**Behaviour (e.g. NOSIE):** Average score/change in behaviour - NOSIE

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not reported adequately

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| Study ID | MAGLIANO2006 |
|---|---|
| General info | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| Method | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Open |
| | **Duration:** No. weeks of treatment - 26 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - 17 Public mental health centres, Italy |
| | **Notes about study methods:** 34 mental health workers from 17 centres in Italy selected 71 families of consumers with schizophrenia to take part in the intervention. Eligible families and participants were randomly assigned by means of a computerised random procedure performed by the co-ordinating centre in Naples. |
| Participants | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia<br>- clinically stable<br>- in treatment with the locale centre for >=6 months<br>- living with at least one adult relative |
| | **Total sample size:** No. randomised - 71 |
| | **Gender:** % female 24% |
| | **Age:** Mean - 35 |
| | **Ethnicity:** Not reported |
| | **Setting:** Outpatient |
| | **History:**<br>[Intervention / Control]<br>Age of onset of illness: 21.7(6.0) / 21.9(6.5)<br>Lifetime voluntary hospital admissions: 2.2(3.3) / 2.4(2.9)<br>Lifetime compulsory admissions: 1.0(2.1) / 0.7(0.9)<br>Months in treatment at mental health centre: 91.7(75.6) / 86.0(72.0) |

**Baseline stats:**
[Intervention / Control]
BPRS negative: 2.4(1.0) / 2.3(0.8)
BPRS positive: 2.4(1.1) / 2.6(1.1)

**Notes about participants:**
[Intervention / Control]
Had attended information sessions on schizophrenia in previous 6 months n(%): 11(26) / 9(31)
Received individual psychotherapy n(%): 12(29) / 8(28)
Had participated in a rehabilitation programme n(%): 22(52) / 16(55)
All participants were taking antipsychotic medication

**Interventions** **Intervention - group 1.:** Family psychoeducation, 18 1-hour sessions; n=42

**Intervention - group 2.:** Waiting list control; n=29

**Notes about the interventions:**
Family Psychoeducation
The intervention was developed by Falloon and consisted of four components: assessment of individual and family needs; information sessions with consumers and their relatives about clinical aspects of schizophrenia, its treatments and early signs of relapse; communication skills training; and problem-solving skills training. After completing the basic training course, professionals started the intervention with the first group of families. Professionals were instructed to carry out at least three 1-hour sessions a month for each family for 6 months. The frequency and location of the sessions were decided on the basis of each family's needs and the professionals' working time and caseloads.

Training
At each centre two professionals (one psychiatrist or psychologist and one nurse, social worker, or rehabilitator) completed a formal training programme in the family psychoeducational intervention developed by Falloon. The training programme included three monthly modules of 2 and a half days each. In the year after the training course, participants attended four supervision meetings and each month they received by phone tutorial support on family work. Participants were also trained in the use of the assessment instruments selected for the study.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes** **Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Assessment of disability

**Satisfaction with treatment:** Carer satisfaction - Family burden
Perception of professional support

**Other:** Social network questionnaire

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**MONTERO2001**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT - For variables not dependent on adherence to intervention (for example, relapse etc) ITT approach was used whereby comparisons included all randomised patients according to the assigned therapy group.

**Type of analysis:** Completer - For a subset of variable including social functioning, dose of antipsychotic medication, EE status etc, analysis was conducted on those patients who completed the full programme.

**Blindness:** Only raters blind

**Duration:** No. weeks of treatment - 52

**Raters:** Independent of treatment

**Design:** Single-centre - outpatient clinics in one catchment area of Valencia, Spain

**Number of people screened, excluded & reasons:** 87 patients were referred and randomised

**Notes about study methods:** Randomisation was carried out by an independent institution using Epiinfo method with sealed envelopes containing random numbers.

**Participants** **Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-III-R

**Inclusion criteria:**
- diagnosis of schizophrenia according to DSM-III-R
- a recent acute psychotic relapse (within the previous 6 months), with or without hospital admission, and be in remission
- aged 15 - 45
- have lived with relatives for the previous 3 months and be planning to remain in the same household for the 12-month period after being enrolled in the study.

**Exclusion criteria:** - Patients with a background of substance misuse were excluded if they were physically dependent at the time of the study

**Total sample size:** No. randomised - 87

**Total sample size:** ITT population - 87 for non-adherence dependent variables

**Gender:** % female 33%

**Age:** Mean 26.8(6.3)

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
[BFT / RG]
Age at onset: 21.4(4.6) / 21.1(4.4)
Length of illness, years: 5.7(4.5) / 5.3(3.6)
Previous admission, % other than index admission: 30 / 30

**Baseline stats:**
[BFT / RG]
PAS: 6.6(3.2) / 5.9(3.2)
DAS-II: 3.8(1.1) / 3.9(0.8)
High EE, n(%): 28(57.1) / 21(42.8)

**Notes about participants:**
[BFT / RG]
Medication, n(%)
Noncompliance: 4(9) / 3(7)
Maintenance dose: 26(56) / 23(56)
High dose: 16(35) / 15(37)

**Interventions** **Intervention - group 1.:** behavioural family therapy (BFT), 12 months; n=46

**Intervention - group 2.:** Relatives Group (RG) 12 months; n=41

**Notes about the interventions:**
Both interventions were on the same schedule: weekly for the first 6 months, every 2 weeks for the next 3 months, and monthly for the last 3 months.

BFT:
The framework addressed each family unit, including the patient, and was carried out at home. It encompassed three different modules introduced sequentially and integrated later: patient and family education about schizophrenia, training in communication skills, and teaching and practice of problem- solving techniques designed to help families think of solutions and apply them.

RG:
Began with two educational sessions about schizophrenia for the patient and relatives, provided individually for each family unit at the health centre. The following sessions were attended by only the relatives, and they aimed to teach problem-solving skills, reduce criticism and over involvement, reduce social contact between patient and relatives, expand social networks, and lower expectations. The participants were invited to take part in the weekly RG that took place at the mental health centre. The RG was designed as an open group: new relatives were incorporated as they were referred to the programme, always after the educational sessions. The mean number of participants (usually one per patient, occasionally two) in each session was 8—10. The sessions lasted approximately 90 minutes.

Training
Three psychiatrists and one psychiatric nurse were trained intensively in behavioural family therapy for 2 months by the team leader who was in turn trained by Prof. Falloon. Another researcher was trained in Leff's strategy and trained the rest of the team. The participating staff were selected according to their interest in integrated therapeutic approaches. Manuals, workbooks and videotapes were used in training. The therapists met weekly with the team leader for monitoring of progress and supervision.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Average score/change in global state - Global PAS, GHQ

**Global state & service outcomes (e.g. CGI):** Relapse and psychotic relapse defined as an increase of 3+ points on at least one of the scales.

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Global DAS-II

**Other:** Family EE level
Knowledge of illness

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

| **Study ID** | **RAN2003** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Cluster randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - 6 townships in western rural China |
| | **Number of people screened, excluded & reasons:** 510 patients identified in 6 townships, 357 met inclusion criteria and randomised, 31 refused consent after randomisation (24 had no carers, 7 were afraid of discrimination by community) |
| | **Notes about study methods:** Random numbers table achieved block randomisation using townships as units. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100 |
| | **Diagnostic tool:** Other method - CCMD-2-R |
| | **Diagnostic tool:** ICD-10 |
| | **Inclusion criteria:**<br>- People with schizophrenia living in one of six townships |

**Exclusion criteria:**
- Schizoaffective psychoses
- Comorbid substance misuse
- Has no relatives

**Total sample size:** No. randomised - FI=132 (adjusted n = 60)

**Gender:** % female 65

**Age:** Mean - 43.5

**Ethnicity:** Chinese

**Setting:** Outpatient

**History:**
[Combo / Drug / Control]
Years of illness: 11.6 (9.5) / 10.6 (9.6) / 12.3 (8.4)

**Baseline stats:**
[Combo / Drug / Control]
Severe symptom/deterioration in clinical status: 52% / 54% / 53%

**Notes about participants:**
Carers [Combo / Drug / Control]:
Female: 40% / 45% / 37%
Age: 47.1 / 45.1 / 49.2
Parent of patient: 29% / 30% / 30%
Spouse of patient: 55% / 52% / 55%

**Interventions**

**Intervention - group 1.:** Family psychoeducation + antipsychotics; n=126

**Intervention - group 2.:** Antipsychotics alone; n=103

**Intervention - group 3.:** Control; n=97

**Notes about the interventions:**
Family psychoeducation:
Building on the psychoeducational family approach and the vulnerability-stress model modified to take account of the characteristics of Chinese rural areas, the main components were as follows:
1. Family education conducted once per month (1.5-3 hours) for 9 months. The purpose was to provide specific advice, support and information to the family, including information relating to mental diseases, treatment and rehabilitation. The patient was encouraged to join the meeting.
2. Multiple family workshops were held once every 3 months, in which general questions were discussed, and relatives shared the experiences of caring for patients.

3. Crisis intervention conducted when necessary (for example, for attempted suicide, aggressive and destructive behaviour). The local village broadcast network was also employed for health education during the first 2 months.
Trained psychiatrists and village doctors conducted all these above-family interventions. Village doctors did not get the same training as psychiatrists, but assisted with the interventions.

Antipsychotics
Long-term injection of haloperidol decanoate (50-125mg/month) and/or an oral depot.

Control
Received no treatment within study. Antipsychotics were neither encouraged nor discouraged, and participants were allowed to seek their own treatment.

Training
Trained psychiatrists and village doctors conducted all the family interventions. Village doctors did not get the same training as psychiatrists, but assisted with the interventions.

**Family/carer involvement:** Both person with schizophrenia and their family/carer

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) - because clustering had not been taken into account by trial authors, rate and sample size were adjusted by the design effect assuming an intracluster correlation coefficient of .02

**Global state & service outcomes (e.g. CGI):** Relapse - defined as change from a normal or no schizophrenic state to a state of schizophrenia by PSE-derived criteria, or a marked worsening of schizophrenic symptoms - (% converted into n) [because clustering had not been taken into account by trial authors, relapse rate and sample size were adjusted by the design effect assuming an intracluster correlation coefficient of .02]

**Global state & service outcomes (e.g. CGI):** Clinically significant response in global state - Clinical Status (% full recovery, significant improvement or severe symptom/deterioration) - added to RevMan under no significant improvement [because clustering had not been taken into account by trial authors, rate and sample size were adjusted by the design effect assuming an intracluster correlation coefficient of .02]

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - Mental disability (% mild, moderate, serious or most serious) defined as mental illness lasting over a year, which to some extent had an impact on family or social functioning. (Label is a composite score of different measures not used in any other paper)

**General and psychosocial functioning (e.g. SFS):** Clinically significant response in general functioning - Ability to work (% full-time, part-time or not able) as not able to work [because clustering had not been taken into account by trial authors, rate and sample size were adjusted by the design effect assuming an intracluster correlation coefficient of .02]

**Non-adherence to study medication:** Non-adherence rate and sample size were adjusted by the design effect assuming an intracluster correlation coefficient of .02

**Other:** Relatives' knowledge of illness (Relatives Investigation Scale and Relatives' Beliefs Scale) - means only reported for single items in the Relatives' Beliefs Scale and not total score

| | |
|---|---|
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Not addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **SO2006** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 6 |
| | **Duration:** Length of follow-up - Also contained a 6 month follow-up but data not used as waiting list control participated in the intervention after the initial 6 weeks |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Multi-centre - 3 sites in Hong Kong |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Carers were randomly assigned by a computer to an active intervention or waiting list control group. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% schizophrenia, schizoaffective or schizophreniform disorder (not broken down any further) |
| | **Diagnostic tool:** ICD-10 |

**Inclusion criteria:**
Inclusion criteria for relatives included
- a family member was experiencing first episode psychosis
- being the major carer of the patient
- living with the patient at time of recruitment
- informed written consent

**Exclusion criteria:**
Relative were not recruited if:
- they were actively receiving psychiatric services
- patient was receiving inpatient treatment

**Total sample size:** No. randomised - 45

**Total sample size:** ITT population - 44 (completers only)

**Gender:** % female 84% female (carers only)

**Age:** Mean 49 (age of carers)

**Ethnicity:** Details not reported

**Setting:** Outpatient

**History:** All participants were experiencing a first-episode of psychosis and were recruited from the Early Assessment Service for Young People with Psychosis (EASY)

**Baseline stats:**
[FI / Control]
PANSS: 54.3(27.4) / 51.4(15.4)

**Interventions** **Intervention - group 1.:** Family Intervention, 6 session, 1.5 hours per week; N = 22

**Intervention - group 2.:** Waiting list control; N = 23

**Notes about the interventions:**
Family Intervention
The first 3 sessions were organised to increase and consolidate the carer's knowledge about psychosis. The last 3 aimed at enhancing skills in managing the patients' illness and their own stress. Major components of the intervention included education on early psychosis and its treatment, handling difficult behaviours, stress management, communication skills and relapse prevention.

Waiting list control
Carers on the waiting list received standard care from the patient's case manager.

Carers in the study were not given any intensive individual or family psychotherapy other than that in the active condition. All patients were

| | |
|---|---|
| | treated with antipsychotic medication with efforts made to ensure that their regular medical service was unaffected.<br><br>Training and supervision<br>A Masters level psychologist ran the sessions under supervision from the first author |
| | **Family/carer involvement:** Only family/carer involved |
| **Outcomes** | **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) |
| | **Other:** The Chinese Ways of Coping Questionnaire<br>The Experience of Caregiving Inventory<br>Level of expressed Emotion<br>Knowledge about psychosis |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Well covered |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **SZMUKLER2003** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial (effectiveness/pragmatic) |
| | **Type of analysis:** ITT - Analysis was planned on an ITT basis |

NB: 49 of the 61 participants from Camberwell completed the follow-up (57/77 of the total sample e.g. Camberwell + Peckham, were followed up.)

**Blindness:** Open

**Duration:** No. weeks of treatment - 36

**Duration:** Length of follow-up - 6 months

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre UK (Main results relate to a defined catchment area in Camberwell)

**Number of people screened, excluded & reasons:** The study aimed to recruit carers of patients experiencing a psychotic disorder being treated by two community mental health teams in a defined catchment area. Of the 146 patients, 61 agreed to participate (42%). Reasons for non-engagement in the programme were: patient objection (12%), carer too busy or cannot make the commitment (29%), carer desires practical help not support (9%), carer not interested (24%).

Further carers from Peckham were sought to increase the power of the study. However as these were not representative of the total population of carers, the results are based on Camberwell with only a brief reference to the total group.

**Notes about study methods:** Randomisation occurred within strata (using permuted blocks with varying block size). Stratification was based on the patient's diagnosis and the carer's relationship to the patient.

Process was conducted by an independent statistician who was not involved again in the trial until after its completion.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 51%

**Diagnosis:** Other schizophrenia related [%] Schizoaffective disorder - % not reported

**Diagnosis:** Other [%] bipolar affective disorder - % not reported; psychotic depression - % not reported

% reported for other diagnosis which included the above and schizoaffective disorder

**Diagnostic tool:** Other method - patients were diagnosed by their consultant

**Total sample size:** No. randomised - 61 (77 including Peckham carers)

**Total sample size:** ITT population - 49 (Camberwell carers only)

**Gender:** % female 82% - carers data

**Age:** Mean 54(14) - carers data

**Ethnicity:** Ethnicity of carers was examined in relation to recruitment into the study. (number recruited / number approached)
- 40/78 white carers
- 18/54 black carers

**Setting:** Other carers of patients experiencing a psychotic disorder being treated by two closely related CMHTs in Camberwell and CMHTs in Peckham.

**Baseline stats:** None reported

**Notes about participants:** A carer was defined as someone in at least monthly face-to-face contact in a supportive role toward the patient and was considered to be in such a role by the patient and themselves.

**Interventions**

**Intervention - group 1.:** Intervention group, 6 individual family settings, 12 fortnightly relatives group over 9 months; n=30 (36 Camberwell + Peckham)

**Intervention - group 2.:** Control, 1 hour session; n=31 (41 Camberwell + Peckham)

**Notes about the interventions:**
Family Intervention
- Based on the programme developed in Melbourne and started with 6 individual family sessions offered in the family home.
- Followed by 12 fortnightly relatives' groups which aimed to consolidate initial gains and allow further opportunities to deal with carers' problems in a supportive environment. Each session ran for 1.5 hours and included a talk given by a speaker with special knowledge or experience of a particular area. This was followed by a general discussion where effective communications were facilitated within a problem-solving framework. Strategies and solutions were shared with in the group.

Control
- Consisted of a single 1 hour session in which the study was described and caregiving problems discussed. Caregivers were given the same aids as those in the intervention group.

Training
The 6 individual sessions and 12 relatives' groups were run by the same carers' support worker. The support worker was an experienced Thorn-trained Community Psychiatric Nurse working under weekly supervision of the research team.

**Family/carer involvement:** Only family/carer involved

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Days in hospital

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Other:** Carer morbidity (Clinical Interview Schedule Revised - CISR); Experience of Caregiving Inventory (ECI); Coping with Life Events and Difficulties Interview (COPI) (effective coping, ineffective coping); Self Evaluation and Social Support Schedule (SESS) (confidants, general support); Severity of caregiving difficulty

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| | |
|---|---|
| **Study ID** | **VALENCIA2007** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment 52 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Mexico |
| | **Number of people screened, excluded & reasons:** 98 participants were randomised, a total of 16 failed to complete the study leaving a final sample of 82 in the analysis. |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- outpatients diagnosed with schizophrenia according to DSM-IV, who were taking antipsychotic medication.<br>- clinically stable in terms of psychotic symptoms (corroborated by PANSS < 60) |

- aged 16-60
- completed at least 6 years of elementary education
- lived with family and resided in Mexico City
- Provided written informed consent.

**Total sample size:** No. randomised - 98 initially randomised, 82 used in the analysis

**Gender:** % female 22%

**Age:** Mean - 29.8(6.8)

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** average age of illness onset = 21.3(5.4)

**Baseline stats:**
[PSST / TAU]
PANSS: 115.2(30.5) / 107.9(22.6)
GPS: 57.5(16.0) / 53.6(12.2)
GPSF: 3.2(0.6) / 3.1(0.6)
GAF: 43.3(6.3) / 44.1(8.0)

**Interventions** **Intervention - group 1.:** PSST; n=43

**Intervention - group 2.:** TAU; n=39

**Notes about the interventions:**
TAU
Provided at the schizophrenia clinic by two clinical psychiatrists who were blind to the treatment conditions. TAU included the following features/tasks: 20-minute monthly appointments during a 1 year period, controlled the prescription of antipsychotic medication based upon the assessment of psychotic symptoms, checked medication compliance, recorded attendance to consultations and registered all information for their clinical files.

In addition to TAU, the experimental group underwent psychosocial skills training (PSST) and family therapy (FT).

PSST
Composed of 7 treatment areas: symptom management, medication management, social relations, occupational, money management, couple relations and family relations based on a therapists training manual. The sessions used six learning activities to teach patients skills acquisition. PSST was in the form of group sessions, 8 participants per group, for up to 1 hour 15 minutes, once a week for a total of 48 sessions over the course of 1 year.

FT
The first part of FT consisted of psychoeducation, which included 8 group sessions where all the patients' relatives received information about the illness, symptoms and medication management. The second part consisted of 4 sessions for each family to improve communication skills, recognition and management of the warning signs of relapse, the importance of medication and its side effects, compliance with antipsychotic medication and keeping appointments with physicians.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAF

**Global state & service outcomes (e.g. CGI):** Relapse - not defined

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - PSFS

**Engagement with services (e.g. SES):** Average score/change in engagement with services - Compliance with antipsychotic medication - defined as patients having taken at least 80% of the prescribed antipsychotic medication.

Therapeutic adherence - 1) patients' attendance at therapy sessions; 2) number of patients who completed the intervention, compared with those who dropped out.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**References of included studies (update)**

**BRADLEY2006**

Bradley G.M.; Couchman G.M.; Perlesz A.; Nguyen A.T.; Singh B.; Riess C. (2006) Multiple-family group treatment for English- and Vietnamese-speaking families living with schizophrenia. *Psychiatric Services57*: 521-530.

**BRESSI2008**

Bressi,C.; Manenti,S.; Frongia,P.; Porcellana,M.; Invernizzi,G. (2008) Systemic family therapy in schizophrenia: A randomized clinical trial of effectiveness. *Psychotherapy and Psychosomatics*. 77(1)

**CARRA2007**

Carra,G.; Montomoli,C.; Clerici,M.; Cazzullo,C.L. (2007) Family interventions for schizophrenia in Italy: Randomized controlled trial. *European Archives of Psychiatry and Clinical Neuroscience*. 257(1): 23 - 30.

**CHENG2005**

Cheng LY; Chan S; (2005) Psychoeducation program for Chinese family carers of members with schizophrenia. *Western Journal of Nursing Research* 27(5): 583-599.

**CHIEN 2004A**

Chien,W.T.; Norman,I.; Thompson,D.R. (2004) A randomized controlled trial of a mutual support group for family caregivers of patients with schizophrenia. *International Journal of Nursing Studies* 41(6): 637 - 649.

**CHIEN2004B**

*Chien,W.T.; Chan,S.W. (2004) One-year follow-up of a multiple-family-group intervention for Chinese families of patients with schizophrenia. *Psychiatric Services* 55(11): 1276 - 1284.

Chien, W.T.; Chan, S.; Morrissey, J.; Thompson, D. (2005) Effectiveness of a mutual support group for families of patients with schizophrenia. *Journal of Advanced Nursing*. 51(6): 595-608.

Chien,W.T.; Chan,S.-W.C.; Thompson,D.R. (2006) Effects of a mutual support group for families of Chinese people with schizophrenia: 18-month follow-up. *British Journal of Psychiatry* 189: 41 - 49.

**CHIEN2007**

Chien,W.T.; Wong,K.F. (2007) A family psychoeducation group program for Chinese people with schizophrenia in Hong Kong. *Psychiatric Services*. 58(7): 1003 - 1006.

**GARETY2008**

Garety, P.A., Fowler, D.G., Freeman, D., Bebbington, P., Dunn, G. & Kuipers, E. (2008) A randomised controlled trial of cognitive behavioural therapy and family intervention for the prevention of relapse and reduction of symptoms in psychosis. *British Journal of Psychiatry* 192: 412-423.

**JENNER2004**

*Jenner,J.A.; Nienhuis,F.J.; Wiersma,D.; van de Willige, G (2004) Hallucination focused integrative treatment: a randomized controlled trial. *Schizophrenia Bulletin* 30(1): 133 - 145.

Jenner,J.A.; Nienhuis,F.J.; van de Willige,G; Wiersma,D. (2006) "Hitting" voices of schizophrenia patients may lastingly reduce persistent auditory hallucinations and their burden: 18-month outcome of a randomized controlled trial. *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie* 51(3): 169 - 177.

**KOPELOWICZ2003**

Kopelowicz,A.; Zarate,R.; Gonzalez Smith, V; Mintz,J.; Liberman,R.P. (2003) Disease management in Latinos with schizophrenia: a family-assisted, skills training approach. *Schizophrenia Bulletin* 29(2): 211 - 227.

