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Compliance therapy for schizophrenia (Review)

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TABLE OF CONTENTS

[Intervention Review]

Compliance therapy for schizophrenia

Andrew McIntosh[1], Louise Conlon[2], Stephen Lawrie[3], Andrew C Stanfield[4]

[1]University of Edinburgh, Royal Edinburgh Hospital, Edinburgh, UK. [2]Department of Psychiatry, Clinical Sciences Institute, University College Hospital, National University of Ireland, Galway, Ireland. [3]Department of Psychiatry, University of Edinburgh, Edinburgh, UK. [4]Division of Psychiatry, University of Edinburgh, Edinburgh, UK

Contact address: Andrew McIntosh, University of Edinburgh, Royal Edinburgh Hospital, Edinburgh, EH10 5HF, UK. andrew.mcintosh@ed.ac.uk.

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ABSTRACT

Background

Schizophrenia is a severe mental illness characterised by delusions and hallucinations. Antipsychotic drugs does reduce these symptoms, but at least half of people given these drugs do not comply with the treatment regimen prescribed.

Objectives

To assess the effects of compliance therapy on antipsychotic medication adherence for people with schizophrenia.

Search methods

Cochrane Schizophrenia Group Trials Register (June 2005).

Selection criteria

We included all randomised controlled trials of 'compliance therapy' for people with schizophrenia or related severe mental disorders.

Data collection and analysis

We independently extracted data and, for dichotomous data, calculated the relative risk (RR), its 95% confidence interval (CI) on an intention to treat basis. We present continuous data using the weighted mean difference statistic.

Main results

We included one trial with relevant and available data (n=56, duration 2 years) comparing compliance therapy with non-specific counseling. The primary outcome 'non-compliance with treatment' showed no significant difference between compliance therapy and non-specific counseling (n=56, RR 1.23 CI 0.74 to 2.05). The compliance therapy did not substantially effect attitudes to treatment (n=50, WMD DAI score -2.10 CI -6.11 to 1.91). Very few people (˜10%) left the study by one year (n=56, RR 0.5 CI 0.1 to 2.51). Mental state seemed unaffected by the therapy (n=50, WMD PANSS score 6.1 CI -4.54 to 16.74) as was insight (n=50, WMD SAI -0.5 CI -2.43 to 1.43), global functioning (n=50, WMD GAF -4.20 CI -16.42 to 8.02) and quality of life (n=50, WMD QLS -3.40 CI -16.25 to 9.45). At both one and two years the average number of days in hospital was non-significantly reduced for those allocated to the compliance therapy.

Authors' conclusions

There is no clear evidence to suggest that compliance therapy is beneficial for people with schizophrenia and related syndromes but more randomised studies are justified and needed in order for this intervention to be fully examined.

PLAIN LANGUAGE SUMMARY

Compliance therapy for schizophrenia

Relapse in people with schizophrenia is common and in many cases attributable to poor compliance with antipsychotic medication. Compliance therapy was developed to specifically address non-compliance with antipsychotic medication. We only found one reasonably good but small trial. It did not show that compliance therapy really effected compliance with medication, psychotic symptoms, or quality of life but it was always too small really to show this for certain. The study did, however, suggest that the compliance therapy may help people spend shorter times in hospital across a two year period, when compared with standard care. There is a need for more studies and we have proposed a design that could be conducted within the confines of routine care for outcomes of interest to everyone involved.

BACKGROUND

Antipsychotic medication has proven efficacy in the treatment of positive symptoms of schizophrenia and the prevention of relapse. In spite of this almost 90% of patients will relapse within the first five years of treatment following an acute episode (Robinson 1999) and in general the illness has a tendency to recur or become chronic (Mason 1996). Several factors have been shown to increase the chance of relapse, but probably the single most important determinant of relapse is the discontinuation of effective antipsychotic drug therapy (Green 1988).