**LEAVEY2004**

Leavey,G.; Gulamhussein,S.; Papadopoulos,C.; Johnson-Sabine,E.; Blizard,B.; King,M. (2004) A randomized controlled trial of a brief intervention for families of patients with a first episode of psychosis. *Psychological Medicine*. 34(3): 423 - 431.

**LI2005**

Li,Z.; Arthur,D. (2005) Family education for people with schizophrenia in Beijing, China: randomised controlled trial. *British Journal of Psychiatry* 187: 339 - 345.

**LINSZEN1996**

Lenior, M.E., Dingemans, P.M.A.J., Linszen, D.H., De Haan, L. & Schene, A.H. (2001) Social functioning and the course of early-onset schizophrenia. *British Journal of Psychiatry* 179: 53-58.

*Linszen,D.; Dingemans,P.; Van der Does,J.W.; Nugter,A.; Scholte,P.; Lenoir,R.; Goldstein,M.J. (1996) Treatment, expressed emotion and relapse in recent onset schizophrenic disorders. *Psychological Medicine* 26(2): 333 - 342.

**MAGLIANO2006**

Magliano,L.; Fiorillo,A.; Malangone,C.; De Rosa,C.; Maj,M.; Maresca,L.; Cavaliere,G.; Delcuratolo,V.; Giannini,M.; Ambra,L.; Malacarne,A.; Gentile,F.; Casale,L.; Raffaeli,M.; Innocente,P.; Salmeri,R.; Cantone,R.; Scordato,M.; Campo,G.; Curreli,R.; Miscali, S., et al. (2006) Patient functioning and family burden in a controlled, real-world trial of family psychoeducation for schizophrenia. *Psychiatric Services* 57(12): 1784 - 1791.

**MONTERO2001**

Montero, I., Asencio, A., Hernandez, I., Masanet, M.J., Lacruz, M., Bellver, F., Iborra, M., Ruiz, I. (2001) Two strategies for family intervention in schizophrenia: A randomised trial in a Mediterranean environment. *Schizophrenia Bulletin* 27(4): 661- 670.

Montero,I.; Hernandez,I.; Asencio,A.; Bellver,F.; Lacruz,M.; Masanet,M.J. (2005) Do all people with schizophrenia receive the same benefit from different family intervention programs?. *Psychiatry Research* 133: 187 - 195.

Montero,I.; Masanet,M.J.; Bellver,F.; Lacruz,M. (2006) The long-term outcome of 2 family intervention strategies in schizophrenia. *Comprehensive Psychiatry* 47(5): 362 - 367.

**RAN2003**

Ran,M.S.; Xiang,M.Z.; Chan,C.L.; Leff,J.; Simpson,P.; Huang,M.S.; Shan,Y.H.; Li,S.G. (2003) Effectiveness of psychoeducational intervention for rural Chinese families experiencing schizophrenia--a randomised controlled trial. *Social Psychiatry and Psychiatric Epidemiology* 38(2): 69 - 75.

**SO2006**

So,H.W.; Chen,E.Y.H.; Chan,R.C.K.; Wong,C.W.; Hung,S.F.; Chung,D.W.S.; Ng,S.M.; Chan,C.L.W. (2006) Efficacy of a brief intervention for carers of people with first-episode psychosis: A waiting list controlled study. *Hong Kong Journal of Psychiatry*. 16(3), 92-100

**SZMUKLER2003**

Szmukler, G., Kuipers, E., Joyce, J., Harris, T., Leese, M., Maphosa, W., Staples, E. (2003) An exploratory randomised controlled trial of a support programme for carers of patients with a psychosis. *Social Psychiatry and Psychiatric Epidemiology* 38: 411-418.

**VALENCIA2007**

Valencia, R., Juarez, M. (2007) A psychosocial skills training approach in Mexican out-patients with schizophrenia. *Psychological Medicine* 37(10): 1393-1402.

**Characteristics of excluded studies (update)**

**BAZZONI2003**

**Reason for exclusion:** Paper not in English

**Leff 2003**

**Reason for exclusion:** Population not in protocol e.g. depression.

**MOTLOVA2002**

**Reason for exclusion:** Foreign language paper

**Stein2003**

**Reason for exclusion:** Conference abstract only

**References of excluded studies (update)**

Bazzoni,A.; Rosicarelli,M.L.; Picardi,A.; Mudu,P.; Roncone,R.; Morosini,P. (2003) A controlled clinical trial of a group intervention for relatives of patients with schizophrenia. *Italian Journal of Psychopathology* 9: 10 - 16.

Leff,J.; Alexander,B.; Asen,E.; Brewin,C.R.; Dayson,D.; Vearnals,S.; Wolff,G. (2003) Modes of action of family interventions in depression and schizophrenia: The same or different? *Journal of Family Therapy* 25(4): 357- 370.

Motlova,L.; Dragomirecka,E.; Spaniel,F.; Selepova,P. (2002) Family psychoeducation in schizophrenia and quality of life in patients and their relatives. *Psychiatrie* 6: 46 - 49.

Stein,M.K.; Glynn,S.M.; Shepherd,J.G.; Rook,K.S.; Vo,M.; Potkin,S.G. (2003) A test of a culturally appropriate family sponsorship program for Caucasian and Vietnamese caregivers of persons with schizophrenia. *Schizophrenia Research* 60: 328 - 329.

## Psychodynamic and psychoanalytic therapies

| Previous guideline review | 1. Review type<br>2. Funding<br>3. Period covered<br>4. Data analysis<br>5. No. of studies<br>6. No. randomised | Interventions | Outcomes reported in review |
|---|---|---|---|
| Malmberg L, Fenton M. Individual psychodynamic psychotherapy and psychoanalysis for schizophrenia and severe mental illness (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2001. Oxford: Update Software. | 1. Systematic review and meta-analysis of RCTs.<br>2. Intramural sources of support to the review: Porvoo Hospital, Finland; Cochrane Schizophrenia Group, UK. Extramural sources of support to the review: Finnish Office for Health Technology Assessment (FinOHTA); Finska Läkaresällskapet.<br>3. Database origin to 1999<br>4. Meta-analysis of Relative Risk and Weighted Mean Difference.<br>5. 3.<br>6. 492 (Total). | 1. Psychodynamic psychotherapy-defined as regular individual therapy sessions with a trained psychotherapist, or a therapist under supervision. Therapy sessions were to be based on a psychodynamic or psychoanalytic model. Sessions could rely on a variety of strategies, including explorative insight-oriented, supportive or directive activity, applied flexibly. However, therapists should use a less strict technique than in psychoanalysis. To be considered well-defined psychodynamic psychotherapy, trialists needed to include working with transference.<br>2. Psychoanalysis- defined as regular individual sessions, planned to last a minimum of 30 minutes, with a trained psychoanalyst three to five times a week. Psychoanalysis was required to have been planned to continue for at least 1 year. Analysts were required to adhere to a strict definition of psychoanalytic technique. To be considered well-defined psychoanalysis, trialists needed to report working at the infantile sexual relations level of psychoanalytic theory.<br>3. Standard care - the care a person would normally receive had they not been included in the research trial. The category 'standard care' also incorporates 'waiting list control groups' where | 1. Committed suicide by 3 years (May 1976)<br>2. Global impression<br>a. Not able to be discharged (May 1976)<br>b. Given medication during 12 months, 3 years follow-up (May 1976)<br>c. Rehospitalised (Gunderson 1984)<br>d. Returned to hospital (O'Brien 1972)<br>e. Not improved at 24 months (O'Brien 1972)<br>f. Discharged from therapy (O'Brien1972)<br>g. Remaining in therapy (O'Brien 1972)<br>h. Not able to perform major household responsibilities (Gunderson 1984)<br>i. Not able to in enjoy a significant relationship (Gunderson 1984)<br>j. Not self supporting (Gunderson 1984)<br>3. Achieved best level of health (Menninger Health Sickness scale: high=good) (May 1976)<br>4. Treatment not considered successful by treatment team (May 1976)<br>5. Leaving the study early (Gunderson 1984)<br>Where possible, outcomes grouped into the time periods 1-6 months (short-term), 7-12 months (medium-term), >12 months (long- |

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|---|---|---|---|
| | | participants receive drug or other interventions.<br>4. Other psychosocial therapies - additional psychological and/or social interventions, such as non-directive counselling, supportive therapy, CBT and other 'talking therapies'.<br>5. No care - this group included people randomised to no treatment or to a waiting list without receiving any care. | term). |
| **Update** | **New studies:** 1 RCT. | | **Notes:** Definition updated |

**Characteristics of included studies (previous guideline)**

| Study | Methods | Participants | Interventions | Outcomes | Notes |
|---|---|---|---|---|---|
| **Gunderson1984** | Allocation: random, no further details.<br>Duration: 2 years, had to stay in therapy for 6 months to be eligible to go onto 2 year follow-up. | Diagnosis: schizophrenia, DSM II & III, diagnosis confirmed three times.<br>Age: 18-35 years.<br>N=164 (almost 2000 screened).<br>Sex: not mentioned.<br>Inclusion criteria: minimal prior treatment, no drug or alcohol problems, no organic illnesses, able to function outside of hospital for 4 consecutive months in some major role without medication in the previous 2 years.<br>Setting: all hospitalised initially, then in community. | 1. Insight-oriented psychotherapy: n=88*.<br>2. Reality-adaptive, supportive psychotherapy: n=76*. | Global impression (rehospitalised, unable to take household responsibilities, unable to have key relationship, not self supporting).<br>Leaving the study early.<br>Unable to use -<br>Cognition (no SD).<br>Ego functioning (no SD).<br>Signs and symptoms of illness (no SD).<br>Use of medication (no SD).<br>Hospitalisation (no SD). | Gunderson reports randomising 95 people. In earlier report of same study (Stanton 1984) 164 people were said to have been randomised. For the 69 dropouts there are no other available data other than leaving the study early. There are only usable data of 95 people staying in therapy beyond 6 months.<br><br>**Allocation concealment B** |
| **May1976** | Allocation: random, no further details.<br>Duration: until discharge or 6-12 months of treatment. Follow up after discharge (and from assigned interventions) up to 5 years. Usable data available for 3 years. | Diagnosis: schizophrenia, no further details.<br>N=228.<br>Sex: male and female.<br>History: first admission with no significant prior treatment.<br>Exclusions: people who were 'obviously not going to be discharged within 2 years', and those whose illness went into remission during 18 day assessment period. | 1. Individual psychotherapy: n=46.<br>2. Ataraxic drugs (trifluperazine): n=48.<br>3. Individual psychotherapy and ataraxic drugs: n=44.<br>4. ECT: n=47.<br>5. Milieu therapy and ataraxic drugs: n=43. | Global impression (discharge from hospital).<br>Follow up.<br>Menninger Health Sickness Scale (MHSS).<br>Medication use after discharge.<br>Best level of functioning.<br>Unable to use -<br>Relapse (no usable data). | **Allocation concealment B** |
| **O'Brien1972** | Allocation: random, no further details.<br>Duration: 20 months. | Diagnosis: schizophrenia, case notes contained clear evidence of a psychotic episode, no further details. | 1. Individual psychotherapy: n=50.<br>2. Group psychotherapy: n=50. | Global impression (rehospitalisation, not improved, discharged, remaining in therapy). | Dropped 13 participants from analysis, but it was clear from which groups, so they were added back in an effort to |

| | | | | | |
|---|---|---|---|---|---|
| | | Sex: 39 male, 61female.<br>Age: mean ~37 years.<br>History: newly discharged from acute inpatient care; mean number of hospitalisations ~2.9. | All participants on medication at the start of the study. | Unable to use -<br>Mental state (BPRS - no usable data, Zung Self Rating Scale - no data).<br>Mental status (Mental Status Scale - no usable data).<br>Social functioning (Social Effectiveness Scale - no usable data).<br>Leaving the study early (no data). | undertake an intention to treat analysis.<br>No details of orientation or frequency of sessions.<br><br>**Allocation concealment B** |

Allocation concealment: A = adequate, B = unclear, C = inadequate, D = allocation concealment was not used as a criterion to assess validity.

**References of included studies (previous guideline)**

**Gunderson 1984 (published data only)**

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May P. (1984) A step forward in research on psychotherapy of schizophrenia. *Schizophrenia Bulletin*; 10(4):604-7.

Muller C. (1984) Psychotherapy in schizophrenia: the end of the pioneers' period. *Schizophrenia Bulletin*; 10(4):618-20.

Stanton AH, Gunderson JG, Knapp PH, Frank AF, Vannicelli ML, Schnitzer R, Rosenthal R. (1984) Effects of psychotherapy in schizophrenia. I. Design and implementation of a controlled study. *Schizophrenia Bulletin*; 10(4):520-63.

**May 1976 (published data only)**

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May PR, Tuma AH, Dixon WJ. (1981) Schizophrenia: a follow-up study of the results of five forms of treatment. *Archives of General Psychiatry* ;38(7):776-84.

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**O'Brien 1972 (published data only)**

Mintz J, O'Brien C, Luborsky L. (1976) Predicting the outcome of psychotherapy for schizophrenics: relative contributions of patient, therapist, and treatment characteristics. *Archives of General Psychiatry*;33(10):1183-6.

* O'Brien CP, Hamm KB, Ray BA, Pierce JF. (1972) Group versus individual psychotherapy with schizophrenics. *Archives of General Psychiatry*; 27:474-8.

**Characteristics of excluded studies (previous guideline)**

| Study | Reason for exclusion |
|---|---|
| **Appelbaum 1986** | Allocation: not randomised, description of organisation of psychotherapy wards. |
| **Armstrong 1991** | Allocation: random.<br>Participants: unclear.<br>Interventions: Life Skills Programme in Day Hospital, vs. Supportive Psychotherapeutic Milieu in Day Hospital.<br>Not psychoanalytic or psychodynamic therapy. |
| **Azima 1959** | Allocation: unclear.<br>Methods: drugs given and observations collected using a double blind method, likely A-B-C-A crossover trial.<br>Interventions: phenobarbital or reserpine, not psychodynamic therapy. |
| **Bellak 1973** | Allocation: not randomised, case report. |
| **Cancro 1987** | Allocation: not randomised, review. |
| **Carpenter 1993** | Allocation: not randomised, review. |
| **Chiesa 1999** | Allocation: random.<br>Exclusion criteria: schizophrenia. |
| **Chodoff 1982** | Allocation: not randomised, review. |
| **Cormier 1987** | Allocation: not randomised, before and after study. |
| **Dyrud 1973** | Allocation: not randomised, review. |
| **Epstein 1981** | Allocation: not randomised, review. |
| **Falloon 1983** | Allocation: random.<br>Participants: people with schizophrenic. N=36.<br>Intervention: family therapy and supportive individual therapy, not psychodynamic therapy. |
| **Friedman 1973** | Allocation: not randomised, review. |
| **Gabbard 1997** | Allocation: not randomised, review. |
| **Gillieron 1980** | Allocation: not randomised, survey and factorial analysis of a questionnaire. |

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|---|---|
| **Glick 1974** | Allocation: random, no further information.<br>Participants: schizophrenia. N=60.<br>Interventions: short vs long hospitalisation, not psychoanalytic therapy. |
| **Guthrie 1997** | Allocation: random.<br>Participants: participants without psychosis.<br>Personal communication from Dr Guthrie. |
| **Harding 1994** | Allocation: not randomised, review. |
| **Hogarty 1997** | Allocation: random, no further details.<br>Participants: people with schizophrenia or schizoaffective disorder. N=186.<br>Interventions: personal therapy, family psychoeducation, combined personal therapy and family psychoeducation or supportive therapy. Personal therapy seemed to have a definition akin to CBT. "Through a process called 'internal coping', personal therapy encouraged the participant to identify the affective, cognitive and physiological experience of stress." |
| **Kaplan 1985** | Allocation: not randomised. |
| **Karon 1969** | Allocation: random.<br>Participants: people with schizophrenia.<br>Interventions: psychoanalytic individual therapy versus ego analytic therapy versus supportive psychotherapy versus medication.<br>Outcomes: psychological tests (Thorndyke Gallup Vocabulary, Porteus Mazes, WAIS IQ test, Visual-Verbal Test), use of medication (no usable data). |
| **Karon 1984** | Allocation: not randomised, review. |
| **Klerman 1984** | Allocation: not randomised, review. |
| **Krull 1987** | Allocation: not randomised, review. |
| **Lindberg 1981** | Allocation: non random, matched pairs retrospective study. |
| **Luborsky 1975** | Allocation: not randomised, review. |
| **Matussek 1974** | Allocation: not randomised, cohort study. |
| **Mueser 1990** | Allocation: not randomised, review and editorial. |
| **Muller 1978** | Allocation: not randomised, review. |
| **Res. committee 1975** | Allocation: not randomised, review. |
| **Resch 1994** | Allocation: not randomised, review. |
| **Roback 1972** | Allocation: random.<br>Participants: hospitalised psychiatric male service users, n=24 (20 diagnosed with schizophrenia).<br>Interventions: interpretive group therapy vs. interactive group therapy.<br>Outcomes: self rating of insight, psychometric tests. Data not usable. |

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|---|---|
| **Rogers 1967** | Allocation: random.<br>Participants: people with schizophrenia, with people without schizophrenia as controls.<br>Interventions: therapeutic relationships. |
| **Rubins 1974** | Allocation: not randomised, review. |
| **Schachter 2001** | Allocation: random.<br>Participants: not unclear if schizophrenia. |
| **Schneider 1993** | Allocation: not randomised, review. |
| **Scott 1995** | Allocation: not randomised, review. |
| **Silverman 1978** | Allocation: not randomised, review. |
| **Sines 1961** | Allocation: participants allocated to 'psychiatric aides'.<br>Participants: 40 with schizophrenia, 7 'mental defectives', and 13 other diagnoses, N=117.<br>Interventions: twice weekly meetings of 50 minutes for the purpose of 'improving the patient's psychiatric and behavioural status'. During the 50 minutes, aides engaged in various activities, none of which resembled psychodynamic therapy. |
| **Sjostrom 1990** | Allocation: random.<br>Participants: people with schizophrenia (DSM III). N=16.<br>Intervention: psychotherapy with dynamic elements versus standard care.<br>Outcomes: no usable data. |
| **Stevens 1973** | Allocation: not randomised, sociological observation of services. |
| **Sverdlov 1980** | Allocation: not randomised, study of remission formation. |
| **Tarrier 1999** | Allocation: random.<br>Participants: people with chronic schizophrenia experiencing residual psychotic symptoms, N=150.<br>Interventions: cognitive behavioural psychotherapy. |
| **Tienari 1986** | Allocation: not randomised, review. |
| **Volterra 1996** | Allocation: random.<br>Participants: people with schizophrenia.<br>Intervention: group and individual psychotherapy (plus haloperidol 2mg/day) versus drug treatment alone.<br>Outcome: no data available (Congress abstract). |
| **Vora 1977** | Allocation: randomised.<br>Participants: clinic attendees who received therapy in excess of 1 year, 53% neurotic, 47% either psychotic or characterological disorders, data not presented for people with schizophrenia alone. |
| **Werbart 1988** | Allocation: not randomised, review. |

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|---|---|
| **Young 1979** | Allocation: random<br>Participants: 141 with schizophrenia and 94 without schizophrenia<br>Interventions: long vs. short hospitalisation and therapists A-B-scores, not psychodynamic psychotherapy. |
| **de Socarraz 1978** | Allocation: random.<br>Participants: people with neuroses, not with schizophrenia. |

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* Cormier HJ, Allard L, Vaillancourt S, Gingras C. (1987) Evaluation d'un programme de sante mentale pour jeunes adultes psychotiques [An evaluation of mental health programs for young adult psychotics. [Special issue: community mental health services for the chronically mentally disabled]]. *Canadian Journal of Community Mental Health*; 6:107-16.

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* de Socarraz ML, Randolph DL. (1978) Responses given by A and B quasi-therapists to differing sexual roles in an intropunitive-neurotic prototype: an analogue study. *Journal of Clinical Psychology;* 34(1):165-70.

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**Falloon 1983**

* Falloon I, Razani J, Moss HB, Boyd JL, McGill CW, Pederson J. (1983) Gemeindenahe Versorgung von Schizophrenen. Eine einjahringe Kontrolluntersuchung bei Familien und Einzeltherapie. [Community management of schizophrenia. A one-year study of family and individual therapy]. *Partnerberatung*; 20(2-3):73-9.

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Falloon IRH, McGill CW, Boyd JL, Pederson J. (1987) Family management in the prevention of morbidity of schizophrenia: social outcome of a two-year longitudinal study. Psychological Medicine; 17(1):59-66.

**Friedman 173**

* Friedman R, Gunderson J, Feinsilver D. (1973) The psychotherapy of schizophrenia: an NIMH program. American Journal of Psychiatry; 130(6):674-7.

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* Gabbard G, Lazar S, Hornberger J, Spiegel D. (1997) The economic impact of psychotherapy: a review. *American Journal of Psychiatry*;154(2):147-55.

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* Krull, F. (1987) Psychotherapie bei schizophrenie: theorie und praxis der einzelbehandlung: eine Übersicht [Individual psychotherapy of schizophrenia: a review of theories and therapeutic practice]. *Fortschritte der Neurologie-Psychiatrie* ; 55(2):54-67.

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* Luborsky L, Singer B, Luborsky L.(1975) Comparative studies of psychotherapies. Is it true that "everyone has one and all must have prizes"? *Archives of General Psychiatry*; 32(8), 995-1008.

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* Scott JE, Dixon LB. (1995) Psychological interventions for schizophrenia. *Schizophrenia Bulletin*; 21(4):621-30.

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**Characteristics of included studies (update)**

| **Study ID** | **DURHAM2003** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial (effectiveness/pragmatic) |
| | **Type of analysis:** ITT - All participants who started allocated treatment were analysed. For missing values, LOCF and imputation from group means were also applied, these had no impact on significant outcomes. |
| | **Type of analysis:** LOCF |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 36 |
| | **Duration:** Length of follow-up - 3 months |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Two adjacent mental health services in Tayside and Fife |
| | **Number of people screened, excluded & reasons:** A total of 274 people were referred for possible inclusion in the trial, of whom 95 (35% of initial referrals) fulfilled the initial criteria, entered the baseline assessment phase and were offered a further screening interview 3 months later. Of these, 66 (24% of initial referrals, 38% of 171 potentially suitable referrals) entered the study and were randomised to treatment conditions. |
| | **Notes about study methods:** Randomisation (sealed envelope technique) administered centrally by non-clinical project coordinator, carried out separately at each treatment centre by permuted blocking. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 89% |
| | **Diagnosis:** Other schizophrenia related [%] Delusional disorder 3%, schizoaffective 8% |

**Diagnostic tool:** DSM-IV

**Diagnostic tool:** ICD-10

**Inclusion criteria:**
- Psychosis with a diagnosis of schizophrenia, schizoaffective disorder or delusional disorder
- Aged 16–65 years
- Known to the psychiatric services as experiencing positive symptoms of persistent and distressing hallucinations or delusions
- Stabilised on antipsychotic medication for at least a 6-month period under the care of a consultant psychiatrist.

**Exclusion criteria:**
- Primary diagnosis of alcoholism or drug misuse
- Evidence of organic brain disease
- History of violence.

**Total sample size:** No. randomised - 66

**Total sample size:** ITT population - 60

**Gender:** % female 32%

**Age:** Mean 36 (10.4)

**Ethnicity:** Not reported

**Setting:** Outpatient

**Setting:** Inpatient

**History:** Mainly middle-aged men with a long history of illness (mean 13 years, range 2-31)

**Baseline stats:**
[CBT / SPT / TAU]
PANSS total score: 101.2 (14.7) / 95.0 (17.7) / 92.4 (17.5)
PSYRATS delusions: 14.1 (4.5) / 12.3 (5.8) / 11.2 (5.6)
PSYRATS hallucinations: 23.0 (11.3) / 23.6 (10.0) / 20.8 (10.9)
Global Assessment Scale: 32.0 (4.8) / 34.9 (7.2) / 34.8 (8.1)

**Notes about participants:**
Medication [CBT / SPT / TAU]
Chlorpromazine equivalents, mg/day [mean (95% CI)]: 604 (392-816) / 747 (527-967) / 630 (333-927)
Four of the 15 patients who were started on an atypical were prescribed clozapine.

**Interventions** **Intervention - group 1.:** CBT; n=22

**Intervention - group 2.:** SPT; n=23

**Intervention - group 3.:** TAU; n=21

**Notes about the interventions:**
CBT
Drew on best practice as exemplified by two treatment manuals. The essential elements were as follows: engagement; analysis of problems; development of a normalising rationale for psychotic experiences; exploration of current coping strategies; acquisition of additional coping strategies for hallucinations and delusions; and focus on accompanying affective symptomatology using relaxation training, personal effectiveness training and problem-solving as appropriate. The overall aims were: to enhance knowledge and acceptance of illness; to encourage the acquisition of specific coping skills for managing hallucinations and delusions; and to develop an understanding of personal vulnerability and how to mitigate its effects.

SPT
Supportive psychotherapy using a previous framework. The approach is psychodynamic in orientation and seeks to understand psychotic experience as a function of being overwhelmed and unable to bear intensely charged emotional experiences. The essential elements of therapy were as follows: provision of non-specific emotional support and empathy; opportunity for the patients to describe the narrative of their lives and the impact of the illness; and working through of transference.

TAU
All participants received usual treatment, focused on community mental health teams. Services include regular psychiatric consultation and contact with a keyworker (typically a trained community psychiatric nurse), with emergency assessment and hospital admission available as required. Facilities in the community include day care, sheltered work, supported accommodation and volunteer befriending. Specialist psychological intervention for psychosis within a cognitive–behavioural framework, although a limited resource, is offered through clinical psychology and clinical nurse specialists.

Training
The CBT arm of the trial was delivered by five clinical nurse specialists with extensive professional experience of severe mental disorder. All had completed a recognised post-registration training in Dundee that mainly focuses on standard CBT for common mental disorders but includes a module on psychosis. All were registered as therapists with the British Association of Behavioural and Cognitive Psychotherapy. One of these five had developed a specialist interest in CBT for psychosis and took the lead role in developing the treatment protocol, training and supervising the other therapists and treating the majority of patients.

None of the CBT therapists saw patients in the supportive psychotherapy arm of the trial, which was delivered by 16 mental health professionals (mainly nursing but also psychiatry and occupational therapy) who were attached to the clinical teams responsible for the patients referred to the trial. All had expressed an interest in developing clinical skills in psychotherapy for patients with psychosis and none had received any formal training in CBT. They were given training and supervision by a consultant psychotherapist, who has consultant responsibility for one of the day hospitals in Dundee and is director of psychotherapy training in Tayside. She took responsibility for developing the supportive psychotherapy protocol and for training and supervising the therapists. All therapists in both treatment conditions were offered bi-weekly supervision for the duration of their contact with patients in the trial.

**Outcomes**

**Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) for end of treatment and FU for both CBT vs SC and CBT vs other active treatment

**Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAS (end of treatment and FU)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS Total for end of treatment and FU
PSYRATS Delusions, PSYRATS Hallucinations

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state: Clinically worthwhile improvement: 25% reduction in PANSS
Clinically important improvement: 50% reduction in PANSS

**Satisfaction with treatment:** Service user satisfaction

**Other:** Antipsychotic use (CPZ equivalents), increase/decrease in antipsychotic doses, discontinuation/change in antipsychotic

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Well covered

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**
**:** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** ++

**References of included studies (update)**

Durham,R.C.; Guthrie,M.; Morton,R.V.; Reid,D.A.; Treliving,L.R.; Fowler,D.; Macdonald,R.R. (2003) Tayside-Fife clinical trial of cognitive-behavioural therapy for medication-resistant psychotic symptoms. Results to 3-month follow-up. *British Journal of Psychiatry* 182: 303 - 311.

**Characteristics of excluded studies (update)**

**ROSENBAUM2005**

**Reason for exclusion:** - Participants not fully randomised - study was conducted in 4 centres, 2 of which only offered a certain type of treatment. Participants were only randomised in the other two centres.

**ROSENBAUM2006[ROSENBAUM2005]**

**Reason for exclusion:** - Primary paper excluded
- Participants not fully randomised - study was conducted in 4 centres, 2 of which only offered a certain type of treatment. Participants were only randomised in the other two centres.

**References of excluded studies (update)**

Rosenbaum,B.; Valbak,K.; Harder,S.; Knudsen,P.; Koster,A.; Lajer,M.; Lindhardt,A.; Winther,G.; Petersen,L.; Jorgensen,P.; Nordentoft,M.; Andreasen,A.H. (2005) The Danish National Schizophrenia Project: prospective, comparative longitudinal treatment study of first-episode psychosis. British Journal of Psychiatry 186: 394 - 399.

Schmid,G.B.; Wanderer,S. (2007) Phantasy therapy: Statistical evaluation of a new approach to group psychotherapy for stationary and ambulatory psychotic patients. *Forschende Komplementarmedizin*.14(4): 216-223.

Rosenbaum B, Valbak K, Harder S, Knudsen P, Koster A, Lajer M, Lindhardt A, Winther G, Peterson L, Jorgensen P, Nordentoft M, Andreasen AH (2006). Treatment of patients with first-episode psychosis: two year outcome data from the Danish National Schizophrenia Project. *World Psychiatry* 5, 100-103

## Psychoeducation

| Previous guideline review | 1. Review type<br>2. Funding<br>3. Period covered<br>4. Data analysis<br>5. No. of studies<br>6. No. randomised | Interventions | Outcomes reported in review |
|---|---|---|---|
| Pekkala E, Merinder L.<br><br>Psychoeducation for schizophrenia (Cochrane Review).<br><br>In: *The Cochrane Library*, Issue 4, 2001. Oxford: Update Software. | 1. Systematic review of RCTs.<br>2. Extramural sources of support to the review: Finnish Office for Health Technology Assessment (FinOHTA) FINLAND; Intramural sources of support to the review: Department of Psychiatry, Porvoo Hospital FINLAND, Department of Psychiatric Demography, Institute of Basic Psychiatric Research, University Hospital of Aarhus DENMARK<br>3. Database origin to 1999.<br>4. Meta-analysis of Relative Risk, weighted mean difference, or standardised mean difference.<br>5. 10 (10, after removing five ineligible trials and adding five new trials).<br>6. 1128 (1070). | 1. All didactic interventions of psychoeducation or patient teaching involving individuals or groups were included. Psychoeducational interventions were defined as any group or individual programme involving interaction between information provider and service user. These programmes address the illness from a multidimensional viewpoints, including familial, social, biological and pharmacological perspectives. Participants are provided with support, information and management strategies. Programmes of 10 sessions or less were considered as 'brief', and 11 or more as 'standard' for the purposes of this review. Interventions including elements of behavioural training, such as social skills or life skills training as well as education performed by patient peers were excluded from this review. Staff education studies were also excluded.<br>2. Standard care was defined as the normal level of psychiatric care provided in the area where the trial was carried out. | Primary outcomes were effects of psychoeducation on:<br>1. Participant compliance, defined as:<br>1.1 Compliance with medication;<br>1.2 Compliance with follow-up.<br>2. Relapse.<br>Secondary outcomes:<br>1. Level of knowledge:<br>1.1 Improvement of understanding of his/her illness and need for treatment;<br>1.2 Level of knowledge about expected and undesired effects of medication.<br>2. Behavioural outcomes:<br>2.1 Level of psychiatric symptoms;<br>2.2 Symptom control skills;<br>2.3 Problem solving skills;<br>2.4 Social skills.<br>3. Family members' level of knowledge:<br>3.1 Family members' understanding of medication and psychiatric illness.<br>4. Service utilisation:<br>4.1 Use of outpatient treatment;<br>4.2 Length of hospitalisation.<br>5. Health economic outcomes:<br>5.1 Treatment costs. |

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| **Update** | **Reclassified:** 1 RCT (Posner1992) included in the previous guideline as family intervention, reclassified as psychoeducation.<br>**Follow up to existing studies:** 3 papers: Bauml1996 (2 papers); Hornung1995 (1 paper).<br>**New studies:** 9 RCTs. | **Notes:**<br>Definition updated |

**Characteristics of included studies (previous guideline)**

| Study | Methods | Participants | Interventions | Outcomes | Notes |
|---|---|---|---|---|---|
| **Atkinson1996** | Allocation: random - no further description.<br>Blinding: not described.<br>Duration: 20 weeks, follow up 3 months.<br>Analysis of dropouts: the data is presented for study group attendees, rather than those allocated to groups. | Diagnosis: schizophrenia SADS and DSM-III-R.<br>N=146.<br>Age: not reported<br>Sex: male 92, female 54.<br>History: community based out-patients good depot clinic attendees, illness length 9-14 years. | 1. Education groups on 8 geographical areas, each session 90 minutes including a break. Sessions alternated between an information and problem solving. Manual outlining the content was given. N=73.<br>2. Waiting list. N=73. | 1. Social functioning: SFS, modified SNS.<br>2. Quality of life: Heinrichs' scale.<br>3. Leaving the study early.<br>Unable to use -<br>1. Compliance with medication (no usable data).<br>2. Mental state: BPRS (no data).<br>3. Knowledge (no data).<br>4. Self-esteem (no data). | Know-ledge + self-esteem assessed but reported elsewhere. |
| **Bauml1996** | Allocation: computerised list block randomisation either to intervention group or control "which was blind to study physician".<br>Blinding: not reported.<br>Duration: 4-5 months and 1 year follow-up.<br>Analysis of dropouts: withdrawals described and analysed. Setting: Inpatients, Munich, Germany. | Diagnosis: schizophrenia, schizophreniform disorder, schizoaffective disease ICD-9, DSM-III-R.<br>N=236.<br>Age: mean 33 years.<br>Sex: male 109, female 127.<br>History: outpatients, GAS mean 49, BPRS mean 42, illness duration mean 7 years, hospitalisations mean 4, first episode 24% of participants. | 1. Information group of eight sessions and information booklet. First four sessions weekly, next four monthly. N=125.<br>2. Control group. N=111. | 1. Medication compliance.<br>2. Relapse.<br>3. Death.<br>4. Knowledge: WFB.<br>5. Illness-related attitudes: KK.<br>6. Expressed emotion: FQ.<br>7. Mental state: BPRS.<br>8. Leaving the study early.<br>9. Global functioning: GAS. | |

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| **Cunningham Owens2001** | Allocation: random numbers in sealed envelopes. Blinding: rater not blind. Duration: 1 session, follow-up by research psychiatrist every 8 weeks approx., over 12 months follow-up. Analysis of dropouts: numbers in each group provided - at baseline, did not differ significantly from completers. Setting: in-patients/day patients at discharge, Scotland, UK. | Diagnosis: schizophrenia (DSM-III-R). N=114. Mean age: ~35, Sex 33 F 81 M. History: at least one previous episode, due for discharge, recommendation for maintenance antipsychotic medication from consultant, mean duration of illness ~9 years, 50% on depot, 56% on antiparkinsonian medication, 25% exclusively on atypicals. | 1. Intervention group: designed to improve understanding of illness and acceptance of medication. Comprised a 15-minute educational video, the content of which was also available in three differently presented booklets. After viewing video, participants offered choice of booklets. Those not taking all three booklets during the 1st session were offered them again at 6 and 12 months. The informational component was didactic in delivery and adopted a medical approach to the understanding of schizophrenia. Designed to enhance factual knowledge and correct erroneous and insight-related misconceptions about the disorder, the risks of relapse and consequences of symptom exacerbation, and to address the question of stigma. Distinction between treatment and maintenance regimes emphasised, as was nature and treatment of side effects from medication. In addition, participants asked which side effects (if any) were the most troublesome to them, and an appropriate treatment was determined by a structured protocol. N=61.<br>2. Control group: standard care. | 1. Leaving the study early.<br>2. Relapse.<br>3. Insight: ITAQ.<br>4. Mental state: Depression (MADRS). | |

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| **Hayashi2001** | Allocation: "randomly allocated" - no further details.<br>Blindness: not stated.<br>Duration: 8 weeks treatment.<br>Setting: Acute inpatients, Tokyo, Japan. | Diagnosis: schizophrenia (DSM IV). N = 54.<br>Age: range 19-59<br>Sex: 54 M<br>History: consecutive admissions, mean previous hospitalisations ~3.<br>Exclusions: mental retardation or organic brain disease. | 1. 3-stage intervention: form working relationship, facilitate collaborative attitude and pursue remedies for sufferings, and psychoeducation approaches. N=27.<br>2. routine inpatient treatment. N=27. | 1. PANSS (Japanese version - positive, negative, general).<br>2. Awareness of Being a Patient Scale (ABPS).<br>Unable to use:<br>1. Maudsley Personality Inventory (no usable data).<br>2. Perceptions of participants scales (instrument non-validated). | |
| **Hornung1995** | Allocation: randomisation in which age, sex, prognosis and medication compliance were balanced by preliminary matching. Randomisation by an independent institution, Zentrum zur Methodischen von Therapiesstudien (ZMBT).<br>Blinding: raters were not blind except compliance rated by independent raters at 1 year.<br>Duration: 15 weeks and follow-up 5 years.<br>Analysis of dropouts: withdrawals partially described, modified ITT mentioned (data unclear). Setting: Out-patients, Muenster, Germany. | Diagnosis: Schizophrenia DSM-III-R with the exception of schizoaffective disorder. N=191.<br>Age: mean 31.9 years (SD 7.8).<br>Sex: male 111, female 80.<br>History: 'chronic', outpatients, > 2 acute episodes in last 5 years, onset of illness mean ~24 years, mean ~4 (SD 3.1) hospitalisations, BPRS mean ~27 (SD 6.4), daily neuroleptic dose mean ~470 mg CPZ (SD 680). | 1. Psychoeducational medication training (PT) + leisure time group (LTG) at 7 study centres: 10 sessions in groups of 4-6 participants with one or two psychotherapists during 15 weeks. First 5 sessions once a week, next five twice a fortnight. N=32.<br>2. PT+key person counselling 10 sessions (KC) +LTG. N=35.<br>3. PT+cognitive psychotherapy=CP N=34<br>4. PT+KC+CP. N=33.<br>5. Control group participants attended a structured but unspecific leisure-time group of same length. N=57. | 1. Relapse.<br>2. Death<br>3. Global functioning: GAS.<br>4. Leaving the study early.<br>Unable to use:<br>1. Medication compliance (no usable data).<br>2. Mental state: BPRS, PANS (no usable data).<br>3. Qualification for medication self-management (no usable data).<br>4. Illness-related attitudes: KK-Skala (no usable data).<br>5. Satisfaction with knowledge (no usable data). | Partici-pants of interven-tions 1,2 and 5 taken into account. |

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| **Jones2001** | Allocation: "randomly allocated" using randomisation chart.<br>Blinding: not reported.<br>Duration: 5 sessions were provided, but the time between sessions was not reported.<br>Analysis of dropouts: intention to treat analysis assumed that the values for psychological variables for participants who did not complete follow-up had not changed.<br>Setting: Outpatients, Glasgow, UK. | Diagnosis: Schizophrenia (F2 on ICD-10). N=112.<br>Age: range 18-75.<br>Sex: 37 F, 75 M.<br>Exclusion criteria: aged over 65, uncertain diagnosis, acutely ill at time of contact, presence of chronic symptoms or physical problems restricting participation, persistent defaulters, recent involvement in an education programme. | "All interventions involved 5 sessions and were intended to increase patients' knowledge about schizophrenia."<br>1. Computer only: 3 types of screen display: (a) general information, (b) personal information from the viewing participant's medical record embedded in more general information, and (c) questionnaires (including medical record audit), plus feedback displays. At end of session, any of the information requested by the participant could be printed out. Each session lasted ~14 minutes. N=56.<br>2. Community psychiatric nurse only: These hour-long sessions covered the same content as the computer system. Personal issues could be introduced by the participant. Participants could also be given a printed summary, but this did not include any personal info. N=28.<br>3. Combined community psychiatric nurse and computer: the 1st session was with the nurse, sessions 2-4 were on the computer, and the final session was again with the nurse. Participants were given relevant printed summaries from sessions. N=28. | 1. Leaving the study early.<br>2. Mental state: improved BPRS.<br>3. Insight: improved ITAQ.<br>4. Global functioning: improved GAF.<br>5. Satisfaction.<br>Unable to use:<br>1. Knowledge and Information about Schizophrenia Schedule (KISS - non-validated scale).<br>2. BPRS, GAF, ITAQ change scores (SDs not reported). | |

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| **Lecompte1996** | Allocation: randomised.<br>Blinding: none.<br>Duration: not reported. | Diagnosis: schizophrenia (DSM III-R).<br>N=64.<br>Age: mean ~36 years.<br>History: at least 2 hospital admissions, noncompliant with medication. | 1. Psychoeducation: medication compliance using "cognitive-behavioral therapeutic strategies" + standard care - (1) enhancement of therapeutic alliance; (2) psychoeducation regarding prognosis and evolution of illness and treatment; (3) perceptual and attitudinal strategies for identifying prodromal symptoms and developing coping strategies; (4) behavioural strategies using reinforcement, modelling, and shaping of compliance behaviour; (5) cognitive restructuring by correcting erroneous beliefs and distorted convictions about the illness, pharmacotherapy, chronicity of illness, necessity of preventive medication, and outcome expectancies. N=32.<br>2. Control: unstructured conversations + standard care. N=32. | 1. Leaving the study early.<br><br>Unable to use:<br>1. Length of time in hospital (no SD). | |
| **Macpherson 1996** | Allocation: random - a random numbers table.<br>Blinding: all ratings were carried out by the author, without blinding procedures.<br>Duration: 1 month.<br>Analysis of dropouts: withdrawals described.<br>Setting: Outpatients, Bristol and Gloucester, UK. | Diagnosis: DSM-III-R schizophrenia.<br>N=67.<br>Age: mean 45.2 years (SD 13).<br>Sex: male 48, female 16.<br>History: largely (54/64) community based, chronic, institutionalised population, at least 6 months cumulative antipsychotic drug exposure and clinical stability.<br>Years in institution mean 12.8 (SD 11.8).<br>Education mean 11 years (SD 1.9). | 1. A single individualised educational session following manual guidelines based on the psychoeducation literature and principles of general health education. N=24.<br>2. Individualised teaching in 3 education sessions 25-35 minutes at weekly intervals. N=23.<br>3. No education. N=20. | 1. Leaving the study early.<br>Unable to use:<br>1. Mental state (no usable data). 2. Insight (no usable data).<br>3. Knowledge (Understanding of Medication Questionnaire - UMQ - instrument non-validated). | All education was performed by the author RM. |

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| **Merinder1999** | Allocation: stratified for gender and for illness duration, randomisation carried out by an independent institution.<br>Blinding: relapse and compliance assessed blindly.<br>Duration: 8 weeks, 1 year follow up.<br>Analysis of dropouts: follow-up of withdrawals reported.<br>Setting: Outpatients, Arhus and Viborg, Denmark. | Diagnosis: schizophrenia (F20.2-F20.9) ICD Danish version, OPCRIT.<br>N=46.<br>Age: median 35.9 years, interquartile range 30.3-39.6 years.<br>Sex: male 23, female 23.<br>History: illness duration median 8.2 years, earlier admissions median 5.<br>In treatment at 2 community psychiatric centres. | 1. Psychoeducational 8 -sessions intervention using didactic, interactive method standardised with a manual for group leaders and a booklet for participants. Weekly group of 5-8 participants conducted separately for participants and relatives. N=24.<br>2. Psychopharmacological treatment, psychosocial rehabilitation efforts and to some extent supportive psychotherapy. N=22. | 1. Relapse.<br>2. Death.<br>3. Global functioning: GAF.<br>4. Leaving the study early.<br>5. Expressed emotion: FQ.<br>6. Insight (IS).<br>7. Mental state: BPRS.<br>8. Satisfaction with services: VSSS.<br><br>Unable to use:<br>1. Knowledge (instrument non-validated). | |

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| **Smith1987** | Allocation: random allocation of families to one of two interventions. Blinding: not reported. Duration: 4 weeks, 6 month follow-up. Analysis of dropouts: NA - no dropouts occurred. Setting: Birmingham, UK. | Diagnosis: schizophrenia - no further details given. No details provided about participant characteristics/history. N=40 family members, from 8 families. | 1. Group condition: 4 weekly educational sessions were conducted by clinical psychologist. Sessions were in semi-structured seminar format involving oral presentation of information and audiovisual aids, including a video. Each session corresponded to one of the following aims: (a) improve relatives' understanding of nature, symptoms, treatment of schizophrenia, (b) improve relatives' "cognitive mastery" of their own situation by applying info to their own circumstances (mainly through an instrumental component in the form of homework assignments), (c) improve relationship and reduce alienation between participant and relatives by changing relatives' attitudes, (d) emphasise importance of maintaining relatives' personal well-being. At the end of the session family members were given a written homework exercise to complete. N=20.<br>2. Postal condition: a typed information booklet (corresponding to one of the information sessions received in the group condition) was sent through the post to family members at weekly intervals over a 4-week period. Each booklet had an appropriate homework exercise attached. N=20. | 1. Leaving the study early.<br>2. Stress: Symptom Rating Test (SRT).<br>Unable to use:<br>1. Knowledge (instrument non-validated). 2. Beliefs about schizophrenia (instrument non-validated). 3. Worry and fear (instrument non-validated). 4. Behavioural disturbance (instrument non-validated) 5. Family distress (instrument non-validated). | |

ABPS: Awareness of Being a Patient Scale (25-item, 4-point scale measuring participants' psychological attitudes toward their psychiatric situation. High ABPS scores indicate a more appropriate patient attitude).
BPRS: Brief Psychiatric Rating Scale (higher scores indicate more severe symptoms).