The discontinuation of effective medication has been termed non-compliance, non-adherence or non-concordance. The term non-compliance emphasises the role of doctors as providing a solution and the patients health beliefs as barriers to be overcome. Other models have been proposed that emphasise the equality between patient and doctor in determining the best treatment option and convey the importance of the therapeutic alliance. The latter model usually describes the discontinuation of effective prescribed medication as non-concordance and emphasises the role of the patient as the most important determinant (Marinker 1997).

Non-concordance with drug therapy is common in schizophrenia; approximately 50% of patients are non-concordant one year after being discharged from hospital (Bartko 1988). Effective interventions for improving antipsychotic drug adherence therefore have the potential to reduce the severity of symptoms of the disorder, prevent future relapse and may improve overall outcome.

Several effective psychosocial interventions are currently available for the treatment of schizophrenia; these include family therapy (Pharoah 2000) and psychoeducational approaches (Pekkala 2002). The mode of effectiveness is however uncertain and may simply result from an improvement in drug compliance. Compliance therapy is a therapy specifically designed to improve concordance with treatment for those with major mental illnesses, but its effectiveness in patients with schizophrenia or other related severe mental illness is uncertain.

OBJECTIVES

The primary objective of this review is to assess the effect of 'compliance therapy' on adherence with antipsychotic medication in people with schizophrenia or related psychoses compared to treatment as usual.

The secondary objective is to determine whether 'compliance therapy' is superior to any other intervention in promoting adherence with antipsychotic medication.

METHODS

Criteria for considering studies for this review

Types of studies

We included all relevant randomised controlled trials (RCTs) in any language.

Types of participants

We included all people with schizophrenia and non-affective psychotic mental illness irrespective of mode of diagnosis, age, sex or duration of illness.

Types of interventions

1. Compliance therapy
An intervention based on motivational interviewing (Miller 1991) where the participant is invited to review their history of illness, symptoms and side-effects and consider the benefits and drawbacks of drug treatment (Hayward 1995). The therapist's focus should be on the discrepancy between the participants beliefs and maladaptive behaviours, and should focus on adaptive behaviours. Other components may include a consideration of issues relating to the stigma of mental illness though this is not necessary or sufficient to fulfil the definition of 'compliance therapy'.

2. Standard care
We defined standard care as the normal level of psychiatric care provided in the area where the trial was undertaken.

3. Other psychosocial interventions
Additional psychological and/or social interventions, such as non-specific counseling and supportive therapy and other 'talking therapies'.

Types of outcome measures

We, a priori, defined the time periods in which we would report outcomes (short term - up to 12 weeks, medium term - 13-26 weeks and long term - more than 26 weeks).

Primary outcomes

1. Patient adherence
1.1 Concordance with antipsychotic medication prescription
1.2 Concordance with follow-up arrangements

Secondary outcomes

1. Death, suicide or natural causes.

2. Leaving the study early.

3. Clinical response
3.1 No clinically significant response in global state - as defined by each of the studies
3.2 Average score/change in global state
3.3 No clinically significant response on psychotic symptoms - as defined by each of the studies
3.4 Average score/change on psychotic symptoms
3.5 No clinically significant response on positive symptoms - as defined by each of the studies
3.6 Average score/change in positive symptoms
3.7 No clinically significant response on negative symptoms - as defined by each of the studies
3.8 Average score/change in negative symptoms.
3.9 No clinically significant response on insight - as defined by each of the studies
3.10 Average score/change in insight

4. Extrapyramidal adverse effects
4.1 Incidence of use of antiparkinson drugs

4.2 No clinically significant extrapyramidal adverse effects - as defined by each of the studies
4.3 Average score/change in extrapyramidal adverse effects

5. Quality of life/satisfaction with care for either recipients of care or carers
5.1 No significant change in quality of life/satisfaction - as defined by each of the studies
5.2 Average score/change in quality of life/satisfaction