FQ: Family Questionnaire (20-items, rated on a 4-point scale. Covers dimensions of Criticism and Emotional Overinvolvement; developed to be a less time-consuming evaluation of EE than Camberwell Family Interview, against which its validity has been tested).
GAF: General Assessment of Functioning (90-point rating scale that assesses psychological, social and occupational functioning).
GAS: Global Assessment Schedule (higher scores indicate better global functioning).
IS: Insight Scale (8-items, scoring 3 factors - Awareness of Illness, Need for treatment, and Attribution of symptoms - on a 3-point scale).
ITAQ: Insight and Treatment Attitudes Questionnaire (higher scores indicate more insight into illness and treatment).
KK: Krankheitskonzeptskala (German) = Concept of Illness Scale (29-items rated on a 5-point Likert scale. The instrument describes 7 dimensions of illness-related attitudes. The higher the score, the higher the expression of the respective item).
MADRS: Montgomery Asberg Depression Rating Scale (higher scores indicate more severe symptoms).
PANSS: Positive and Negative Syndrome Scale (30 7-point items and three subscales: two 7-item subscales for positive and negative symptoms, and a 16-item subscale covering general psychopathy).
SFS: Social Functioning Schedule (lower scores indicate improved behaviour/function).
SNS: Social Network Schedule (measures number of social contacts in a given time period).
SRT: Symptom Rating Test (30-item measure of stress symptoms incorporating anxiety, depression, somatic, and inadequacy subscales).
VSSS: Verona Service Satisfaction Scale (54-items covering 7 dimensions of satisfaction with service, each rated on a 5-point Likert scale).
WFB: Wissensfragebogen (German) = Knowledge Questionnaire (20 multiple-choice items with a maximum total score of 70, and a minimum of -43).

**References of included studies (previous guideline)**

**Atkinson 1996 (published data only)**

*Atkinson JM, Coia DA, Gilmour WH, Harper JP. (1996) The impact of education groups for people with schizophrenia on social functioning and quality of life. *British Journal of Psychiatry*; 168:199-204.

**Bäuml 1996 (published data only)**

*Bäuml J, Kissling W, Pitschel-Walz G. (1996) Psychoedukative gruppen für schizophrene patienten: Einfluss auf wissensstand und compliance. *Nervenheilkunde* 6;15:145-50.

Bäuml,J.; Pitschel-Walz,G.; Volz,A.; Engel,R.R.; Kessling,W. (2007) Psychoeducation in schizophrenia: 7-year follow-up concerning rehospitalization and days in hospital in the Munich Psychosis Information Project Study. *Journal of Clinical Psychiatry.* 68(6): 854 - 861.

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Pitschel-Walz G, Engel RR. (1997) Psychoedukation in der Schizophreniebehandlung [Psychoeducation in the treatment of schizophrenia]. *Psycho*; 23(1):22-36.

Pitschel-Walz,G.; Bäuml,J.; Bender,W.; Engel,R.R.; Wagner,M.; Kissling,W. (2006) Psychoeducation and compliance in the treatment of schizophrenia: results of the Munich Psychosis Information Project Study. *Journal of Clinical Psychiatry* 67(3): 443 - 452.

**Cunningham Owens 2001**

*Cunningham Owens DG, Carroll A, Fattah S, Clyde Z, Coffey I, Johnstone EC. (2001) A randomized, controlled trial of a brief interventional package for schizophrenic out-patients. *Acta Psychiatrica Scandinavica*; 103:362-9.

**Hayashi 2001 {published data only}**

*Hayashi N, Yamashina M, Igarashi Y, Kazamatsuri H. (2001) Improvement of patient attitude toward treatment among inpatients with schizophrenia and its related factors: Controlled study of psychological approach. *Comprehensive Psychiatry*; 42(3):240-246.

**Hornung 1995 (published data only)**

Buchkremer G, Klingberg S, Holle R, Schulze Monking H, Hornung WP. (1997) Psychoeducational psychotherapy for schizophrenic patients and their key relatives or care-givers: results of a two-year follow-up. *Acta Psychiatrica Scandinavica*; 96(6):483-91.

Feldmann,R.; Hornung,W.P.; Prein,B.; Buchkremer,G.; Arolt,V. (2002) Timing of psychoeducational psychotherapeutic interventions in schizophrenic patients. *European Archives of Psychiatry and Clinical Neuroscience* 252(3): 115 - 119.

*Hornung W P, Holle R, Schulze Monking H, Klingberg S, Buchkremer, G. (1995) Psychoedukativ-psychotherapeutische Behandlung von schizophrenen Patienten und ihren Bezugspersonen. Ergebnisse einer 1-Jahres-Katamnese [Psychoeducational-psychotherapeutic treatment of schizophrenic patients and their caregivers. Results of a one-year catamnestic study]. *Nervenarzt*; 66:828-34.

Hornung WP, Klingberg S, Feldmann R, Schonauer K, Schulze Monking H. (1998) Collaboration with drug treatment by schizophrenic patients with and without psychoeducational training: results of a one-year follow-up. *Acta Psychiatrica Scandinavica*; 97(3):213-9.

Hornung WP, Buchkremer G, Redbrake M, Klingberg S. (1993) Patientmodifizierte Medikation: Wie gehen schizophrene Patienten mit ihren Neuroleptika um? *Nervenarzt*; 64:434-9.

Hornung WP, Feldman R, Klingberg S, Buchkremer G, Reker T. (1999) Long-term effects of a psychoeducational psychotherapeutic intervention for schizophrenic outpatients and their key-persons - results of a five-year follow-up. *European Archives of Psychiatry and Clinical Neuroscience*; 249:162-7.

Hornung WP, Kieserg A, Feldman R, Buchkremer G. (1996) Psychoeducational training for schizophrenic patients: background, procedure and empirical findings. *Patient Education and Counseling*; 29:257-68.

Hornung WP, Schonauer K, Feldmann R, Monking HS. (1998) Medikationsbezogene Einstellungen chronisch schizophrener Patienten. Eine Follow-up Untersuchung 24 Monate nach psychoedukativer Intervention [Medication-related attitudes of chronic schizophrenic patients. A follow-up study after psycho-educational intervention]. *Psychiatrische Praxis*; 25(1):25-8.

**Jones 2001**

*Jones RB, Atkinson JM, Coia DA, Paterson L, Morton AR, McKenna K, Craig N, Morrison J, Gilmour WH. (2001) Randomised trial of personalised computer based information for patients with schizophrenia. *British Medical Journal;* 322:835-40.

**Lecompte 1996**

* Lecompte, D., Pelc, I. (1996). A cognitive-behavioral program to improve compliance with medication in patients with schizophrenia. *International Journal of Mental Health*, *25 (1)*, 51-6.

**Macpherson 1996 (published data only)**

*Macpherson R, Jerrom B, Hughes A. (1996) A controlled study of education about drug treatment in schizophrenia. *British Journal of Psychiatry;* 168:709-17.

**Merinder 1999 (published data only)**

*Merinder LB, Viuff AG, Laugesen H, Clemmensen K, Misfelt S, Espensen B. (1999) Patient and relative education in community psychiatry: a randomised controlled trial regarding its effectiveness. *Social Psychiatry and Psychiatric Epidemiology*; 34(6):287-94.

Merinder LB, Viufff AG, Laugesen H, Clemendsen K, Misfelt S, Espensen B. (1998) Effects of psychoeducative methods; a randomized controlled study. *Nordic Journal of Psychiatry supplement*; 41:144.

**Smith 1987**

*Smith JV, Birchwood MJ. (1987) Specific and Non-specific effects of educational Intervention with families living with a schizophrenic relative. *British Journal of Psychiatry*; 150:645-52.

**Characteristics of excluded studies (previous guideline)**

| Study | Reason for exclusion |
|---|---|
| **Angunawela 1998** | Allocation: random.<br>Participants: adults with general psychiatric problems: schizophrenia 21%, affective disorder 57%, neurotic, personality, other non-psychotic disorder 14% and others 8%. No analyses on diagnostic subgroups.<br>Intervention: participant information leaflet vs. usual information. |
| **Azrin 1998** | Allocation: participants matched and randomly assigned.<br>Participants: chronically mentally ill participants: schizophrenia, bipolar and major depressive disorder. No analyses on diagnostic subgroups. |
| **Boczkowski 1985** | Allocation: random.<br>Participants: people with schizophrenia.<br>Interventions: psychoeducation vs. control group.<br>Outcomes: no usable data. |
| **Borell 1995** | Allocation: random.<br>Participants: schizophrenia DSM-III.<br>Interventions: information programme versus control waiting list group<br>Outcomes: no usable data. |
| **Chaplin 1998** | Allocation: random.<br>Participants: diagnosis functional psychosis, not limited to participants with schizophrenia. No analyses on diagnostic subgroups. |
| **Eckman 1992** | Allocation: random.<br>Participants: schizophrenia DSM-III-R criteria.<br>Intervention: skills training versus supportive group psychotherapy. No psychoeducation. |
| **Goulet 1993** | Allocation: random.<br>Participants: schizophrenia or schizophreniform or schizoaffective disorder DSM-III.<br>Intervention: Uses Medication Management module of Liberman's social skills programme. |
| **Haas 1988** | Allocation: random.<br>Participants: schizophrenia DSM-III, schizoaffective or schizophreniform disorder.<br>Intervention: Fits GDG Family Intervention definition. |
| **Herz 1996** | Allocation: random.<br>Participants: DSM-III-R schizophrenia or schizoaffective disorder.<br>Intervention: Psychoeducation as part of Multimodal Intervention. |
| **Goldman 1988** | Allocation: random.<br>Participants: people with schizophrenia. |

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| | Interventions: didactic program versus standard ward activities<br>Outcomes: no usable data (means, no standard deviations), number of dropouts unclear. |
| **Hogarty 1986** | Allocation: random.<br>Participants: schizophrenia or schizoaffective disorder.<br>Intervention: family intervention with minimal psychoeducation versus social skills training versus combination of family intervention and social skills training versus drug treatment. |
| **Kelly 1990** | Allocation: random.<br>Participants: non-psychoses 7-11%, schizophrenia 59-71%, no analyses of diagnostic subgroups. |
| **Kleinman 1993** | Allocation: block randomisation after stratifying for hospital affiliation.<br>Participants: schizophrenia DSM-III.<br>Intervention: educational process group versus single educational session. No standard care group. |
| **Kopelowicz 1998** | Allocation: random.<br>Participants: DSM-IV schizophrenia or schizoaffective disorder<br>Intervention: community re-entry program, not psychoeducation. |
| **Kuipers 1994** | Allocation: random.<br>Participants: chronic mentally ill service users: schizophrenia and affective disorder.<br>Interventions: structured medication education versus unstructured teaching. No standard care group. |
| **Mak 1997** | Allocation: random.<br>Participants: schizophrenia DSM-III out-patients.<br>Intervention: group and individual behavioural family management with psychoeducation provided through printed information versus conventional care. (Psychoeducation component did not involve interaction between information provider and recipients and was thus excluded from the review.) |
| **Razali 1995** | Allocation: random.<br>Participants: schizophrenic disorder (DSM-III-R).<br>Intervention: Very limited intervention concerned solely with medication compliance. |
| **Tarrier 1988** | Allocation: random.<br>Participants: schizophrenia (PSE).<br>Intervention: Various treatment groups combined in such a way that effects of psychoeducation cannot be determined. |
| **McGill 1983** | Allocation: random.<br>Participants: PSE schizophrenia.<br>Intervention: complex family therapy intervention versus individual supportive psychotherapy. |
| **Xiong 1994** | Allocation: random.<br>Participants: DSM-III-R schizophrenia.<br>Intervention: family intervention with minimal psychoeducation versus standard care. |

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| **Youssef 1987** | Allocation: random.<br>Participants: diagnosis unclear: schizoaffective or affective disorder, data not available for a non-affective subgroup.<br>Intervention: education sessions versus standard care. |
| **Zhang 1994** | Allocation: random.<br>Participants: schizophrenia.<br>Intervention: family intervention with minimal psychoeducation versus standard care. |

**References of excluded studies (previous guideline)**

**Angunawela 1998**

* Angunawela II, Mullee MA. (1998) Drug information for the mentally ill: a randomised controlled trial. *International Journal of Psychiatry in Clinical Practice*; 2:121-7.

**Azrin 1998**

* Azrin NH, Teichner G. (1998) Evaluation of an instructional program for improving medication compliance for chronically mentally ill outpatients. *Behaviour Research and Therapy*;36(9):849-61.

**Boczkowski 1985**

* Boczkowski JA, Zeichner A, DeSanto N. (1985) Neuroleptic compliance among chronic schizophrenic outpatients: an intervention outcome report. *Journal of Consulting and Clinical Psychology*; 53:666-71.

**Borell 1995**

* Borell P, Orhagen T, d'Elia G. (1995) Sjukdomsrelaterad information vid schizofreni: klinisk tillämpning och effekter [Feasibility and effects of a patient information program in schizophrenia]. *Scandinavian Journal of Behaviour Therapy*; 24(3-4):75-86.

**Chaplin 1998**

* Chaplin R, Kent A. (1998) Informing patients about tardive dyskinesia. *British Journal of Psychiatry*; 172:78-81.

**Eckman 1992**

* Eckman TA, Wirshing WC, Marder SR, Liberman RP, Johnston-Cronk K, Zimmermann K, et al. (1992) Technique for training schizophrenic patients in illness self-management: a controlled trial. *American Journal of Psychiatry*; 149(11):1549-55.

**Goldman 1988**

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**Goulet 1993**

*Goulet J, Lalonde P, Lavoie G, Jodoin F. (1993) Effets d'une éducation au traitement neuroleptique chez de jeunes psychotiques. *Revue Canadienne de Psychiatrie*; 38(8):571-3.

**Haas 1988**

Clarkin JF, Glick ID, Haas G, Spencer JH. (1991) The effects of inpatient family intervention on treatment outcome. In: Mirin, S.M., Gossett, J.T., Grob, M.C., eds. *Psychiatric Treatment: Advances in Outcome Research*, pp. 47-59. Washington, DC & London: American Psychiatric Press.

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Glick ID, Clarkin JF, Haas GL, Spencer JH, Chen CL. (1991) A randomized clinical trial of inpatient family intervention: VI. Mediating variables and outcome. *Family Process*; 30:85-99.

Glick ID, Spencer JH, Clarkin JF, Haas GL, Lewis AB, Peyser J et al. (1990) A randomized clinical trial of inpatient family intervention: IV. Followup results for subjects with schizophrenia. *Schizophrenia Research*; 3:187-200.

Haas GL, Glick ID, Clarkin JF, Spencer JH, Lewis AB. (1990) Gender and schizophrenia outcome: a clinical trial of an inpatient family intervention. *Schizophrenia Bulletin*; 16(2):277-92.

Haas GL, Glick ID, Clarkin JF, Spencer JH, Lewis AB, Peyser J, et al. (1988) Inpatient family intervention: a randomized clinical trial: II. Results at hospital discharge. *Archives of General Psychiatry*; 45(3):217-24.

Spencer JH, Glick ID, Haas GL, Clarkin JF, Lewis AB, Peyser J, et al. (1988) A randomized clinical trial of inpatient family intervention: III. Effects at 6-month and 18-month follow-ups. *American Journal of Psychiatry*; 145(9):1115-21.

**Herz 1996**

Herz MI. (1996) Psychosocial treatment. *Psychiatric Annals*; 26:531-5.

*Herz MI, Lamberti JS, Minz J, Scott R, O'Dell SP, McCartan L et al. (2000) A program for relapse prevention in schizophrenia: a controlled study. *Archives of General Psychiatry*; 57:277-83.

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Hogarty GE, Anderson CM, Reiss DJ, Kornblith SJ, Greenwald DP, Ulrich RF, et al. (1991) Family psychoeducation, social skills training, and maintenance chemotherapy in the aftercare treatment of schizophrenia. II. Two-year effects of a controlled study on relapse and adjustment. *Archives of General Psychiatry;* 48(4):340-7.

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**Kopelowicz 1998**

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**Kuipers 1994**

* Kuipers J, Bell C, Davidhizar R, Cosgray R, Fawley R. (1994) Knowledge and attitudes of chronic mentally ill patients. *Journal of Advanced Nursing*; 20(3):450-6.

**Mak 1997**

Mak KY, Wong MC, Ma LK, Fung SC. (1997) A cost-effectiveness study of a community-based family management rehabilitation programme for schizophrenic outpatients in Hong Kong: a six-month report. *Hong Kong Journal of Psychiatry*; 7(2):26-35.

**McGill 1983**

* McGill CW, Falloon IR, Boyd JL, Wood-Siverio C. (1983) Family educational intervention in the treatment of schizophrenia. *Hospital and Community Psychiatry;* 34(10):934-8.

**Razali 1995**

*Razali MS, Yahua H. (1995) Compliance with treatment in schizophrenia: a drug intervention program in a developing country. *Acta Psychiatrica Scandinavica*; 91:331-5.

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**Tarrier 1988**

Barrowclough C, Tarrier N. (1990) Social functioning in schizophrenic patients. *Social Psychiatry and Psychiatric Epidemiology*; 25:125-9.

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* Xiong W, Phillips MR, Hu X, Wang R, Dai Q, Kleinman J, et al. (1994) Family-based intervention for schizophrenic patients in China. A randomised controlled trial. *British Journal of Psychiatry*; 165(2):239-47.

**Youssef 1987**

* Youssef FA. (1987) Discharge planning for psychiatric patients: the effects of a family-patient teaching programme. *Journal of Advanced Nursing*; 12(5):611-6.

**Zhang 1994**

* Zhang M, Wang M, Li J, Phillips MR. (1994) Randomised-control trial of family intervention for 78 first episode male schizophrenic patients. An 18-month study in Suzhou, Jiangsu. *British Journal of Psychiatry*; 165 (Suppl 24):96-102.

**Characteristics of included studies (update)**

| **Study ID** | **BECHDOLF2004** |
|---|---|
| **General info** | **Funding source:** Not mentioned. But Soleduc is a registered psychoeducation programme of Sanofi-Aventis - same drug company for amisulpride (all participants were on amisulpride) |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All included participants |
| | **Blindness:** Open |
| | **Duration:** No. weeks of treatment - 52 weeks (although intervention was only delivered at 3 time points, baseline, 6 and 12 months - 7 sessions each time) |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Multi-centre - 51 sites in France |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Each participating centre received a randomisation list with the order of patient assignment - no further details reported. |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] % not reported |
| | **Diagnosis:** Other schizophrenia related [%] % not reported |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia spectrum disorder |
| | **Exclusion criteria:**<br>- Patients hospitalised for >120 days in previous year<br>- requiring other antipsychotics apart from amisulpride |
| | **Total sample size:** No. randomised - 220 |

**Total sample size:** ITT population - 220

**Gender:** % female 38%

**Age:** Mean 33

**Ethnicity:** Not reported

**History:**
[Psychoeducation / control]
Mean duration of schizophrenia, months: 97.8 / 111.3
Previous hospitalisations: 4.7 / 5.9

**Baseline stats:**
[Psychoeducation / control]
PANSS positive: 16.6(6.0) / 17.6(7.2)
PANSS negative: 22.3(7.1) / 21.2(7.1)

**Notes about participants:**
[Psychoeducation / Control]
Substance misuse (%)
Smokers: 71.2 / 71.6
Alcohol: 6.3 / 5.5

**Interventions** **Intervention - group 1.:** Psychoeducation, 7 sessions 3 times during intervention period (baseline, 6 months and 12 months; N = 111

**Intervention - group 2.:** Control (psychosocial group training), 7 sessions at 3 time points (baseline, 6 months and 12 months; N = 109

**Notes about the interventions:**
All participants were on amisulpride 50-800mg/day

Psychoeducation
Soleduc programme which comprises 8 specific modules delivered via video cassette:
- The disease and its evolution
- Patient responsibility for treatment compliance
- Antipsychotic treatment
- Psychotherapeutic treatment
- Methods of care and specialised follow-up
- Reintegration
- Psychosocial rehabilitation

Control
Psychosocial training group in which patients were orally informed about schizophrenia and its treatment according to the standards of each centre.

Training
The Soleduc modules were delivered by nurse staff under the supervision of a psychiatrist.

**Outcomes**

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - Data not presented in a usable form

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not reported adequately - No mention of allocation concealment in the randomisation list

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed - Differences in severity of illness

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Poorly addressed - No usable data presented for symptoms and functioning

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**BECHDOLF2004**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT

**Blindness:** Only raters blind

**Duration:** No. weeks of treatment - 8

**Duration:** Length of follow-up - 6 and 24 months

**Raters:** Independent of treatment

**Design:** Single-centre - Cologne, Germany

**Number of people screened, excluded & reasons:** During the study period, 189 patients fulfilled inclusion criteria. 57 patients were not approached, either because they were involuntary admissions, formally detained under the Mental Health Act and could therefore not be included in RCTs or because during their inpatient stay, patient flow was too small to form a group of eight patients to start a group intervention. Of the remaining 132 subjects whose consent to enter the trial was sought, there was a 33.4% non-participation rate (n = 44) due to refusal, non-German speaking, inability to complete assessment or rapid discharge.

**Notes about study methods:** Randomisation by computer-generated random numbers for blocks of 8 participants. Results were placed in sealed envelopes and only opened at the time of treatment allocation

**Participants**

**Diagnosis:**
Schizophrenia [% of sample] ICD-10: F 20, F 23, F 25
[CBT / Psychoeducation]
ICD-10 diagnoses, n (%)
F 20: 32 (80.0) / 37 (77.1)
F 23: – (0.0) / 2 (4.1)
F 25: 8 (20.0) / 9 (18.8)

**Diagnosis:** Other schizophrenia related [%]

**Diagnostic tool:** ICD-10

**Exclusion criteria:**
- primary diagnosis of drug or alcohol dependence, organic brain disease, learning disability or hearing impairment

**Total sample size:** No. randomised - 88

**Gender:** % female - 55

**Age:** Mean - 32

**Age:** Range - 18-64

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[CBT / psychoeducation]
Time since diagnosis, months: 56.7 (65.4) / 50.0 (58.7)
Mean number of admissions: 2.6 (3.8) / 2.4 (3.2)

**Baseline stats:**
[CBT / Psychoeducation]
PANSS total: 13.6 (5.3) / 15.1 (5.6)

**Notes about participants:** Medication use: The mean dosages of typical antipsychotics converted to chlorpromazine equivalents were nearly the same at baseline and follow-up evaluations, although there was a wide range of dosage within the treatment groups (pre-treatment [mg mean (SD)]: CBT 431.7 (201.0), PE 375.0 (349.5); post-treatment: CBT 158.8 (73.3), PE 520.0 (413.3); follow-up: CBT 358.3 (340.4), PE 361.4 (340.9)]. All patients were treated with neuroleptics, most with atypicals (pretreatment: CBT 80%, PE 85%; post-treatment: CBT 93.5%, PE 87.8%; follow-up: CBT 88.9%, PE 89.2%). Around one-third of patients studied also received antidepressive medication (pretreatment: CBT 26.3%, PE 25.0%; post-treatment: CBT 25.8%, PE 38.9%; follow-up: CBT 31.0%, PE 28.9%). No significant differences emerged between treatment groups at pre- and post-treatment or follow-up.

**Interventions** **Intervention - group 1.:** Group CBT, 16 sessions, n=40

**Intervention - group 2.:** Group psychoeducational programme, 8 sessions, n=48

**Notes about the interventions:** All interventions were an adjunct to routine hospital care and patients remained under the medical supervision of the responsible consultant psychiatrist who alone determined the pharmacological regime, timing of discharge and readmission.

Group CBT:
Based on a manualised approach which used coping strategy enhancement, problem solving and relapse prevention in patients with psychosis.

Group psychoeducational programme:
The PE programme was similar to the PE group training for patients.

Training:
Groups of both interventions were led by an experienced and CBT trained psychiatrist or clinical psychologist

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol) - added to RevMan for FU

**Global state & service outcomes (e.g. CGI):** Relapse was defined by a rating of at least 5 and a 2-point increase compared with the previous assessment in at least one of the items of the positive syndrome subscale of the PANSS

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation - defined in accordance with Buchkremer and co-workers (26) by a 36-hour full hospitalisation or a 5-day partial hospitalisation because of an exacerbation of acute psychotic symptoms.

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS general, positive, negative

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - Clinical significant change was calculated by a two-fold criterion: (i) improvement of PANSS global score >2 SD beyond the mean of the intake sample at follow-up and (ii) reliable change index exceeds 1.96. The latter is calculated by dividing the absolute magnitude of change by the SE of the change score (follow-up minus pretest) for

| | |
|---|---|
| | FU |
| | **Non-adherence to study medication:** Non-adherence - Compliance with medication |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Adequately addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

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| **Study ID** | **CATHER2005** |
| **General info** | **Funding source:** Pharmaceutical industry |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT defined as having completed at least 4 out of 16 sessions |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 16 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - Two outpatient clinics in Boston |
| | **Notes about study methods:** Randomisation performed by independent member of the research team and stratified by PANSS and gender |
| **Participants** | **Diagnosis:** Other schizophrenia related [%] Schizoaffective 39% |
| | **Diagnosis:** Schizophrenia [% of sample] 61% |
| | **Diagnostic tool:** DSM-IV |

**Inclusion criteria:**
- 18–65 years of age
- English speaking
- Treated with olanzapine for at least 6 months and at a stable dose for at least 30 days
- Exhibiting residual psychotic symptoms as defined by two ratings of mild or one rating of moderate on Psychosis items of PANSS.

**Exclusion criteria:**
- Known or suspected organic brain disorder
- Substance use disorder in the past 3 months
- A conceptual disorganisation rating on the PANSS of moderate or higher
- Previous exposure to the study treatments.

**Total sample size:** No. randomised - 30

**Total sample size:** ITT population - 28

**Gender:** % female 43%

**Age:** Mean - 40.4 (11.96)

**Ethnicity:** White 68%
Hispanic 4%
Black 29%

**Setting:** Outpatient

**History:** Mean years of illness: 18 (13.1)

**Baseline stats:**
Average for the whole sample:
PANSS total: 51.1 (12.6)
PSYRATS-total: 33.3 (13.7)
Auditory hallucinations: 85.7%
SFS: 118.5 (21.5)

**Notes about participants:** Medication: Olanzapine doses ranged from 5 to 40mg with a mean daily dose of 19.7 (8.6) mg. 33% of participants were taking another antipsychotic in addition to olanzapine.

**Interventions**

**Intervention - group 1.:** Functional CBT: 16 weekly sessions; n=15

**Intervention - group 2.:** Psychoeducation; n=13

**Notes about the interventions:**
Functional CBT
Comprises several modules: education, coping skills, cognitive restructuring, behavioural experiments and goal-setting (including those

typically used in current CBT interventions). Patients are taught skills for managing persistent positive symptoms that interfere with accomplishing certain activities or goals. For example, rather than discussing hallucinations or delusions as 'real' or 'unreal', fCBT focuses on whether psychotic symptoms and responses to these symptoms block attainment of specific goals. This approach helps ensure that therapists always have a context for challenging maladaptive responses to symptoms.

Psychoeducation
Team Solutions is a psychoeducational intervention developed and sponsored by Eli Lilly & Co. to teach patients about schizophrenia and the principles of its management, with the aim of promoting reintegration. The programme is not medication-specific and includes a video, patient workbook and instructor's manual and was delivered in an individual format. The programme is organised into 10 modules including, promoting understanding of the illness and of symptoms of schizophrenia, identifying members of the treatment team and their roles, learning about medication and side effects, preventing relapse, and coping with symptoms.

Training
Treatment was delivered by nine therapists with an average of 7.8 years (SD=4.77) of experience conducting CBT. Weekly supervision meetings were held to discuss cases and ensure protocol adherence.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS, PSYRATS - total score

**Mental state (e.g. BPRS, PANSS, BDI):** Clinically significant response in mental state - Clinically significant improvement defined as 20% reduction in PANSS Positive subscale

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SFS - but may need to look at change scores as two groups were different at baseline.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

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|---|---|
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed |
| | **2.1 How well was the study done to minimise bias?:** + |
| **Study ID** | **CHABANNES2008** |
| **General info** | **Funding source:** Not mentioned but Soleduc is a registered psychoeducation programme of Sanofi-Aventis - same drug company for amisulpride (all participants were on amisulpride) |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - All included participants |
| | **Blindness:** Open |
| | **Duration:** No. weeks of treatment - 52 weeks (although intervention was only delivered at 3 time points, baseline, 6 and 12 months - 7 sessions each time) |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Multi-centre - 51 sites in France |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Each participating centre received a randomisation list with the order of patient assignment - no further details reported. |
| **Participants** | **Diagnosis:** Other schizophrenia related [%] % not reported |
| | **Diagnosis:** Schizophrenia [% of sample] % not reported |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia spectrum disorder |
| | **Exclusion criteria:**<br>- Patients hospitalised for >120 days in previous year<br>- requiring other antipsychotics apart from amisulpride |
| | **Total sample size:** No. randomised - 220 |
| | **Total sample size:** ITT population - 220 |
| | **Gender:** % female 38% |
| | **Age:** Mean - 33 |
| | **Ethnicity:** Not reported |

**History:**
[Psychoeducation / control]
Mean duration of schizophrenia, months: 97.8 / 111.3
Previous hospitalisations: 4.7 / 5.9

**Baseline stats:**
[Psychoeducation / control]
PANSS positive: 16.6(6.0) / 17.6(7.2)
PANSS negative: 22.3(7.1) / 21.2(7.1)

**Notes about participants:**
[Psychoeducation / Control]
Substance misuse (%)
Smokers: 71.2 / 71.6
Alcohol: 6.3 / 5.5

**Interventions**

**Intervention - group 1.:** Psychoeducation, 7 sessions 3 times during intervention period (baseline, 6 months and 12 months; N = 111

**Intervention - group 2.:** Control (psychosocial group training), 7 sessions at 3 time points (baseline, 6 months and 12 months; N = 109

**Notes about the interventions:**
All participants were on amisulpride 50-800mg/day

Psychoeducation
Soleduc programme which comprises 8 specific modules delivered via video cassette:
- The disease and its evolution
- Patient responsibility for treatment compliance
- Antipsychotic treatment
- Psychotherapeutic treatment
- Methods of care and specialised follow-up
- Reintegration
- Psychosocial rehabilitation

Control
Psychosocial training group in which patients were orally informed about schizophrenia and its treatment according to the standards of each centre.

Training
The Soleduc modules were delivered by nurse staff under the supervision of a psychiatrist.

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|---|---|
| **Outcomes** | **Global state & service outcomes (e.g. CGI):** Re-hospitalisation |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - Data not presented in a usable form |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not reported adequately - No mention of allocation concealment in the randomisation list |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed - Differences in severity of illness |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Poorly addressed - No usable data presented for symptoms and functioning |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **CHAN2007A** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer - Analysis of post-treatment and follow-up appears to include all randomised participants. |
| | **Blindness:** No mention |
| | **Duration:** Length of follow-up - 12 months |
| | **Duration:** No. weeks of treatment - 2 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - acute psychiatric unit, Hong Kong, China |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |

**Participants**

**Diagnosis:** Schizophrenia [% of sample] % not reported

**Diagnosis:** Other schizophrenia related [%] schizoaffective disorder - % not reported

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- diagnosis of schizophrenia or schizoaffective disorder with DSM-IV criteria
- stable mental condition after admission to the acute unit
- primary education level or above
- participated in either the TRIP or WOT programmes voluntarily

**Exclusion criteria:**
- comorbid diagnosis of substance misuse, organic brain syndromes or mental retardation

**Total sample size:** No. randomised - 81

**Gender:** % female 0%

**Age:** Range - 18-63

**Age:** Mean - 35.82

**Ethnicity:** Not reported

**Setting:** Inpatient

**History:**
[TRIP / WOT]
No. of previous admissions, %:
0-2: 57.9 / 62.9
3-5: 26.3 / 18.5
6-8: 5.3 / 7.4
10 or above: 10.5 / 11.1

**Baseline stats:** baseline symptom measures not reported

**Interventions**

**Intervention - group 1.:** TRIP, 10 50-minute sessions over 2 weeks; n=44

**Intervention - group 2.:** WOT, n=37

**Notes about the interventions:**
Transforming Relapse and Instilling Prosperity (TRIP)
A ward-based illness management programme which comprises the notions of relapse reduction and health promotion. It utilises strategies from illness management as described in the literature. The 10 sessions can be categorised into two themes, illness orientation and health orientation. The sessions follow a semi-structured format of didactic presentation of topics followed by open discussion.

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|---|---|
| | Ward occupational therapy (WOT)<br>WOT is based on the activities health approach that aims to maintain activities during hospitalisation by providing normal routine selected by the patient from a typical array of work, rest and leisure activities. |
| **Outcomes** | **Global state & service outcomes (e.g. CGI):** Re-hospitalisation - Relapse was defined as the number of re-hospitalisations |
| | **Other:** Medical outcomes study SF-36; SUMD |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?: +** |
| **Study ID** | **LITTRELL2003** |
| **General info** | **Funding source:** Pharmaceutical industry |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Open |
| | **Duration:** Length of follow-up - 2 months |
| | **Duration:** No. weeks of treatment - 16 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Multi-centre - Referrals came from local community health centres and private practice psychiatrists, US |
| | **Number of people screened, excluded & reasons:** Not reported |

**Notes about study methods:** Randomisation procedure not reported

**Participants** **Diagnosis:** Schizophrenia [% of sample] 77%

**Diagnosis:** Other schizophrenia related [%] 23%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- aged 18+
- DSM-IV diagnosis of schizophrenia or schizoaffective disorder
- taking conventional antipsychotics >=3 months immediately before study
- compliant with antipsychotic drug treatment as prescribed

**Total sample size:** No. randomised 70

**Gender:** % female 39%

**Age:** Mean 34

**Ethnicity:** Caucasian - 74%
African American - 26%

Analysis looked at sex and race differences in weight gain.

**Setting:** Outpatient

**History:**
[Psychoeducation / TAU]
Age of onset: 19.31(3.06) / 20.91(3.86)

**Notes about participants:** The most commonly prescribed conventional antipsychotic was haloperidol (39%), and 13% of the sample were taking decanoate formulations.

**Interventions** **Intervention - group 1.:** Psychoeducation, 16 weekly 1 hour sessions; n=35

**Intervention - group 2.:** TAU; n=35

**Notes about the interventions:**
All participants began treatment with olanzapine at study entry with use of a stepped initiation conversion process. Olanzapine dosage (range 5-20mg/day) was adjusted as needed based on the patients' responses and side effects. Concomitant medications for residual and breakthrough symptoms were allowed at the clinician's discretion and included lithium (n=6), valporate (n=3) and SSRIs (n=13). No pharmacological interventions for weight gain were permitted.

Psychoeducation
- Intervention group attended a psychoeducation class using the "Solutions of Wellness" modules. The programme is not specific to

medications and it is formulated specifically for use with people with schizophrenia.
- Consists of two written modules: "Nutrition, Wellness, and Living a Healthy Lifestyle" and "Fitness and Exercise".
-The classes included different formats such as individual work, dyads, small and large group work.
- Patient participation included reading aloud, discussing tropics in groups, completing written exercises, taking quizzes and playing educational games.

**Outcomes** **Other:** Weight Gain; Weight Change; BMI; BMI change

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not reported adequately

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** +

**Study ID** **SHIN2002**

**General info** **Funding source:** Not mentioned

**Published or unpublished data?:** Published

**Method** **Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Blindness:** Only raters blind

**Duration:** No. weeks of treatment - 10

**Raters:** Independent of treatment

**Design:** Single-centre - US

**Number of people screened, excluded & reasons:** Participants were recruited from a pool of 110 Korean patients with chronic mental illness.
-65 patients met diagnostic criteria for study entry.
-48 consented to participate.

**Notes about study methods:** Randomisation procedure not reported

**Participants** **Diagnosis:** Schizophrenia [% of sample] not reported

**Diagnosis:** Other schizophrenia related [%] % with schizoaffective disorder and schizophreniform disorder not reported

**Diagnostic tool:** DSM-IV

**Inclusion criteria:** - Any patient with a diagnosis of schizophrenia, schizoaffective disorder, or schizophreniform disorder

**Total sample size:** No. randomised - 48

**Gender:** % female 58%

**Age:** Mean - 37

**Age:** Range - 22-53

**Ethnicity:** all participants were Korean-American

**Setting:** Outpatient

**History:**
[Experimental group / control group]
Number of hospitalisations: 2.71(1.76) / 1.21(1.18)
Time since last hospitalisation, months: 7.17(6.43) / 12.67(19.30)

**Baseline stats:**
[Experimental / Control]
BPRS total: 91.88(9.76) / 91.83(6.70)
Stigma-Devaluation Scale: 18.54(2.40) / 20.21(2.43)
Family Crisis Oriented Personal Evaluation Scale
total: 80.92(8.22) / 81.02(6.88)

**Notes about participants:**
[Experimental / Control]
Years in US: 14.25(3.00) / 15.08(4.38)
Living arrangement, n(%):
Living away from family: 7(29.2) / 4(16.7)
Living with family: 17(70.8) / 20(83.3)

**Interventions** **Intervention - group 1.:** Experimental group - psychoeducational group; n=24

**Intervention - group 2.:** Control; n=24

**Notes about the interventions**
TAU - Control
The control group received 10 Individual supportive therapy (IST) sessions, each 45 minutes in duration. All of the sessions were conducted in Korean.

Psychoeducation:
In addition to TAU at the clinic (IST), treatment included 10 weekly psychoeducational group sessions each 90 minutes long. Each session included a variety of educational techniques designed to enhance the participants' learning and to maintain their attention. The curriculum included modules on definitions of illness, medications and side effects, relapse prevention, crisis and illness management, stigma, communication and stress management skills, self-help, and community resources. In addition traditional disease concepts were integrated.

To reinforce the interventions, parallel sessions, also conducted in Korean, were offered to family members of all participants.

**Outcomes**

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS

**Other:** Stigma-Devaluation Scale; Family Crisis Oriented Personal Evaluation Scale.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not reported adequately

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

**Study ID**

**SIBITZ2007**

**General info**

**Funding source:** Not mentioned

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT - all patients allocated to the booster condition who attended at least one booster session and all patients allocated to the non-booster session were included in the analysis.

However patients who had no existent follow-up data and patients who had missing values on any of the covariates used were not included.

**Blindness:** No mention

**Duration:** No. weeks of treatment - All participants underwent a 9-week psychoeducation programme. Completers of this programme were then randomised to receive booster sessions over 36 weeks.

**Duration:** Length of follow-up - 12 months (including the 9 months where participants were having monthly booster sessions)

**Raters:** Not stated to be independent of treatment

**Design:** Multi-centre - outpatient centres in Vienna, Austria

**Number of people screened, excluded & reasons:** 172 referred by psychiatrists, of these 16 DNA, 8 failed to met study criteria, 7 refused to participate and 10 DNA any psychoeducation sessions.

Of the 131 participants who attended at least one session of psychoeducation, 103 went on to attend 5 or more sessions. These were classified as completers and were subsequently randomised into either booster or non-booster conditions.

**Notes about study methods:** block-randomisation at the end of the 9-week psychoeducation programme

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 70%

**Diagnosis:** Other schizophrenia related [%] schizoaffective disorder - 30%

**Diagnostic tool:** ICD-10

**Inclusion criteria:**
- ICD-10 diagnosis of schizophrenia or schizoaffective disorder
- aged 19-65
- considered sufficiently motivated and stable to be able to benefit from the programme to be entered into the booster stage
- completed at least 5 sessions in the 9-week programme.

**Total sample size:** No. randomised - 103

**Total sample size:** ITT population - 87

**Gender:** % female 54%

**Age:** Mean 36

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
[Booster / Non-booster]
Age at onset of illness: 23.4(6.3) / 25.7(7.4)
Years of illness: 12.5(8.7) / 11.0(9.0)

**Baseline stats:**
[Booster / non-booster]
PANSS total: 72.7(14.2) / 74.6(12.7)
SDSS: 56.9(13.9) / 57.9(13.0)

**Notes about participants:**
[Booster / Non-booster]
Ongoing treatment in the community, n(%)
psychotherapy: 25(52.1) / 19(34.5)
antipsychotic medication: 45(93.8) / 49(94.2)

**Interventions**

**Intervention - group 1.:** Booster, 9 monthly sessions; n=48

**Intervention - group 2.:** Non-booster (TAU); n=55

**Notes about the interventions:**
Psychoeducation programme
Prior to randomisation participants underwent 9 weekly 75 minute meetings. The following four illness-related topics were covered: concept of illness, symptoms and early warning signs, medication and illness related stigma. In addition the following QoL topics dealt with: improving well-being, how to make friends, how to actively plan and manage everyday life and how to create a more pleasant environment.

Booster sessions
Consisted of an extension programme of monthly meetings for 9 months. The booster sessions were based on the original manual and conducted in order to systematically repeat and discuss topics which the patients were familiar with from participating in the original seminar in more detail. At the request of participants, a few new topics (for example, how to manage aggression and problems with partners) were incorporated.

Non-booster
Participants received TAU

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SDSS

**Satisfaction with treatment:** Service user satisfaction - DAI

**Quality of Life:** Average score/change in quality of life – Quality of Life Index

**Other:** Illness concept scale; questionnaire of competence and control; knowledge questionnaire; health locus of control

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not addressed

**2.1 How well was the study done to minimise bias?:** +

**Study ID**

**VREELAND2006**

**General info**

**Funding source:** Pharmaceutical industry

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** ITT - The repeated measures used in the analysis were the participants' scores on any given variable at each testing session (baseline, midpoint, and endpoint).

**Blindness:** Single-blind

**Duration:** No. weeks of treatment - 24

**Raters:** Independent of treatment

**Design:** Single-centre - US

**Number of people screened, excluded & reasons:** 74 participants initially volunteered but 3 were not included in the final analysis because of missing data at time point 1.

**Notes about study methods:** Randomisation was based on a table of random numbers.

**Participants**

**Diagnosis:** Other schizophrenia related [%] schizoaffective disorder - % not reported

**Diagnosis:** Schizophrenia [% of sample] % not reported

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- partial hospitalisation clients who met DSM-IV criteria for schizophrenia or schizoaffective disorder.
- attended the partial hospitalisation programme at least 2 days per week.

**Exclusion criteria:**
- clinical records indicating presence of comorbid diagnosis of dementia or mental retardation.
- evidence of severely impaired mental function on Shipley Institute of Living Scale
- unable or unwilling to give informed consent
- Had previously been exposed to more than one Team Solutions workbook
- evidence of significant risk of suicide

**Total sample size:** No. randomised - 74

**Total sample size:** ITT population - unclear

**Gender:** % female 56%

**Age:** Range 22-64

**Ethnicity:** Hispanic - 9%
African American - 32%
European American - 56%
Other or no data - 3%

**Setting:** Inpatient

**History:** No details about disorder history, medication, onset etc. reported

**Baseline stats:**
[Team Solution / Control]
KASQ: 14.5(5.0) / 15.8(4.9)
TSCKAS: 11.9(3.2) / 12.2(2.7)
GAF-DIS: 47.4(10.7) / 48.8(13.8)
CGI: 4.6(0.7) / 4.5(0.8)
PANSS General: 33.5(8.7) / 33.6(8.2)
PGWB: 69.8(21.4) / 69.5(18.1)
IAPSRS: 3.0(0.4) / 2.8(0.1)

**Interventions** **Intervention - group 1.:** Team Solutions; n=40

**Intervention - group 2.:** Control; n=34

**Notes about the interventions:**
TAU
All participants were attending the partial hospitalisation programme for at least 2 days per week. The programme offered psychosocial treatment including participation in prevocational work areas, goal-orientated recreational groups, social skills training, and psycho-educational groups on topics such as medication education, stress management, physical health issues, nutrition and exercise, and independent living.

Team Solutions.
In addition to TAU the experimental group also took part in Team Solutions groups. Groups met twice each day, 2 days per week for 24 weeks. There were three 8-week sessions, with two workbooks being covered in each session. Team Solutions is designed to education patients about their illness and how to manage it. Topics include understanding the symptoms of mental illness, why and how psychiatric medications work and are an important part of treatment, relapse prevention and coping strategies, and how to avoid crises.

**Outcomes** **Global state & service outcomes (e.g. CGI):** Average score/change in global state - CGI; GAF-DIS

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**Engagement with services (e.g. SES):** Average score/change in engagement with services- TCI; ROMI; IAPSRS Toolkit

**Satisfaction with treatment:** Service user satisfaction – Recovery Attitudes Questionnaire (RAQ)

**Quality of Life:** Average score/change in quality of life - PGWB

**Other:** KASQ; Team Solutions Comprehensive Knowledge Assessment Scale (TSCKAS); Scale to Assess Unawareness of Mental Disorder (SUMD)

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis).**

**:** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| **Study ID** | **XIANG2006** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT - Applied to missing outcome variables, however 5 participants who dropped out were completely excluded from analysis. |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 8 |
| | **Duration:** Length of follow-up - 24 weeks post-treatment |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Community in Beijing, China |
| | **Number of people screened, excluded & reasons:** 4,500 patients with schizophrenia on clinic register, 150 randomly selected and approached, 96 met criteria and randomised |
| | **Notes about study methods:** Randomisation by computer-generated numbers tables |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100 |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV schizophrenia diagnosis<br>- Age 18-60<br>- Chinese literate<br>- Clinically stable for >=3 months prior to entry, as defined by PANSS items P2, P3, P5 and P9 sum <=10 with no single item <=4<br>- At least one family member cohabiting with patient<br>- Willing and able to provide informed consent. |
| | **Exclusion criteria:**<br>- Acute medical or neurological conditions<br>- History of substance misuse other than nicotine. |

**Total sample size:** ITT population - 91

**Total sample size:** No. randomised - 96

**Gender:** % female 51%

**Age:** Mean - 39

**Ethnicity:** Details not reported

**Setting:** Outpatient

**History:**
[CRM Group / SC Group]
Number of admissions: 2.33(2.39) / 2.04(2.31)
Age at onset: 22.57(6.17) / 25.50(9.10)
Duration of illness, years: 14.80(8.43) / 14.52(9.91)

**Baseline stats:**
[CRM group / SC group]
PANSS positive: 9.7(4.1) / 9.6(3.6)
PANSS negative: 12.9(4.3) / 14.2(5.0)
PANSS general: 24.9(5.4) / 25.4(5.6)
SDSS: 5.82(2.3) / 6.8(3.1)

**Notes about participants:**
[CRM Group / SC Group]
Daily dose in chlorpromazine equivalents, mg: 421.11(192.61) / 459.37(180.32)

**Interventions**

**Intervention - group 1.:** Community re-entry module, 16x twice weekly 1-hour sessions; n=48

**Intervention - group 2.:** Supportive counselling, 16x twice-weekly 1-hour sessions; n=48

**Notes about the interventions:**
Community re-entry module (CRM)
One of the Social and Independent Living Skills Modules developed by the Intervention Research Center for Major Mental Illness at the University of California. Each group session involved 6-8 patients, focusing on education on medications and symptoms, assessment and planning for discharge and re-entry into community, monitoring signs of relapse and developing emergency plan. Materials including handouts, workbooks, video tapes, homework assignments etc. were used.