6. Costs
6.1 Direct and indirect

Search methods for identification of studies

Electronic searches

We searched the Cochrane Schizophrenia Group's Trials Register (latest update June 2005)
using the phrase:

[((*complian* or *educat* or *concord* or *adhere* or *psychoed* or *non-com* or *refus*) in REFERENCE) and ((*complian* or *educat* or *concord* or *adhere* or *psychoed* or *non-com* or *refus*) in STUDY)]

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

Searching other resources

1. Reference searching
We inspected the references of all identified studies for more trials.

Data collection and analysis

1. Selection of trials
Two reviewers (AM,SL) independently searched for trials, identified potentially relevant abstracts and assessed full papers for inclusion and methodological quality. We resolved any disagreement by discussion.

2. Quality assessment
The search for trials was performed independently by two reviewers, as described in the Cochrane Collaboration Reviewers' Handbook (Higgins 2005). When disputes arose as to which category a trial was allocated, resolution was attempted by discussion. When this was not possible and further information was necessary to clarify into which category to allocate the trial, data was not entered and the trial was allocated to the list of those awaiting assessment. We only included trials in category A or B in this review.

3. Data management
3.1 Data extraction
This was performed independently by at least two reviewers and the authors of trials were contacted to provide missing data where possible.

3.2 Intention-to-treat analysis
We excluded data from studies where more than 50% of participants in any group were lost to follow-up. We were to have performed a sensitivity analysis to assess the impact of this decision. In studies with less than 50% dropout rate, we considered those who left early as having a negative outcome.

4. Data analysis
4.1 Binary data
For binary outcomes we calculated an estimation of the relative risk (RR) and its 95% confidence interval (CI) and the number needed to treat statistic (NNT).

4.2 Continuous data
4.2.1 Skewed data: continuous data on clinical and social outcomes are often not normally distributed. To avoid the pitfall of applying parametric tests to non-parametric data we applied the following standards to all data before inclusion: i. standard deviations and means were reported in the paper or were obtainable from the authors; ii. when a scale starts from a finite number (such as 0), the standard deviation, when multiplied by 2, was less than the mean (as otherwise the mean was unlikely to be an appropriate measure of the centre of the distribution (Altman 1996). Endpoint scores on scales often have a finite start and end point and this rule can be applied to them.

4.2.2 Summary statistic: for continuous outcomes we estimated a weighted mean difference (WMD) between groups.

4.2.3 Valid scales: we only included continuous data from rating scales if the measuring instrument had been described in a peer-reviewed journal and the instrument was either a self report or completed by an independent rater or relative (not the therapist) (Marshall 2000).

4.2.4 Endpoint versus change data: where possible, we presented endpoint data and if both endpoint and change data were available for the same outcomes then we only reported the former in this review.

4.2.5 Cluster trials: Studies increasingly employ 'cluster randomisation' (such as randomisation by clinician or practice) but analysis and pooling of clustered data poses problems: Firstly, authors often fail to account for intra class correlation in clustered studies, leading to a 'unit of analysis' error (Divine 1992) - whereby p values are spuriously low, confidence intervals unduly narrow and statistical significance overestimated - causing type I errors (Bland 1997, Gulliford 1999). Secondly, RevMan does not currently support meta-analytic pooling of clustered dichotomous data, even when these are correctly analysed by the authors of primary studies, since the 'design effect' (a statistical correction for clustering) cannot be incorporated.

Where clustering was not accounted for in primary studies, we would have presented these data in a table, with an (*) symbol - to indicate the presence of a probable unit of analysis error. Subsequent versions of this review will seek to contact first authors of studies to seek intra-class correlation co-efficients of their clustered data and to adjust for these using accepted methods (Gulliford 1999). Where clustering has been incorporated into the analysis of primary studies, then we would have also presented these data in a table. No further secondary analysis (including meta-analytic pooling) will be attempted until there is consensus on the best methods of doing so, and until RevMan, or any other software, allows this. A Cochrane Statistical Methods Workgroup is currently addressing this issue. In the interim, individual studies will be very crudely classified as positive or negative, according to whether a statistically significant result ($p<0.05$) was obtained for the outcome in question, using an analytic method that allowed for clustering.

5. Test for heterogeneity
Firstly, we were to consider all the included studies within any comparison to judge clinical heterogeneity. Then we used visual inspection of graphs to investigate the possibility of statistical heterogeneity. This was supplemented using, primarily, the I-squared statistic. This provides an estimate of the percentage of variability due to heterogeneity rather than chance alone. Where the I-squared estimate was greater than or equal to 75%, we interpreted it as indicating the presence of high levels of heterogeneity (Higgins 2005). If inconsistency was high, we would not summate the data, but the data were to be presented separately and we would have investigated the reasons for heterogeneity. The studies responsible for heterogeneity were not to be added to the main body of homogeneous trials by us, but summated and presented separately and reasons for heterogeneity investigated.

6. Addressing publication bias
We entered data from all identified and selected trials into a funnel graph (trial effect against trial size) in an attempt to investigate the likelihood of overt publication bias (Egger 1997).

7. Sensitivity analyses
7.1 We would have performed a sensitivity analysis to assess the impact of our decision to exclude trials with more than 50% loss of participants.

7.2 We would have performed a further sensitivity analysis to assess the impact of the inclusion of studies where the adherence of participants was not assessed by a 'highly objective method' such as pill counts or negligible blood levels.

RESULTS

Description of studies

1. Excluded
Several studies evaluated interventions based on cognitive behaviour therapy or motivational interviewing which had relevance to our review. Typically, however, the interventions under evaluation within studies involved more than simple compliance therapy. Therefore if family group therapy was also part of the treatment intervention we had to exclude these studies. We identified many such studies which we could have listed under excluded studies but we decided to describe only trials for which the focus was medication compliance and appeared to be based upon the principals of motivational interviewing.

We had to exclude Kemp 1996 because the participants also included some people with 'primary affective disorder'. We contacted the study authors but they were unable to provide data excluding ineligible patients. We made a post-hoc decision on the minimum proportion of people with schizophrenia that should be in an included study. Following consultation with colleagues, we decided to widen our inclusion criteria to include studies where >80% of randomised people were diagnosed with schizophrenia or related psychotic illness. Kemp 1996 did not meet these revised inclusion criterion. Spooren 1998 also included people with mood and substance misuse disorders. In this case we did not contact the authors because the intervention also did not meet our inclusion criteria as it involved aspects of family therapy and psychoeducation. We felt this to be broader than our definition of compliance therapy. Finally we also excluded Barrowclough 2001 because it provided a family or caregiver as part of the experimental intervention.

2. Ongoing studies
We did not identify any ongoing studies.

3. Awaiting assessment
We identified one potentially relevant study published in Chinese (Xu 1999) which is currently awaiting assessment.

4. Included
We only identified one small (n=56) study for inclusion in this review (O'Donnell 2003).

4.1 Length of trials
The single included trial was conducted over a period of two years, although all data except 'inpatient days' were available only at one-year follow up.

4.2 Participants in O'Donnell 2003 were consenting patients from 94 consecutive admissions to inpatient care. These people were aged 18-65 with an an IQ of more than 80. All were fluent English speakers and had no evidence of organic disease. An operational (DSM III-R) diagnosis of schizophrenia was confirmed using a structured clinical interview (SCID).

4.3 Setting
O'Donnell 2003 was conduced in an urban catchment area of Dublin, Ireland.

4.4 Study size
O'Donnell 2003 randomised 56 people.

4.5 Interventions
O'Donnell 2003 defined compliance therapy as a cognitive behavioural intervention with techniques adopted from motivational interviewing, cognitive therapy and psychoeducation. Compliance therapy was conducted according to a manual (Kemp 1996) and delivered over five sessions, each lasting 30-60 minutes. The patient's illness history, understanding of illness, ambivalence to treatment, maintenance treatment and stigma regarding mental illness were reviewed during the therapy sessions. The control therapy 'non-specific counseling' also consisted of five sessions of 30-60 minutes each. However, when patients raised matters relating to medication, they were advised to discuss these matters with their treating teams.