Supportive counselling (SC)
Developed by Chaoyang Mental Health Care Center based on the psychosocial intervention model, consisting of group-based semi-structured counselling discussing particular topics, including symptoms and prognosis, medication, long-term management, relapse monitoring and

| | |
|---|---|
| | prevention. General psychoeducation was also offered. Basic counselling techniques included listening, facilitation and mirroring. |
| **Outcomes** | **Global state & service outcomes (e.g. CGI):** Relapse defined as 1) hospitalisation (for at least 36 hours due to exacerbation of psychotic symptoms), 2) attempted suicide, or 3) having deteriorated on the four PANSS psychosis items (one item rated as 6 or 7, or two items rated as 5 or more). |
| | **Global state & service outcomes (e.g. CGI):** Re-hospitalisation |
| | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS |
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SDSS |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Well covered |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |

| | |
|---|---|
| **Study ID** | **XIANG2007** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** All analyses were conducted on an ITT basis |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 24 months |
| | **Duration:** No. weeks of treatment - 4 |

**Raters:** Independent of treatment

**Design:** Single-centre - Chaoyang Mental Health Care Institute, China

**Number of people screened, excluded & reasons:** 483 inpatients were assessed for eligibility: 45 refused to participate, 335 were excluded for not meeting the study criteria for the following reasons (n): age beyond range (57), not clinically stable (183), no plan to discharge (67), other reasons (28). 103 participants were randomly allocated.

**Notes about study methods:** Randomisation procedure not reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- inpatients with a diagnosis of schizophrenia according to the DSM-IV
- aged 18-60
- clinically stable for 1 month before recruitment and about to begin their pre-discharge home leave (routine in this area). Clinical stability defined as sum of the four psychotic symptoms of the PANSS <=10 with none of the items scoring 4+
- admission was voluntary
- at least 1 family member would be cohabiting with the patient after discharge
- no employment immediately after discharge

**Exclusion criteria:**
- presence of ongoing acute medical or neurological conditions
- current or history of drugs and substance misuse other than nicotine.

**Total sample size:** No. randomised - 103

**Total sample size:** ITT population - 94 completed the research interview over the 25 month follow-up period.

**Gender:** % female 53%

**Age:** Mean 38.6

**Ethnicity:** Details not reported

**Setting:** Inpatient

**History:**
[CRM / group psychoeducation]
Duration of illness, years: 15.26(9.13) / 15.60(9.96)
Age at onset: 22.09(6.60) / 24.16(8.45)
Number of admissions: 2.18(2.25) / 1.86(1.82)

**Baseline stats:**
[CRM / Group psychoeducation]

PANSS positive: 8.58(3.88) / 8.86(3.39)
PANSS negative: 12.06(4.85) / 12.30(5.19)
PANSS general: 21.08(5.16) / 21.37(5.55)

**Notes about participants:**
[CRM / Group psychoeducation]
Daily antipsychotic dose, chlorpromazine equivalents, mg: 435(199) / 446(193)

**Interventions**

**Intervention - group 1.:** Community Re-Entry Module (CRM), 16 x 1 hour sessions (4 sessions per week); n=53

**Intervention - group 2.:** Group psychoeducation: 16 x 1 hour sessions, (4 sessions per week); n=50

**Notes about the interventions:**
Community re-entry module (CRM)
One of the Social and Independent Living Skills Modules developed by the Intervention Research Center for Major Mental Illness at the University of California. Each group session involved 6-8 patients, focusing on education on medications and symptoms, assessment and planning for discharge and re-entry into community, monitoring signs of relapse and developing emergency plan. Materials including handouts, workbooks, video tapes, homework assignments etc. were used.

Group psychoeducation
Participants randomised to this group received an equally intensive programme of group psychoeducation, a standard psychosocial intervention in many parts of China. Participants were placed into subgroups of 6-8 members.

The opportunity to attend quarterly, community-based workshops following discharge was offered to both study groups as part of a routine intervention to reinforce the use in the community of skills acquired during admission. Family members in both groups were encouraged to participant in these workshops, which were 4 hours long and delivered by mental health workers.

Training
Two experienced psychiatric nurses were responsible for delivery of both intervention (one nurse CRM, one psychoeducation). Both received a week's training to familiarise themselves with the interventions.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation - a stay of at least 36 hours as a results of exacerbation of psychiatric symptoms.

**Global state & service outcomes (e.g. CGI):** Relapse - if patient was admitted to hospital, attempted suicide, or deteriorated with >=1 of the 4 psychotic items of the PANSS rated as >=6 or >=2 items rated <=5

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - SDSS

**Other:** ITAQ

Re-employment - defined as >=3 consecutive months of salaried employment.

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Adequately addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

**References of included studies (update)**

**BECHDOLF2004**

*Bechdolf,A.; Knost,B.; Kuntermann,C.; Schiller,S.; Klosterktter,J.; Hambrecht,M.; Pukrop,R. (2004) A randomized comparison of group cognitive-behavioural therapy and group psychoeducation in patients with schizophrenia. *Acta Psychiatrica Scandinavica* 110: 21 - 28.

Bechdolf,A.; Kohn,D.; Knost,B.; Pukrop,R.; Klosterkotter,J. (2005) A randomized comparison of group cognitive-behavioural therapy and group psychoeducation in acute patients with schizophrenia: outcome at 24 months. *Acta Psychiatrica Scandinavica* 112(3): 173 - 179.

**CATHER2005**

Cather,C.; Penn,D.; Otto,M.W.; Yovel,I.; Mueser,K.T.; Goff,D.C. (2005) A pilot study of functional Cognitive Behavioral Therapy (fCBT) for schizophrenia. *Schizophrenia Research* 74: 201 - 209.

**CHABANNES2008**

Chabannes,J.P.; Bazin,N.; Leguay,D.; Nuss,P.; Peretti,C.S.; Tatu,P.; Hameg,A.; Garay,R.P.; Ferreri,M. (2008) Two-year study of relapse prevention by a new education program in schizophrenic patients treated with the same antipsychotic drug. *European Psychiatry: the Journal of the Association of European Psychiatrists* 23: 8 - 13.

**CHAN2007A**

Chan,S.H.; Lee,S.W.; Chan,I.W. (2007) TRIP: a psycho-educational programme in Hong Kong for people with schizophrenia. *Occupational Therapy International.* 14(2): 86 - 98.

**LITTRELL2003**

Littrell,K.H.; Hilligoss,N.M.; Kirshner,C.D.; Petty,R.G.; Johnson,C.G. (2003) The effects of an educational intervention on antipsychotic-induced weight gain. *Journal of Nursing Scholarship* 35(3): 237 - 241.

**SHIN2002**

Shin,S.K.; Lukens,E.P. (2002) Effects of psychoeducation for Korean Americans with chronic mental illness. *Psychiatric Services*; 53(9): 1125 - 1131.

**SIBITZ2007**

Sibitz,I.; Amering,M.; Gossler,R.; Unger,A.; Katschnig,H. (2007) One-year outcome of low-intensity booster sessions versus care as usual in psychosis patients after a short-term psychoeducational intervention. *European Psychiatry: the Journal of the Association of European Psychiatrists*. 22(4): 203 - 210.

**VREELAND2006**

Vreeland,B.; Minsky,S.; Yanos,P.T.; Menza,M.; Gara,M.; Kim,E.; Toto,A.M.; Allen,L. (2006) Efficacy of the team solutions program for educating patients about illness management and treatment. *Psychiatric Services*; 57(6): 822 - 828.

**XIANG2006**

Xiang,Y.; Weng,Y.; Li,W.; Gao,L.; Chen,G.; Xie,L.; Chang,Y.; Tang,W.K.; Ungvari,G.S. (2006) Training patients with schizophrenia with the community re-entry module: a controlled study. *Social Psychiatry and Psychiatric Epidemiology* 41(6): 464 - 469.

**XIANG2007**

Xiang,Y.T.; Weng,Y.Z.; Li,W.Y.; Gao,L.; Chen,G.L.; Xie,L.; Chang,Y.L.; Tang,W.K.; Ungvari,G.S. (2007) Efficacy of the Community Re-Entry Module for patients with schizophrenia in Beijing, China: outcome at 2-year follow-up. *British Journal of Psychiatry*. 190: 49 - 56.

**Characteristics of excluded studies (update)**

**AGUGLIA2007**

**Reason for exclusion:** Participants not randomised

**Bechdolf 2002**

**Reason for exclusion:** Conference abstract

**GRAEBER2003**

**Reason for exclusion:** Co-morbid

**References of excluded studies (update)**

Aguglia, E., Pascolo-Fabrici, E., Bertossi, F., & Bassi, M. (2007) Psychoeducational intervention and prevention of relapse among schizophrenic disorders in the Italian community psychiatric network. *Clinical Practice and Epidemiology in Mental Health* 3: 7.

Bechdolf,A.; Knost,B.; Kuntermann,C.; Schiller,S.; Hambrecht,M.; Klosterkotter,J.; Pukrop,R. (2002) Coping-oriented versus psychoeducational group therapy for post acute patients with schizophrenia: results of a 6 month follow-up. *Schizophrenia Research* 53: 264 - 265.

Graeber,D.A.; Moyers,T.B.; Griffith,G.; Guajardo,E.; Tonigan,S. (2003) Addictions services. A pilot study comparing motivational interviewing and an educational intervention in patients with schizophrenia and alcohol use disorders. *Community Mental Health Journal*. 39(3): 189 - 202.

## Social skills training

| Author | 1. Review type<br>2. Funding<br>3. Period covered<br>4. Data analysis<br>5. No. of studies<br>6. No. randomised | Interventions | Reported Outcomes |
|---|---|---|---|
| Pilling S, Bebbington P, Kuipers E, Garety P, Geddes J, Martindale B, Orbach G, Morgan C. (2002)<br><br>Psychological treatments in schizophrenia II: meta-analyses of randomized controlled trials of social skills training and cognitive remediation.<br><br>*Psychological Medicine*, 32, 783-791. | 1. Systematic review of RCTs.<br>2. Intramural sources of support to the review: University College London. Extramural sources of support to the review: Department of Health, UK.<br>3. Database origin to 1999<br>4. Meta-analysis of Odds Ratio and Standardised Mean Difference.<br>5. 9 (9 after removing 1 ineligible trial and adding 1 new trial).<br>6. 471 (436). | 1. Social skills training programmes, defined as any structured psychosocial intervention, whether group or individual, aimed at enhancing the social performance and reducing the distress and difficulty in social situations. The key components are: a). a careful behaviourally based assessment of a range of social and interpersonal skills; b) an importance placed on both verbal and non-verbal communication; and c) the individual's ability to (i) perceive and process relevant social cues; and (ii) respond to and provide appropriate social reinforcement.<br><br>This approach has the goal of building up individual behavioural elements into complex behaviours. The aim is to develop more effective social communication. There is | 1. Mental state:<br>a. Relapse/Readmission<br>b. Unable to discharge from hospital<br>c. Number of days in hospital<br>d. Continuous ratings of mental state (BPRS/ SCL-90)<br>2. Compliance:<br>a. Non-compliance with treatment<br>3. Behaviour:<br>a. Harm<br>4. Social functioning:<br>a. Changes in social skills<br>b. Global adjustment<br>c. Social adjustment<br>d. Profile of Adaptation of Life<br>e. Changes in Quality of life<br><br>Outcomes were divided into short term (<6 months), medium term (7-12 months) and long term (> 1 year). |

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| | | considerable emphasis not just on clinic-based interventions (including modelling, role-play and social reinforcement) but also the setting of homework tasks and the generalisability of the treatment.<br><br>Programmes where social skills training was a component part of a more complex rehabilitation intervention are excluded. This includes instances where major components of treatment were token economies, life skills training and other similar milieu-based interventions which may include an element of social skills training in a broader programme.<br><br>2. Control treatment, defined as standard care without a dedicated programme of the type described above. | |
| **Update** | **Reclassified studies:** 1 RCT (Eckmann1992).<br>**Studies previously included, but excluded from update:** 1 RCT (Finch1977).<br>**New studies:** 12 RCTs.<br>**Awaiting assessment:** 1 trial (KERN2005) | | **Notes:**<br>Definition updated |

**Characteristics of included studies (previous guideline)**

| Study | Methods | Participants | Interventions | Outcomes | Notes |
|---|---|---|---|---|---|
| **Bellack1984** | Allocation: random.<br>Blinding: single, raters blind.<br>Duration: 12 weeks, 1 year follow-up.<br>Setting: day hospital programme, Western Psychiatric Institute and Clinic, Pittsburgh, Pennsylvania, US. | Diagnosis: schizophrenia (Feighner criteria). N=64.<br>Age: range 18-58 years, mean 32.7.<br>Sex: 38 M, 16 F.<br>History: mean number of prior hospitalisations 4.9, mean duration of illness 10.8 years. | 1. Social skills training: 3 hours per week, focusing on basic social networking and interpersonal stress reduction, using instruction, modelling, role-play, feedback, home work + day hospital programme. N=44.*<br>2. Day hospital programme alone: group therapies, i.e. current issues, relaxation therapy, group and individual supportive therapy. N=20. | Leaving the study early.<br>Relapse / readmission.<br><br>Unable to use: Hopkins Symptom Checklist (mental state - no SD). Psychiatric Status Schedule (mental state - no SD). Wolpe-Lazarus Assertiveness Test (changes in social skills - no SD). Behavioral Role Play Test (overall social skill - no SD). | Therapists: two therapists "followed a highly structured treatment manual" - no further details about professional background or training provided.<br><br>* Initially two social skills groups that "varied slightly in their application," but as there were no differences in outcomes the trialists amalgamated these data.<br><br>**Allocation concealment B** |
| **Daniels1998** | Allocation: randomised.<br>Blinding: none.<br>Duration: 8 weeks, 16 sessions twice weekly.<br>Setting: outpatients and day patients, Long Island, NY. | Diagnosis: schizophrenia, schizoaffective.<br>N=40*.<br>Age: mean ~33 years, range 19-61.<br>History: mean age of onset ~22 years, SD ~ 9; mean number of hospitalisations ~3, SD ~3. | 1. IBT ("interactive-behavioral training"): group based +standard care. N=20.<br>2. Standard care: including medication. N=20. | 1. Mental state (BPRS, SANS).<br>2. Quality of life (QLS).<br>3. Global state (CGI, GAF).<br>4. Social functioning (Behavioral Assessment Task - BAT). | * "Six of the 40 participants did not complete the study and were therefore excluded from the... analysis." However, number of dropouts not given separately for treatment conditions. N=20 used for each group in Cochrane Analysis (Cormac et al.).<br><br>**Allocation concealment B** |

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| **Dobson1995** | Allocation: randomised - no further details.<br>Blinding: not specified, but assessments were not completed by group therapists, and treatments were not led by the investigators.<br>Duration: 9 week treatment, follow-up at 6 months and 1 year after end of treatment.<br>Setting: day hospital programme, Foothills Hospital, Calgary, Alberta, Canada. | Diagnosis: schizophrenia (Structured Clinical Interview for DSM-III-R). N=33.<br>Age: treatment group mean 33.73 (SD 8.92), control group mean 35.69 (SD 7.23).<br>Sex: 16 M, 12 F (excluding 5 drop-outs, as sex is not specified).<br>History: months of previous hospitalisation - treatment group mean 10 (SD 13.4), control group mean 15.5 (SD 27.35).<br>Exclusions: if subjects received social skills training in the 2 years before assessment, if organicity or alcohol or drug addiction was noted on hospital chart, or if they had received electroconvulsive therapy within the previous 6 months. | 1. Social skills training: four 1-hour sessions per week of communication skills, assertiveness training, using instruction, role-play, modelling, feedback, homework. N=18.<br>2. Social milieu: structured activities including supportive discussion groups, exercise groups, and activity groups. N=15. | Leaving the study early.<br>Relapse / readmission.<br>Length of stay in hospital.<br>Unable to use:<br>Medication dosages (no usable data).<br>PANSS (mental state - no usable data). | Therapists: experienced nurse therapists and one predoctoral psychology intern.<br><br>**Allocation concealment B** |
| **Finch & Wallace1977** | Allocation: randomised - no further details.<br>Blinding: raters blind.<br>Duration: 4 weeks.<br>Setting: inpatient treatment ward, Sepulveda Veterans Administration Medical Center, California, US. | Diagnosis: schizophrenia (DSM-III). N=16.<br>Sex: all males.<br>Age: range 21-40, mean 29.<br>History: mean length of past admission ~3 years. | 1. Social skills training: three 1-hour sessions per week of discussing difficult interpersonal situations, using modelling, role-play, feedback, homework. N=8.<br>2. Standard care. N=8. | Unable to be discharged.<br>Unable to use:<br>Wolpe-Lazarus Assertiveness Test (changes in social skills - no SD).<br>Employment (reported on experimental subjects only). | Therapists: two advanced clinical psychology graduate students (male and female).<br><br>**Allocation concealment B** |

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|---|---|---|---|---|---|
| **Hayes1995** | Allocation: random.<br>Blinding: raters blind.<br>Duration: 18 weeks, plus 9 booster sessions over a 6 month follow-up.<br>Setting: range of mental health services, Queensland, Australia. | Diagnosis: schizophrenia (DSM-III-R). N=63*.<br>Age: mean 36 (SD=10).<br>Sex: 47 M, 16 F.<br>History: mean duration of illness 11 years (SD 10), not currently experiencing psychotic symptoms (assessed on BPRS), presence of residual impairment (score of less than or equal to 60 on GAS, clinical judgment of social skills deficit based on a review of videotaped Simulated Social Interaction Test). | 1. Social skills: two 75-minute sessions per week (36 sessions altogether) emphasising interpersonal skills, social problem solving, positive time use skills. Using instructions, modelling, rehearsal, feedback, homework. N=32*.<br>2. Discussion group: focused on topics of interpersonal relations and purposeful use of time, promoting self disclosure. N=32*. | BPRS (mental state).<br>GAS (global adjustment).<br><br>SCON (conversational social skill).<br>Unable to use:<br>Relapse (data not presented separately for experimental groups).<br>Leaving the study early (same as above).<br>SSIT anxiety and skill scores (social skill), SSQ (social skill), APES (social engagement/participation), QLS (quality of life), SANS (mental state), use of free time (community functioning). | Therapists: two masters-level clinical psychologists, two occupational therapists, two social workers, one registered psychiatric nurse.<br>Training: all therapists received a comprehensive written treatment manual for their respective treatment condition, which they read in conjunction with 10 hours of training in treatment administration.<br>Supervision: all treatment sessions were videotaped and monitored by the investigators in weekly supervision sessions.<br>*Although the total number of participants (N=63) was provided in the study, the exact number randomly assigned to each treatment condition was not provided. Hence, the conservative estimate of n=32 was made for each of the two treatment groups.<br><br>**Allocation concealment B** |

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| **Liberman1998** | Allocation: random.<br>Blinding: medication prescribers blind to treatment allocation.<br>Duration: 6 months, 18 months follow-up after end of treatment.<br>Setting: outpatients, West Los Angeles Veterans Administration Medical Center, California, US. | Diagnosis: schizophrenia (persistent and unremitting form - no further information given).<br>N=84.<br>Age: mean 37.1 (SD 8.8).<br>Sex: all males.<br>History: mean duration of illness 14.8 years (SD 8.0). | 1. Social skills training: 12 hours weekly (3 hours daily, 4 days per week), involving basic conversation, recreation for leisure, medication and symptom management.<br>N=42.<br>2. Occupational therapy training: expressive, artistic and recreational activities.<br>N=42. | Leaving the study early. LQLS (quality of life).<br>Profile of Adaptation to Life: efficacy.<br>*Changes in scores rather than raw scores reported in all outcomes.<br>Unable to use: Independent Living Skills Survey.<br>Rosenberg Self-Esteem Scale.<br>BPRS.<br>GAS.<br>(None of the above could be used because standard deviations were more than half of the means). | Therapists for treatment group: occupational therapist and three paraprofessionals<br>Therapists for control group: three occupational therapists.<br>Supervision: faithfulness of the module leaders to the procedures in the trainer's manuals were rated weekly by their supervisor through use of observational checklist.<br><br>**Allocation concealment B** |

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|---|---|---|---|---|---|
| **Lukoff1986** | Allocation: random<br>Blinding: raters (psychiatrists) blind.<br>Duration: 10 weeks, 2 year follow-up after end of treatment.<br>Setting: inpatient units, California, US. | Diagnosis: schizophrenia (DSM-III and CATEGO Class S Criteria, elicited by Present State Examination).<br>N=28.<br>Age: unavailable.<br>Sex: all males.<br>History: unavailable. | 1. Social skills + token economy: daily morning sessions, twice-weekly afternoon sessions of role play exercises, assertive behaviour, anger control, problem solving + weekly behavioural family therapy session. N=14<br>2. Holistic health programme + token economy: 30-minute exercise in the morning, yoga, meditation, stress education, mobilising positive belief sessions, building self-esteem sessions. N=14. | Leaving the study early. Relapse / readmission.<br>SCL-90 (mental state).<br>NGI (global adjustment).<br>Unable to use: Psychiatric Assessment Scale (PAS). Tennessee Self-Concept Test (TSC). | Therapists: two doctoral level psychologists, two master's level psychologists, one recreation therapist, and predoctoral psychology interns.<br><br>**Allocation concealment B** |
| **Marder1996** | Allocation: random.<br>Blinding: none<br>Duration: 2 years.<br>Setting: outpatients, West Los Angeles Veterans Administration Medical Center, California, US. | Diagnosis: schizophrenia (DSM-III-R).<br>N=80.<br>Age: treatment group mean 38.5 (SD 9.0), control group mean 37.9 (SD 8.6).<br>Sex: all males.<br>History: mean duration of illness - treatment group mean 12.5 years (SD 8.9), control group mean 13.4 years (SD 9.0), mean age at onset of illness - treatment group mean 25.5 (SD 5.7), control group mean 24.4 years (SD 4.8). | 1. Social skills training: 90-minute sessions, twice weekly, for first 6 months, then weekly, to compensate for schizophrenic symptoms and cognitive deficits, using cognitive restructuring principles, repeated behavioural rehearsal, video modelling, social reinforcement, homework. N=43.<br>2. Supportive group psychotherapy: encouraging participants to set personal goals and harness group dynamics, explore problems and obstacles. N=37. | Leaving the study early. Relapse / readmission.<br>SAS (social adjustment).<br>Unable to use: exacerbation in symptoms (no usable data). | Therapists: therapy administered by one or two leaders who were doctoral and master's level psychologists, an occupational therapist, and a social science technician. Therapist for control condition was a doctoral-level psychologist.<br><br>**Allocation concealment B** |

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| **Peniston1988** | Allocation: random.<br>Blinding: raters blind.<br>Duration: 9 months.<br>Setting: inpatients in secure psychiatric wards, Fort Lyon Veterans Administration Medical Center, Colorado, US. | Diagnosis: chronic schizophrenia (DSM-III).<br>N=28.<br>Sex: all males.<br>Age: treatment group mean 40.28 (SD 12.80), control group mean 43.71 (SD 14.48).<br>History: high frequency of physical assaults/self injurious behaviour during last 9 months, mean length of present hospitalization 6.07 years. | 1. Group assertive training: twice weekly (72 half-hour sessions altogether), focused on a series of threatening interpersonal situations, using rehearsal, modelling, feedback, and reinforcement. N=14.<br>2. Standard care. N=14. | Leaving the study early. Unable to be discharged.<br>Harm to others.<br>Harm to self.<br>Unable to use:<br>None. | Therapists: experimenter and co-therapist - no further details provided.<br><br>**Allocation concealment B** |

**References of included studies (previous guideline)**

**Bellack 1984 {published data only}**

Bellack AS, Turner SM, Hersen M, Luber RF. (1984) An examination of the efficacy of social skills training for chronic schizophrenic patients. *Hospital and Community Psychiatry*; 35(10):1023-8.