4.6 Outcomes and outcome scales/interviews

4.6.1 Patient adherence
O'Donnell 2003 measured compliance with medication using a structured clinical interview (Adams 1993). This uses a four point scale: 1 for 0-24% compliance (non-compliant or consistently irregular), 2 for 25-49% compliance (frequently irregular), 3 for 50-74% compliance (irregular) and 4 for 75-100% compliance (regular). The trialists sought further information from family members and health professionals to adjust compliance ratings. O'Donnell 2003 rated people who scored less than or equal to three on this scale as having sub-optimal compliance.

4.6.2 Attitudes to medication
Attitudes to medication were rated using the Drug Attitude Inventory (DAI, Hogan 1983). This is a self report questionnaire containing 30 (long form) or 10 (short form) items relating to the

need and likely effects of medication. Each item is scored TRUE/FALSE with higher scores describing more positive attitudes to medication.

4.6.3 Mental state
Symptoms were measured using the positive and negative syndrome scale (PANSS, Kay 1987), a 30 item observer-rated scale with each item rated from one (absent) to seven (extreme). The rater determines the severity of the symptom by reference to particular criteria. The scale is divided into three sub scales: negative symptoms (seven items), positive symptoms (seven items) and general psychopathology (16 items).

4.6.4 Insight
This was measured using the schedule for assessment of insight (SAI, David 1990), a scale made up of three distinct components: (a) adherence to treatment, (b) recognition of having a mental illness and (c) ability to recognise psychotic phenomena as abnormal.

4.6.5 Global functioning
Global functioning was assessed using the 90-point global assessment of functioning scale (GAF, Endicott 1976). The GAF scale is rated with respect to psychological and occupational functioning.

4.6.6 Quality of life
O'Donnell 2003 rates quality of life using the Heinrichs Quality of Life Scale (QLS, Heinrichs 1984), a 21 item scale with each item rated 0-6. The scale is rated by semi-structured interview providing information on symptoms and functioning in the previous four weeks. The scale provides scores along the following dimensions (interpersonal relations and social network, instrumental role functioning, intrapsychic foundations and common objects and activities).

Risk of bias in included studies

1. Randomisation
O'Donnell 2003 stated that the study was randomised using "odd and even digits from a standard table of random numbers". The method of randomisation was poorly described and the method of allocation concealment was not stated.

2. Blinding of outcome assessment
In O'Donnell 2003 outcomes were rated by a researcher who was said to be blind to the intervention delivered. No details are given regarding how this blinding was maintained or of testing of the blinding.

3. Non-entry and treatment dropout
O'Donnell 2003 accounted for all participants at each stage of the trial. However, reasons for dropout during and following period were not given, except in respect of one person who died before they could provide outcome data.

4. Outcome reporting
Dichotomous outcomes were reported for all study people, whether they completed therapy or not. Continuous outcomes were reported at one year follow up (24 randomised to non-specific counseling and 26 randomised to compliance therapy) although it is unclear whether all people who completed follow up provided data for every outcome.

5. Overall quality
O'Donnell 2003 falls within category B of The Cochrane Collaboration Reviewers' Handbook (Higgins 2005) and is therefore at moderate risk of biased results.

Effects of interventions

1. The search
The original search in March 2002 yielded 482 references from which we sought 102 papers in full text. We contacted the authors of Kemp 1996 for further data, but ultimately the study did not fulfil our inclusion criteria. The original search was updated in 2004, yielding 179 additional articles, from which we sought 20 articles in full text. One study met our inclusion criteria (O'Donnell 2003). The original search was updated again in June 2005 and a further 50 articles identified, none of which met our inclusion criteria.

2. COMPARISON 1. COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELING

2.1 Attitudes to treatment
2.1.1 Non-compliance with medication
Dichotomous data on medication compliance was given in O'Donnell 2003 which compared compliance therapy with non-specific counseling, given as a supplement to usual care. The results at one year tended to favour the control group (n=56, RR 1.23 CI 0.74 to 2.05) but showed no statistically significant difference.

2.1.2 Attitude scores
Continuous data on attitudes to treatment in one study also showed no significant difference between compliance therapy and non-specific counseling (1 study, n=50, WMD -2.10 CI -6.11 to 1.91).

2.1.3 Compliance with follow-up arrangements
No useable data were available for this outcome.

2.2 Death, suicide or natural causes
In O'Donnell 2003 one death is reported in the compliance therapy arm of the trial. No deaths were reported in patients randomised to the non-specific counseling.

2.3 Leaving the study early
O'Donnell 2003 reports how four people left the non-specific counseling arm of the trial (two did not complete therapy and two refused follow-up) and two left the compliance therapy arm of the trial (one did not complete therapy, one death occurred) (n=56, RR 0.5 CI 0.1 to 2.51).

2.4 Mental state
We found no significant difference in terms of average PANSS scores (n=50, WMD 6.1 CI -4.54 to 16.74) although the results tended to non-significantly favour non-specific counseling over compliance therapy.

2.5 Insight
No significant difference was found in terms of the average score on the scale used (SAI, n=50, WMD -0.5 CI -2.43 to 1.43).

2.6 Extrapyramidal adverse effects
No study reported this outcome.

2.7 Global functioning
O'Donnell 2003 found no significant difference in terms of the average scores on the GAF measure (n=50, WMD -4.20 CI -16.42 to 8.02).

2.8 Quality of life
O'Donnell 2003 reports data but found no significant difference was found between compliance therapy and non-specific counseling (n=50, WMD QLS -3.40 CI -16.25 to 9.45).

2.9 Service use
The average number of days in hospital was reduced for those allocated to the compliance therapy but data are skewed and we are unclear if these differences are statistically significant.

2.10 Costs
We found no useable data for this outcome.

3. Sensitivity analyses
Sensitivity analyses were not possible given the paucity of data.

DISCUSSION

1. General issues
1.1 Paucity of data
The greatest problem we found in assessing the efficacy of compliance therapy for people with schizophrenia was the lack of suitably conducted trials. In Kemp 1996, where a trial assessing compliance therapy had indeed been conducted, unfortunately the sample included people with affective disorders. We were unable to obtain any new data from this study for only participants relevant to this review.

Given that the only eligible study we found involved only 56 people, whatever the findings of this study, compliance therapy must therefore still be considered an experimental intervention.

1.2 Reporting of data
O'Donnell 2003 is quite clearly reported. If better concealment of allocation had taken place the results may have been less prone to bias.

2. COMPARISON 1. COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELING

2.1 Attitudes to treatment
By one year there is no convincing evidence that compliance therapy improves adherence with prescribed medication compared to non-specific counseling, when given in addition to routine care. Of course ODonnell 2003 is small, and may have failed to detect a significant advantage of either compliance therapy or non-specific counseling due to low statistical power. When the Drug Attitude Inventory is used to score attitude to medication, however, it too does not really suggest any effect of the compliance therapy.

2.2 Death
There are far too little data for us to be able to draw any conclusion regarding this outcome.

2.3 Leaving the study early
What is notable here is that few left this study by one year (˜10%) in stark contrast to many trials undertaken in order to evaluate drug treatments. There is no suggestion that compliance therapy is off putting but there are too few data for us to be certain.

2.4 Mental state, insight, adverse effects and global functioning
There is no evidence from the O'Donnell 2003 study that compliance therapy is associated with a better clinical response than non-specific counseling on the series of scales used to measure these parameters.