**Daniels 1998 {published data only}**

Daniels L. (1998) A group cognitive-behavioural and process-oriented approach to treating the social impairment and negative symptoms associated with chronic mental illness. *Journal of Psychotherapy Practice and Research*; 7:167-76.

**Dobson 1995 {published data only}**

Dobson DJG, McDougall G, Busheikin J, Aldous J. (1995) Effects of social skills training and social milieu treatment on symptoms of schizophrenia. *Psychiatric Services;* 46(4):376-80.

**Finch & Wallace 1977 {published data only}**

Wallace CJ, Boone SE. (1983) Cognitive factors in the social skills of schizophrenic patients: implications for treatment. *Nebraska Symposium on Motivation*; 31:283-317 (study 2).

**Hayes 1995 {published data only}**

Hayes RL, Halford W, Varghese FT. (1995) Social skills training with chronic schizophrenic patients: effects on negative symptoms and community functioning. *Behavior Therapy*; 26:433-49.

**Liberman 1998 {published data only}**

Liberman RP, Wallace CJ, Blackwell G, Kopelowicz A, Vaccaro VJ, Mintz J. (1998) Skills training versus psychosocial occupational therapy for persons with persistent schizophrenia. *American Journal of Psychiatry*; 155(8):1087-91.

**Lukoff 1986 {published data only}**

Lukoff D, Wallace CJ, Liberman R, Burke K. (1986) A holistic program for chronic schizophrenic patients. *Schizophrenia Bulletin*; 12:274-82.

Liberman RP, Wallace J, Falloon IRH, Vaughn CE. (1981) Interpersonal problem-solving therapy for schizophrenics and their families. *Comphrehensive Psychiatry*; 22(6):627-30.

Wallace CJ, Boone SE. (1983) Cognitive factors in the social skills of schizophrenic patients: implications for treatment. *Nebraska Symposium on Motivation*; 31:283-317 (study 3).

Wallace C, Liberman RP. (1985) Social skills training for patients with schizophrenia: a controlled clinical trial. A controlled clinical trial. *Psychiatry Research*, 15 (3), 239-247.

Ayers T, Liberman RP, Wallace CJ. (1984) Subjective response to antipsychotic drugs: failure to replicate predications of outcome. *Journal of Clinical Psychopharmacology*; 4(2):89-93.

**Marder 1996 {published data only}**

Marder SR, Wirshing WC, Mintz J, McKenzie J, Johnston K, Eckman TA, Lebell M, Zimmerman K, Liberman RP. (1996) Two year outcome of social skills training and group psychotherapy for outpatients with schizophrenia. *American Journal of Psychiatry*; 153(12):1585-92.

**Peniston 1988 {published data only}**

Peniston E, Kulkosky P. (1988) Group assertion and contingent time-out procedures in the control of assaultive behaviors in schizophrenics. *Medical Psychotherapy*; 1:131-41

**Characteristics of excluded studies (previous guideline)**

| Study | Reason for exclusion |
|---|---|
| **Bedell 1989** | Allocation: Not randomised - people in intensive residential treatment unit compared with people treated in state hospital. |
| **Carpenter 1986** | Allocation randomised<br>Intervention: Had social skills training component but broadly family intervention |
| **DeCarlo 1985** | Allocation: randomised.<br>Participants: various diagnoses including schizophrenia and depression - not clear what proportion of the sample is schizophrenic. |
| **Eisler 1978** | Allocation: random<br>Participants: schizophrenic + non-psychotic (analysed separately).<br>Interventions: Social skills training, social skills training with modelling, and practice control.<br>Outcomes: No usable data (all main effects, statistics). |
| **Falloon 1977** | Allocation: random<br>Intervention: social skills training as a component of family intervention |
| **Foxx 1985** | Allocation: random.<br>Participants: Those with schizophrenia.<br>Design: multiple baseline design - experimental and control group both trained in social skills. |
| **Hannes 1976** | Allocation: randomised.<br>Participants: Those with schizophrenia.<br>Interventions: normal activity, current events discussion, cooperative arts and crafts project, and dyad discussion - none of which meet social skills training criteria. |
| **Hayes 1992** | Allocation: No allocation to two experimental groups - intra subject replication design. |
| **Hogarty 1986** | Allocation: No random, calendar randomisation according to available therapist time. |
| **Jerrell 1994** | Allocation: random.<br>Participants: people with severe mental illness, dually diagnosed with substance disorder. |
| **Kim 1997** | Allocation: random<br>Intervention: Very broad, had many components, including family intervention. Not social skills training. |
| **Morgan 1968** | Allocation: Not randomised. |
| **Rice 1979** | Subjects: male arsonists, with various diagnoses, mainly personality disorder. |

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|---|---|
| **Tourney 1960** | Allocation: Not randomised |
| **Wirshing 1992** | Allocation: random.<br>Participants: schizophrenic.<br>Intervention: 'structured and modularised skills training' - not social skills training: focus on medication management and symptom management. |

**Characteristics of included studies (update)**

| **Study ID** | **BROWN1983** |
|---|---|
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 7 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - US |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** Other DSM |
| | **Inclusion criteria:**<br>- inpatients diagnosed with schizophrenia according to DSM-III criteria<br>- chronic schizophrenia |
| | **Exclusion criteria:**<br>- Significant history of drug abuse or alcoholism |
| | **Total sample size:** No. randomised 28 |
| | **Total sample size:** ITT population 25 - completers only |

**Gender:** % female 0

**Age:** Mean 35

**Ethnicity:** 11% - Black
4% - Asian

**Setting:** Inpatient

**History:** 97% had >4 previous hospitalisations

**Baseline stats:** Not reported

**Interventions** **Intervention - group 1.:** Social Skills Training, 7 weeks for 4 hours a day, 5 days a week; N=14

**Intervention - group 2.:** Rehabilitation, 7 weeks for 4 hours a day, 5 days a week; N=14

**Notes about the interventions:**
Social skills training
- Training occurred over six modules: interpersonal, nutrition, health, finance, time management and community networks. The interpersonal skills modules included topographic behaviours such as eye contact, proximity, vocal tone and verbal content, with the remaining five modules including instrumental skills for effective community living.
- Life skills training employed active learning which included behavioural rehearsal, in vivo activities and homework assignments.

Rehabilitation group
Traditional veterans rehabilitation group used to control for therapist time and attention and included activities such as art, recreation and occupational therapy.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - Zung Depression Rating Scale
- Hamilton Depression Rating Scale
- Social Anxiety Scale

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Life Skills Inventory (LSI)

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

**Study ID**

**CHIEN2003**

**General info**

**Funding source:** Not mentioned

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Blindness:** No mention

**Duration:** Length of follow-up - 1 month

**Duration:** No. weeks of treatment - 4

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre - Taiwan

**Number of people screened, excluded & reasons:** 84 participants were included, a total of 8 withdraw either before or during the study. Reasons for withdrawal included inter-hospital transfer, refusal to participate, transfer to a different ward, unable to participate in less than half of the training sessions.

78 participants were randomised

**Notes about study methods:**
Randomisation procedure:
Each participant was assigned a number. A table of random numbers was used to select 28 participants from the first subgroup, and randomly assign 14 of them to the experimental group or control group. This same procedure was repeated within the second and third subgroups of participants.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100

**Diagnostic tool:** DSM-IV

**Total sample size:** No. randomised 78

**Gender:** % female 45

**Age:** Mean - 41.77

**Setting:** Inpatient

**History:**
[Experimental/Control]
Social skills training history n(%):
Have: 10(28.6) / 9(20.9)
Have not: 25(71.4) / 34(79.1)

**Baseline stats:**
[Experimental Group / Control Group]
PSS: 20.51(3.44) / 22.42(3.94)
NSS: 25.43(3.43) / 27.63(4.21)
GPS: 52.20(5.88) / 56.12(5.99)
SARS: 8.20(1.80) / 8.65(1.84)
IAS: 52.66(10.67) / 52.58(10.95)

**Interventions** **Intervention - group 1.:** Experimental Group; n=35

**Intervention - group 2.:** Control Group; n=43

**Notes about the interventions:**
Control Group:
Routine nursing care treatment

Experimental group:
In addition to TAU, the experimental group received 8 group social skills training sessions. The main objective was to advance the social skills abilities via a 60-minute social skills training course twice a week for 4 weeks each month. Training methods of social skills were divided into five parts: explanation, demonstration, role-play, feedback and social enhancement, and a homework assignment.

**Outcomes** **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Interaction Anxiousness Scale (IAS); Interpersonal Communication Satisfaction Scale; The Assertive Skill Scale

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Adequately addressed

**1.3 An adequate concealment method is used.:** Poorly addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

| **Study ID** | **CHOI2006** |
|---|---|
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 26 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Korea |
| | **Number of people screened, excluded & reasons:** 34 participants were included in the study. Of these 7 did not complete the SCET because of employment and moving to other areas, and 9 did not complete the standard psychiatric rehabilitation training due to employment, hospitalisation and refusal to complete measures. |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 97% |
| | **Diagnosis:** Other schizophrenia related [%] Schizoaffective disorder - 3% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV criteria for schizophrenia or schizoaffective disorder<br>- Stable antipsychotic medications |

- aged 18-60

**Exclusion criteria:**
- suspected organic brain pathology
- concurrent substance misuse or dependence
- severe mental retardation

**Total sample size:** No. randomised - 34

**Gender:** % female 44%

**Age:** Mean 32

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:**
[SCET Group / Control Group]
Duration of illness: 9.29(4.86) / 13.08(6.29)

**Baseline stats:**
[SCET Group / Control Group]
PA: 23.82(8.31) / 17.24(6.47)
SBST: 34.47(12.78) / 28.24(10.53)
ERT: 13.65(3.14) / 10.12(3.89)

**Interventions**

**Intervention - group 1.:** SCET - Social Cognition Enhancement Training ; n=17

**Intervention - group 2.:** Control; n=17

**Notes about the interventions:**
Standard Psychiatric Rehabilitation Training (Control):
-Comprehensive training designed to improve daily coping skills, optimise medication adherence, and increase social and occupational functioning.

SCET:
-In addition to the above, SCET was delivered on a group basis for 1.5 hours twice weekly. The package consisted of 36 sessions over approx 6 months. The sessions were conducted in accordance with the manual. SCET aims to improve social cognitive abilities such as context appraisal and perspective taking. Four column cartoons are employed as major training material in social cognitive exercises in which participants are encouraged to perceive social cues in each piece of the cartoon, arrange the four pieces in order based on contextual information and provide coherent explanations of the social situation in each cartoon. SCET also provides an opportunity to discuss how to solve problems in a social situation similar to that depicted in the cartoon.

**Outcomes**

**Cognitive functioning:** Average score/change in cognitive functioning - PA; SBST; ERT

| | |
|---|---|
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Well covered |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **GLYNN2002** |
| **General info** | **Funding source:** Pharmaceutical industry |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer - See ITT for details. |
| | **Type of analysis:** ITT - Paper reports data on all those followed-up at 60 weeks regardless of whether they completed the intervention. However the paper does not report outcomes on 18 people who after randomisation withdrew from the study before receiving any of the allocated intervention |
| | **Blindness:** Double-blind - Randomisation to the two drug conditions was double-blind |
| | **Blindness:** Only raters blind to the allocation of participants to the SST conditions. |
| | **Duration:** No. weeks of treatment - 60 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - Veteran affairs outpatient clinic, LA, US |
| | **Number of people screened, excluded & reasons:** 110 registered or eligible patients. 47 were excluded from random assignment due to (n): unable to stabilise on medication (10), could not tolerate haloperidol/side effects (8), withdrew against medical advice (5), missing (7), |

withdrew consent (7), become non compliant (3), moved (3), decided against skills training (2), severe substance misuse (2)

**Notes about study methods:** Randomisation procedure not reported (for both drug and SST randomisations)

**Participants**

**Diagnosis:** Schizophrenia [% of sample] % not reported

**Diagnosis:** Other schizophrenia related [%] % schizoaffective disorder not reported

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- DSM-IV diagnosis of schizophrenia or schizoaffective disorder
- >=2 documented episodes of acute schizophrenic illness or >=2 years of continuing psychotic symptoms
- Stabilised as an outpatient >=1 month
- Willingness to tolerate haloperidol and risperidone
- No significant organic or medical problems precluding learning or attendance at group sessions
- No evidence of substance misuse in previous 6 months
- Informed consent
- Aged 18-60

**Exclusion criteria:**
- Participants unable to stabilise during the 2-month pre-randomisation period

**Total sample size:** No. randomised - 63

**Total sample size:** ITT population - 46

**Gender:** % female 8%

**Age:** Mean - 43

**Ethnicity:**
[Clinic based SST / clinic based + in-vivo SST]
Ethnicity n(%):
Caucasian: 16(50) / 12(38.7)
African American: 10(31.3) / 15(48.4)
Hispanic: 4(12.5) / 4(12.9)
Asian: 2(6.3) / 0(0.0)

**Setting:** Outpatient

**History:**
[Clinic based SST / Clinic based SST + invivo SST]
Age of illness onset: 24.3(4.8) / 25.8(6.2)
Number of previous hospitalisations: 8.2(9.9) / 7.1(9.0)

**Baseline stats:** [Clinic based SST / Clinic based SST + in-vivo]
BPRS total: 42.1(10.70 / 42.2(10.2)

**Interventions** **Intervention - group 1.:** Clinic based social skills training alone, 64 x 90 minute sessions and 24 X 1 hour sessions; N = 32

**Intervention - group 2.:** Clinic based social skills training + in-vivo skills amplification: 64 x 90 minute sessions and 24 X 1 hour sessions (clinic based sessions). 52 x75 minute meetings

**Notes about the interventions:**
Stabilisation and medication assignment:
- All patients entered a 2-month stabilisation period in which current antipsychotic medication was gradually replaced with open-label haloperidol. Participants were not randomly assigned to SST conditions until they were clinically stable defined as: >=2 months during which none of BPRS ratings on thought disturbance or paranoid clusters changed by >1 point.
- 2 weeks prior to randomisation, medication for all patients changed to 8mg/day haloperidol

Random assignment into drug conditions
-Patients discontinued open-label haloperidol and were randomised on to either haloperidol or risperidone. The initial dose for each drop was 2 mg t.i.d + 6mg at bedtime. The dose could be increased but only for a psychotic exacerbation.
- Patients unable to tolerate haloperidol or risperidone were removed from the double-blind component and treated with alterative treatments. All these patients were encouraged to continue with the SST conditions.

Behaviourally orientated clinical social skills training
- Consisted of a series of social skills training modules (UCLA) administered in a group setting. Modules included medication management, symptom self-management, social problem solving and successful living skills.

In-vivo amplified skills training.
- aimed to support the use of the clinic-based skills within the community.
- manual-based intervention with 60 specific activities scheduled to coincide with the clinic-based training. The in-vivo skills programme had four objectives: 1) support completion of clinic assignments in the community, 2) identify opportunities for skills use in the community, 3) reinforce opportunity for skills use in the community and 4) establish a liaison with or develop a natural support systems to maintain gains from training.

**Outcomes** **Death:** Natural causes

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Time to relapse - Data not useable

**Global state & service outcomes (e.g. CGI):** Relapse - defined as worsening from baseline of >=4 points on the sum of the BPRS cluster scores for thought disturbance and hostile-suspiciousness, or an increase >=3 or more on either of these clusters. In addition, the sum of the scores for >=1 of these clusters needed to be >=4

| | |
|---|---|
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning |
| | **Quality of Life:** Average score/change in quality of life |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Adequately addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Well covered |
| | **1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed The paper states that "no meaningful medication effect existed in the data, thus we dropped the medication effects from the models evaluating psychosocial interventions" |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **GRANHOLM2005** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** ITT analyses were used to examine all outcome variables. Missing data were replaced by within-group means of the missing values. |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 24 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - All centres were based in the US |
| | **Number of people screened, excluded & reasons:** 87 participants were screened; 11 were excluded due to: refusal to complete baseline assessment (n=4), disabling medical illness (n=4), current substance misuse (n=3) |

**Notes about study methods:** A stratified randomisation procedure was used to assign participants to treatments within sites, with the constraint of equal numbers of patients from each site would be assigned to the two conditions according to a sequential list of random numbers.

**Participants**

**Diagnosis:** Other schizophrenia related [%] Schizoaffective disorder = 37%

**Diagnosis:** Schizophrenia [% of sample] 63%

**Diagnostic tool:** DSM-IV

**Exclusion criteria:** - disabling medical problems that would interfere with testing
- absence of medical records to inform diagnosis
- diagnosis of dependence on substances other than nicotine or caffeine within the past 6 months

**Total sample size:** No. randomised - 76

**Total sample size:** ITT population - 76

**Gender:** % female 73.5%

**Age:** Range 42-74

**Age:** Mean 54

**Ethnicity:** 78% were of Caucasian ethnicity

**Setting:** Other community-dwelling patients

**History:**
[TAU +CBSST / TAU]
Age at onset: 26.4(10.9) / 24.7(10.0)
Illness duration: 30.1(11.3) / 28.4(10.5)

**Baseline stats:**
[TAU + CBSST / TAU]
Beck cognitive insight scale: 4.1(5.3) / 5.9(4.7)
PANSS: 51.5(13.2) / 56.1(14.8)
HAM-D: 13.5(9.0) / 14.2(8.8)
Independent Living Skills Survey: 0.69(0.10) / 0.71(0.09)
UCSD Performance-based skills Assessment: 0.73(0.18) / 0.67(0.17)

**Notes about participants:**
participant mediation
1+ atypical antipsychotics = 46
typical antipsychotics = 17
both typical and atypical = 7

No antipsychotic medication = 6

**Interventions** **Intervention - group 1.:** TAU + CBST (Cognitive behavioural social skills training); n=37

**Intervention - group 2.:** TAU control; n=39

**Notes about the interventions:**
TAU
Patients continued in whatever ongoing care they were receiving. No medication guidelines were provided as part of this protocol. To characterise TAU, a standardised service utilisation interview was administered to all participants. 82% reported a psychotropic medication visit in the 6 weeks preceding study entry. 19% reported receiving any form of psychotherapy.

CBSST
CBSST was conducted in 24 weekly 2-hour group sessions. The treatment manual included a patient workbook that contained homework forms. CBSST targeted the multidimensional deficits that lead to disability in aging patients with schizophrenia. The social skills training modules were based on modules in the UCLA social and independent living skills series, whilst the cognitive components were developed specifically for patients with schizophrenia. The age-relevant content modifications included identifying and challenging ageist beliefs, age-relevant role-playing situations and age-specific problem solving. The modules were repeated to compensate for cognitive impairment.

**Outcomes** **Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS; HAM-D; Beck Cognitive Insight Scale; Comprehensive Module Test.

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Independent living Skills Survey; UCSD Performance-Based Skills Assessment

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Well covered

**1.3 An adequate concealment method is used.:** Adequately addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Well covered

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Well covered

**2.1 How well was the study done to minimise bias?: ++**

| | |
|---|---|
| **Study ID** | **PATTERSON2003** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 3months |
| | **Duration:** No. weeks of treatment - 12 |
| | **Raters:** Independent of treatment |
| | **Design:** Multi-centre - 4 board and care centres in San Diego, US |
| | **Number of people screened, excluded & reasons:** No details reported. |
| | **Notes about study methods:** Eight Board and Care facilities in San Diego, each with at least 20 middle-aged or older patients agreed to participate in the project. From this sample of eight facilities, four were randomly chosen for the present study. Ten patients were recruited from each site |
| **Participants** | **Diagnosis:** Other schizophrenia related [%] Schizoaffective disorder - 22% |
| | **Diagnosis:** Schizophrenia [% of sample] schizophrenia - 53% |
| | **Diagnosis:** Other [%] Mood disorder with psychotic features - 25% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- aged >40 years<br>- patients with longstanding psychotic disorders<br>- patients with a DSM-IV chart diagnosis of schizophrenia, schizoaffective disorder, or psychotic mood disorder |
| | **Exclusion criteria:**<br>- DSM-IV diagnosis of dementia<br>- serious suicide risk<br>- could not complete the assessment battery<br>- participating in any other psychosocial intervention or drug research at the time of study intake |
| | **Total sample size:** No. randomised - 40 |

**Total sample size:** ITT population - 32 completers used in the analysis

**Gender:** % female 31%

**Age:** Mean 45

**Ethnicity:** African American - 13%
Hispanic - 3%
Asian American - 3%
White - 78%
Other - 3%

**Setting:** Other Board and Care facility

**History:**
[FAST intervention / TAU]
Duration of illness, years: 21.3(11.8) / 20.9(12.3)

**Baseline stats:**
[FAST intervention / TAU]
UPSA: 31.9(11.8) / 40.3(8.3)
PANSS positive: 12.5(5.6) / 10.4(4.0)
PANSS negative: 16.9(6.6) / 10.1(3.2)
PANSS general: 25.0(6.2) / 22.3(3.7)
HAM-D: 7.8(6.1) / 4.6(2.8)
QWB: 0.53(0.08) / 0.49(0.08)

**Notes about participants:**
[FAST intervention / TAU]
On antipsychotics, n(%): 16(100) / 15(94)
Daily neuroleptic dose (mg, chlorpromazine equivalent): 436.2(659.1) / 461.5(598.14)

**Interventions** **Intervention - group 1.:** FAST intervention, twice-weekly, 120-minute group sessions for 12 weeks; N=20

**Intervention - group 2.:** Control n=20

**Notes about the interventions:**
Functional Adaptation Skills Training (FAST)
Based on a Social and Independent Living Programme, a manualised social-cognitive theory-based behavioural intervention was created. The intervention focused on improving six areas of everyday functioning: medication management, social skills, communication skills, organisation and planning, transportation, and financial management. FAST consisted of 24 semi-weekly, 120 minute group sessions.

TAU

| | |
|---|---|
| | All participants received their usual medications. Participants were queried about their participation in other interventions. None of the patients reported participating in any other psychosocial intervention during the study |
| **Outcomes** | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS; Ham-D |
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - UPSA |
| | **Quality of Life:** Average score/change in quality of life - QWB |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Well covered |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not reported adequately |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **PATTERSON2006** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer subset of the ITT group who, in addition to completing both a baseline and follow-up assessment, attended at least 25% of all group sessions. |
| | **Type of analysis:** ITT - consisted of participants who attended at least one session of their assigned intervention and completed both a baseline and follow-up assessment. |
| | **Blindness:** Only raters blind |
| | **Duration:** Length of follow-up - 6 months |

**Duration:** No. weeks of treatment - 24 weeks

**Raters:** Independent of treatment

**Design:** Multi-centre - 25 Board and Care facilities in San Diego County, US

**Number of people screened, excluded & reasons:** 465 patients were screened and 219 excluded. Reasons for exclusion include: failure to meet inclusion criteria (n=144), refused to participate (n=67), other (n=8)

**Notes about study methods:** Once at least five consent forms had been received from a particular Board and Care centre, all participating patients from that Board and Care were randomised.

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 80.5%

**Diagnosis:** Other schizophrenia related [%] schizoaffective disorder - 19.5%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- aged >40 years
- patients with longstanding psychotic disorders
- patients with a DSM-IV chart diagnosis of schizophrenia or schizoaffective disorder

**Exclusion criteria:**
- DSM-IV diagnosis of dementia
- serious suicide risk
- could not complete the assessment battery
- participating in any other psychosocial intervention or drug research at the time of study intake

**Total sample size:** No. randomised - 240

**Total sample size:** ITT population - 195

**Gender:** % female 35%

**Age:** Mean 51

**Ethnicity:** Caucasian - 53%
Hispanic - 25%
African-American - 13.5%
Asian-American - 4%
Native American - 3%
Other - 1.5%

**Setting:** Other Board and Care facilities

**History:**
[FAST intervention / AC]

Duration of illness, years: 11.6(2.8) / 11.7(2.6)

**Baseline stats:**
[FAST intervention / AC]
UPSA total: 60.3(2.4) / 64.9(2.5)
SSPA: 24.9(0.9) / 27.9(0.9)
MMAA: 14.9(1.1) / 14.8(1.2)
PANSS total: 59.9(2.5) / 62.8(2.7)
HAM-D: 9.9(0.9) / 9.8(0.9)
QWB: 53.9(1.5) / 56.3(1.5)

**Notes about participants:**
[FAST intervention / AC]
Daily neuroleptic dose, mg: 476.5(635.4) / 438.7(472.1)

**Interventions** **Intervention - group 1.:** FAST intervention, 24 weekly sessions of 120 minutes; N=124

**Intervention - group 2.:** Attention Control (AC), 24 weekly 120 minute sessions; n=116

**Notes about the interventions:**
Functional Adaptation Skills Training (FAST)
Based on a Social and Independent Living Programme, a manualised social-cognitive theory-based behavioural intervention was created. The intervention focused on improving six areas of everyday functioning: medication management, social skills, communication skills, organisation and planning, transportation, and financial management. FAST consisted of 24 weekly, 120 minute group sessions.

Attention Control (AC)
individuals received their medication as usual and participated in 24 weekly, 120-minute group sessions that provided a supportive environment for addressing personal problems.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS; HAM-D

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - UPSA; SSPA

**Quality of Life:** Average score/change in quality of life - QWB

**Other:** MMAA

**Quality** **1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not reported adequately

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Poorly addressed

**1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** 20-50%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Well covered

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Adequately addressed

**2.1 How well was the study done to minimise bias?: +**

| **Study ID** | **PINTO1999** |
|---|---|
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** No mention |
| | **Duration:** No. weeks of treatment - 36 |
| | **Raters:** Not stated to be independent of treatment |
| | **Design:** Single-centre - Naples, Italy |
| | **Number of people screened, excluded & reasons:** Not reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- DSM-IV diagnosis of schizophrenia<br>- No evidence of current substance misuse or organic pathology<br>- Treatment-refractory schizophrenia as documented by >=2 previous neuroleptic drug trials of at least 6 weeks at a dose of >600mg chlorpromazine equivalent |
| | **Total sample size:** No. randomised - 41 |

**Total sample size:** ITT population - 37 completers

**Gender:** % female 31%

**Age:** Mean - 34

**Ethnicity:** Not reported

**Setting:** Outpatient

**Setting:** Inpatient

**History:**
[CBT+SST / Supportive therapy]
Illness duration, years: 9.2(3.3) / 8.2(2.9)
Hospital admissions: 11.6(7.9) / 11.7(6.6)

**Baseline stats:**
[CBT+SST / Supportive therapy]
BPRS: 83.1(21.7) / 81.7(20.6)

**Notes about participants:**
All participants were on clozapine
[CBT+SST / supportive therapy]
Clozapine dose, mg: 552.6(129.6) / 547.2(109.1)

**Interventions** **Intervention - group 1.:** CBT+SST, 6 months; N = 20

**Intervention - group 2.:** Supportive therapy, 6 months; N=21

**Notes about the interventions:**
CBT+SST
The CBT intervention focussed on improving clients abilities to manage their current psychotic symptoms and was based on a treatment manual. Skills training methods were used to improve social behaviours including self-case, medication self-management, social conversation, interpersonal problem solving, self-directed recreation, family communication and management of personal resources. Both the CBT and SST components involved rehearsal, positive reinforcement, in vivo exercises and homework assignments.

Supportive therapy
Individual supportive therapy sessions included basic psychoeducation about the nature and treatment of schizophrenia, active listening, empathy and reassurance, reinforcement of the clients; health-promoting initiatives, help in managing a crisis and advocacy of the clients' needs.

**Outcomes** **Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS, SANS, SAPS

| | |
|---|---|
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?:** + |
| **Study ID** | **RONCONE2004** |
| **General info** | **Funding source:** Not mentioned |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind |
| | **Duration:** No. weeks of treatment - 24 |
| | **Raters:** Independent of treatment |
| | **Design:** Single-centre - day hospital service, Italy |
| | **Number of people screened, excluded & reasons:** No details reported |
| | **Notes about study methods:** Randomisation procedure not reported |
| **Participants** | **Diagnosis:** Schizophrenia [% of sample] 100% |
| | **Diagnostic tool:** DSM-IV |
| | **Inclusion criteria:**<br>- in touch with services for >=2 years |

- presented no evidence of organic brain disease
- did not have a history of substance misuse

**Total sample size:** No. randomised - 20

**Gender:** % female 35%

**Age:** Mean - 33

**Age:** Range - 25-41

**Ethnicity:** No details reported

**Setting:** Inpatient

**History:**
[Rehabilitation Group / Control Group]
Mean duration of illness, years: 16.9(8.05) / 11.1(6.9)

**Baseline stats:**
[Rehabilitation Group / Control Group]
BPRS cluster Negative: 8.8(4.9) / 10.1(3.7)
Verbal fluency: 6.06(4.9) / 7.5(1.7)
WCST total errors: 51.4(29.7) / 48.6(20.4)
Tower of London: 19.3(5.7) / 20.6(7.1)
ToM 1st level: 1.06(0.57) / 0.78(0.52)
ToM 2nd level: 0.63(0.62) / 0.70(0.67)
Social disability: 41 / 39

**Notes about participants:** All participants were undergoing antipsychotic treatment and had no plans to change medication during the treatment phase.

**Interventions** **Intervention - group 1.:** Rehabilitation, up to 1 hour per week x22; n=10

**Intervention - group 2.:** Control; n=10

**Notes about the interventions:**
Rehabilitation
Intervention programme was aimed at teaching and learning how to change participants' cognitive structure by transforming their passive and dependent cognitive style to an autonomous one. The method was to enhance the participants' capacity to modify wrong beliefs and their thinking strategies by exposure to new experiences. The treatment goal is reached by acquiring the six sub-objectives. The treatment sessions were conducted in groups of 10 patients with 5 therapists. In every session, after 30 minutes of training work, there was a pause of 5 minutes to help participants relax and to be a reward for participating in the group work.

| | |
|---|---|
| | Control<br>Treated only with antipsychotic medication and supportive psychotherapy when necessary |
| **Outcomes** | **Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - BPRS negative symptom cluster |
| | **General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - Accertamento Disabilita - Italian version of the DAS |
| | **Cognitive functioning:** Average score/change in cognitive functioning - Verbal fluency; Tower of London; ToM (1st level); ToM (2nd level); Mach IV; emotion recognition |
| **Quality** | **1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed |
| | **1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately |
| | **1.3 An adequate concealment method is used.:** Not addressed |
| | **1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed |
| | **1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed |
| | **1.6 The only difference between groups is the treatment under investigation.:** Poorly addressed - Control group in addition to medication were also offered supportive psychotherapy as necessary (paper does not report % utilising this service) |
| | **1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered |
| | **1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20% |
| | **1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not reported adequately |
| | **1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable |
| | **2.1 How well was the study done to minimise bias?: +** |

| | |
|---|---|
| **Study ID** | **UCOK2006** |
| **General info** | **Funding source:** Non-industry support |
| | **Published or unpublished data?:** Published |
| **Method** | **Type of study:** Individual randomised trial |
| | **Type of analysis:** Completer |
| | **Blindness:** Only raters blind to performance on other tests but does not explicitly state that they were blind to treatment allocation. |
| | **Duration:** No. weeks of treatment - 6 |

**Raters:** Not stated to be independent of treatment

**Design:** Single-centre - Turkey

**Number of people screened, excluded & reasons:** 63 patients were screened and randomised. One patient was excluded from the analysis due to psychotic symptom exacerbation.

**Notes about study methods:** Randomisation procedure not reported

**Participants** **Diagnosis:** Schizophrenia [% of sample] 100%

**Inclusion criteria:**
- age 18-45
- no neurological or medical conditions, such as epilepsy, history of head trauma
- no diagnosis of alcohol or substance misuse
- all patients were in the remission phase of the illness.

**Total sample size:** No. randomised - 63

**Gender:** % female 46%

**Age:** Mean - 28.32(6.92)

**Setting:** Outpatient

**History:** Mean duration of illness was 7 years(4.77) and number of previous hospitalisations was 1.83(2.24)

**Baseline stats:**
[Training Group / Control Group]
CGI: 3.87(1.14) / 3.92(0.75)
BPRS-total: 42.34(8.56) / 40.92(7.26)
WCST - correct answers: 66.53(23.43) / 64.91(23)
DST total: 7(2.46) / 7.24(2)
CPT-hit rate: 93.7(13.9) / 92.3(11.5)
AIPSS total: 11.7(4.5) / 11(4.3)

**Notes about participants:** All patients were taking antipsychotics (76.1% atypical, 15.8% typical, and 7.9% combination of atypical and low dose typical).
- Mean dose in typical antipsychotics in chlorpromazine equivalents = 388mg. Mean dose was 13.4mg for olanzapine (n=18), 355mg for clozapine (n=16), 4.7mg for risperidone (n=10), 600mg for quetiapine (n=3), and 600 mg for amisulpride (n=1)
-16% were using anticholinergics.
-approx 50% of patients had attended a supportive group psychotherapy programme.

**Interventions** **Intervention - group 1.:** Training group; n=32

**Intervention - group 2.:** Control; n=30

**Notes about the interventions:**
Control: TAU

Social problem solving training group
In addition to TAU, received 6 weeks problem solving training in a group modality. The group used the problem solving training techniques used in a previous approach. During the sessions the therapist would describe what the interpersonal problem was and then repeat the steps of problem solving methods by writing them on the board. Patients are then asked to repeat these steps. Two sample interpersonal problems brought by patients or the therapist are then discussed using the board in each session. Two solutions to these interpersonal problems are then acted out using role-play.

**Outcomes**

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning - AIPSS

**Other:** Scores on the BPRS, WCST, and the CPT were assessed to determine which parameters contributed most to the post-training AIPSS (social skills outcome) score.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Adequately addressed

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Not reported adequately

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Adequately addressed

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Adequately addressed

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Not addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?: +**

**Study ID**

**VALENCIA2007**

**General info**

**Funding source:** Non-industry support

**Published or unpublished data?:** Published

**Method**

**Type of study:** Individual randomised trial

**Type of analysis:** Completer

**Blindness:** Only raters blind

**Duration:** No. weeks of treatment - 52

**Raters:** Independent of treatment

**Design:** Single-centre - Mexico

**Number of people screened, excluded & reasons:** 98 participants were randomised, a total of 16 failed to complete the study leaving a final sample of 82 in the analysis.

**Notes about study methods:** Randomisation procedure not reported

**Participants**

**Diagnosis:** Schizophrenia [% of sample] 100%

**Diagnostic tool:** DSM-IV

**Inclusion criteria:**
- outpatients diagnosed with schizophrenia according to DSM-IV, who were taking antipsychotic medication.
- clinically stable in terms of psychotic symptoms (corroborated by PANSS < 60)
- aged 16-60
- completed at least 6 years of elementary education
- lived with family and resided in Mexico City
- Provided written informed consent.

**Total sample size:** No. randomised - 98 initially randomised, 82 used in the analysis

**Gender:** % female 22%

**Age:** Mean 29.8(6.8)

**Ethnicity:** Not reported

**Setting:** Outpatient

**History:** average age of illness onset = 21.3(5.4)

**Baseline stats:**
[PSST / TAU]
PANSS: 115.2(30.5) / 107.9(22.6)
GPS: 57.5(16.0) / 53.6(12.2)
GPSF: 3.2(0.6) / 3.1(0.6)
GAF: 43.3(6.3) / 44.1(8.0)

**Interventions**

**Intervention - group 1.:** PSST; n=43

**Intervention - group 2.:** TAU; n=39

**Notes about the interventions**
TAU
Provided at the schizophrenia clinic by two clinical psychiatrists who were blind to the treatment conditions. TAU included the following features/tasks: 20-minute monthly appointments during a 1 year period, controlled the prescription of antipsychotic medication based upon the assessment of psychotic symptoms, checked medication compliance, recorded attendance to consultations and registered all information for their clinical files.

In addition to TAU, the experimental group underwent psychosocial skills training (PSST) and family therapy (FT).

PSST
Composed of 7 treatment areas: symptom management, medication management, social relations, occupational, money management, couple relations and family relations based on a therapists training manual (Valencia et al 2001). The sessions used six learning activities to teach patients skills acquisition. PSST was in the form of group sessions, 8 participants per group, for up to 1 hour 15 minutes, once a week for a total of 48 sessions over the course of 1 year.

FT
The first part of FT consisted of psychoeducation, which included 8 group sessions where all the patients' relatives received information about the illness, symptoms and medication management. The second part consisted of 4 sessions for each family to improve communication skills, recognition and management of the warning signs of relapse, the importance of medication and its side effects, compliance with antipsychotic medication and keeping appointments with physicians.

**Outcomes**

**Leaving the study early:** Leaving due to any reason (non-adherence to study protocol)

**Global state & service outcomes (e.g. CGI):** Re-hospitalisation

**Global state & service outcomes (e.g. CGI):** Average score/change in global state - GAF

**Global state & service outcomes (e.g. CGI):** Relapse - not defined

**Mental state (e.g. BPRS, PANSS, BDI):** Average score/change in mental state - PANSS

**General and psychosocial functioning (e.g. SFS):** Average score/change in general functioning – Patient-Specific Functional Scale (PSFS)

**Engagement with services (e.g. SES):** Average score/change in engagement with services - Compliance with antipsychotic medication - defined as patients having taken at least 80% of the prescribed antipsychotic medication.

Therapeutic adherence - 1) patients' attendance at therapy sessions 2) number of patients who completed the intervention, compared to those who dropped out.

**Quality**

**1.1 The study addresses an appropriate and clearly focused question.:** Well covered

**1.2 The assignment of subjects to treatment groups is randomised.:** Not reported adequately

**1.3 An adequate concealment method is used.:** Not addressed

**1.4 Subjects and investigators are kept 'blind' about treatment allocation.:** Poorly addressed

**1.5 The treatment and control groups are similar at the start of the trial.:** Adequately addressed

**1.6 The only difference between groups is the treatment under investigation.:** Well covered

**1.7 All relevant outcomes are measured in a standard, valid and reliable way.:** Well covered

**1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?:** <20%

**1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention-to-treat analysis). :** Poorly addressed

**1.10 Where the study is carried out at more than one site, results are comparable for all sites.:** Not applicable

**2.1 How well was the study done to minimise bias?:** +

**References of included studies (update)**

**BROWN1983**

Brown, M.A.; Munford, A.M. (1983) Life skills training for chronic schizophrenics. *Journal of Nervous and Mental Disease* 171(8): 466-470.

**CHIEN2003**

Chien,H.C.; Ku,C.H.; Lu,R.B.; Chu,H.; Tao,Y.H.; Chou,K.R. (2003) Effects of social skills training on improving social skills of patients with schizophrenia. *Archives of Psychiatric Nursing* 17(5): 228 - 236.

**CHOI2006**

Choi,K.H.; Kwon,J.H. (2006) Social cognition enhancement training for schizophrenia: a preliminary randomized controlled trial. *Community Mental Health Journal* 42(2): 177 - 187.

**GLYNN2002**

Glynn,S.M.; Marder,S.R.; Liberman,R.P.; Blair,K.; Wirshing,W.C.; Wirshing,D.A.; Ross,D.; Mintz,J. (2002) Supplementing clinic-based skills training with manual-based community support sessions: effects on social adjustment of patients with schizophrenia. *American Journal of Psychiatry* 159(5): 829 - 837.

**GRANHOLM2005**

Granholm,E.; McQuaid,J.R.; Link,P.C.; Fish,S.; Patterson,T.; Jeste,D.V. (2008) Neuropsychological predictors of functional outcome in Cognitive Behavioral Social Skills Training for older people with schizophrenia. *Schizophrenia Research*. 100(1-3): 133-143.

*Granholm,E.; McQuaid,J.R.; McClure,F.S.; Auslander,L.A.; Perivoliotis,D.; Pedrelli,P.; Patterson,T.; Jeste,D.V. (2005) A randomized, controlled trial of cognitive behavioral social skills training for middle-aged and older outpatients with chronic schizophrenia. *American Journal of Psychiatry* 162(3): 520 - 529.

Granholm,E.; McQuaid,J.R.; McClure,F.S.; Link,P.C.; Perivoliotis,D.; Gottlieb,J.D.; Patterson,T.L.; Jeste,D.V. (2007) Randomized controlled trial of cognitive behavioral social skills training for older people with schizophrenia: 12-month follow-up. *Journal of Clinical Psychiatry* 68: 730 - 737.

**NG2007**

Ng,R.M.K.; Cheung,M.S.L. (2007) Social skills training in Hong Kong Chinese patients with chronic schizophrenia. *Hong Kong Journal of Psychiatry*. 16(1): 14 - 20.

**PATTERSON2003**

Mausbach,B.T.; Cardenas,V.; McKibbin,C.L.; Jeste,D.V.; Patterson,T.L. (2008) Reducing emergency medical service use in patients with chronic psychotic disorders: results from the FAST intervention study. *Behaviour Research & Therapy*. 46(1): 145 - 153.

*Patterson TL, McKibbin C, Taylor M, Goldman S, Davila-Fraga W, Bucardo J, Jeste DV. (2003) Functional adaptation skills training (FAST): a pilot psychosocial intervention study in middle-aged and older patients with chronic psychotic disorders. *American Journal of Geriatric Psychiatry*. 11(1): 17-23.

**PATTERSON2003**

Patterson,T.L.; Mausbach,B.T.; McKibbin,C.; Goldman,S.; Bucardo,J.; Jeste,D.V. (2006) Functional adaptation skills training (FAST): a randomized trial of a psychosocial intervention for middle-aged and older patients with chronic psychotic disorders. *Schizophrenia Research* 86(1-3): 291 - 299.

**PINTO1999**

Pinto, A., La Pia, S., Mennella, R., Giorgio, D. & DeSimone, L. (1999) Cognitive-behavioural therapy and clozapine for clients with treatment-refractory schizophrenia. *Psychiatric Services* 50(7): 901-904.

**RONCONE2004**

Roncone,R.; Mazza,M.; Frangou,I.; De Risio,A.; Ussorio,D.; Tozzini,C.; Casacchia,M. (2004) Rehabilitation of theory of mind deficit in schizophrenia: A pilot study of metacognitive strategies in group treatment. *Neuropsychological Rehabilitation* 14(4): 421 - 435.

**UCOK2006**

Ucok,A.; Cakir,S.; Duman,Z.C.; Dicigil,A.; Kandemir,P.; Atli,H. (2006) Cognitive predictors of skill acquisition on social problem solving in patients with schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience* 256(6): 388 - 394.

**VALENCIA2007**

Valencia, R., Juarez, M. (2007) A psychosocial skills training approach in Mexican out-patients with schizophrenia. *Psychological Medicine* 37(10): 1393-1402.

**Characteristics of excluded studies (update)**

**ANZAI2002**

**Reason for exclusion:** Does not meet criteria for intervention

**FUENTES2007**

**Reason for exclusion:** N<10

**GRANHOLM2002**

**Reason for exclusion:** - letter to editor

**PATTERSON2005**

**Reason for exclusion:** n<10 in comparison group

**SEO2007**

**Reason for exclusion:** Non-RCT

**References of excluded studies (update)**

Anzai, N., Yoneda, S., Kumagai, N., Nakamura, Y., Ikebuchi, E. & Liberman, R.P. (2002) Training persons with schizophrenia in illness self-management: A randomised controlled trial in Japan. *Psychiatric Services* 53(5): 545-547.

Fuentes, I.; Garcia,S.; Ruiz,J.C.; Soler,M.J.; Roder,V. (2007) Social perception training in schizophrenia: A pilot study. *International Journal of Psychology and*

*Psychological Therapy* 7(1): 1-12.

Granholm,E.; McQuaid,J.R.; McClure,F.S.; Pedrelli,P.; Jeste,D.V. (2002) A randomized controlled pilot study of cognitive behavioral social skills training for older patients with schizophrenia. *Schizophrenia Research* 53: 167 - 169.

Patterson,T.L.; Bucardo,J.; McKibbin,C.L.; Mausbach,B.T.; Moore,D.; Barrio,C.; Goldman,S.R.; Jeste,D.V. (2005) Development and pilot testing of a new psychosocial intervention for older Latinos with chronic psychosis. *Schizophrenia Bulletin* 31(4): 922 - 930.

Seo,J.M.; Ahn,S.; Byun,E.K.; Kim,C.K. (2007) Social skills training as nursing intervention to improve the social skills and self-esteem of inpatients with chronic schizophrenia. *Archives of Psychiatric Nursing*.21(6): 317 - 326.