2.5 Quality of life
O'Donnell 2003 used a quality of life measure but, again, found no evidence of a real change caused by the experimental intervention. Again, this small study may have failed to detect a significant advantage of either compliance therapy or non-specific counseling on quality of life due to low statistical power.

2.6 Service use: Inpatient bed occupancy
There is a real difficulty interpreting these continuous data that are so skewed. It is intriguing that both one and two year follow up data were suggesting that the compliance therapy group were consistently less using hospital than those allocated to the standard care. For this result, more than any other, this trial should be repeated and more data produced. O'Donnell 2003 has generated an important hypothesis that compliance therapy may not generate much change in standard measures of mental state, quality of life and global functioning, but it may reduce time spent in hospital care.

AUTHORS' CONCLUSIONS

Implications for practice

1. For people with schizophrenia
There is no evidence to suggest that compliance therapy is helpful in terms of adherence, psychotic symptoms or quality of life. The compliance therapy approach may, however, reduce the time spent in hospital, although this is not known for certain. People with schizophrenia should be reassured that this is an experimental approach that has not been shown to cause harm and may really help reduce hospitalization. It would seem that this approach is likely to be safe to be the focus of a randomised trial as there is no evidence it causes harm and some that it may do some tangible good.

2. For clinicians
There is little or no evidence to support or refute the use of compliance therapy in usual clinical care. More trials are needed to clarify whether it has any beneficial effect for people with schizophrenia and it is here that clinicians could help create good evidence. If compliance therapy really could reduce admission times across 24 months it could be have a major part to play in the routine care of people with schizophrenia.

3. For managers and policy makers
If the reduction of time spent in hospital could be replicated, compliance therapy could significantly contribute to improved care and cost savings. There is not enough evidence upon which to base policy but there should be.

Implications for research

1. General
O'Donnell 2003 was well reported but more information on allocation concealment would have been useful. Full compliance with CONSORT (Moher 2001) would have been helpful. Other data from two excluded studies would have been most helpful as, in reality, at least as many people with schizophrenia again as were in O'Donnell 2003 have been randomised to compliance therapy in trials. However, relevant data from Kemp 1996 and Spooren 1998 were not possible to extricate from information on the effects of

the therapy on a series of other mental health conditions. A central repository of data from past trials would have been useful but is likely to be many years off.

2. More well designed, conducted and reported randomised trials
Future trials, such as the one we have outlined in Table 1, should ensure that a clear description of the interventions is given and that any effects of compliance therapy are not confounded by other potentially active interventions. We do feel that such a study is justified from the results of O'Donnell 2003 as this small trial did suggest a real saving of days in hospital care. Such a study would only be meaningful, however, if undertaken within usual resources available to routine care and measure outcomes of relevance to clinicians and recipients of care as well as researchers. Study samples should include people with schizophrenia and closely related disorders, or at least allow data on this group of people to be extracted from the paper.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

O'Donnell 2003

Methods	Allocation: 'table of random numbers', concealment: unclear. Blindness: patients and therapists not blind, assessors blind, although no details are given. Duration: 2 years. Setting: in hospital at start of study.
Participants	Diagnosis: schizophrenia (DSM-III-R) and IQ>80. N=56. Age: 18-65, mean 32 years. Sex: 41 men, 15 women. History: 7 first episode schizophrenia.
Interventions	1. Compliance therapy: administered according to manual of Kemp and David, given over 5 sessions of 30-60 minutes. N=28. 2. Non-specific' counseling: delivered over 5 sessions of 30-60 minutes duration. N=28.
Outcomes	Compliance: clinical interview. Attitudes to treatment: DAI. Insight: SAI. Mental state: PANSS.

O'Donnell 2003 *(Continued)*	Level of functioning: GAF. Quality of life: QLS. Service use: bed occupancy.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

General abbreviations:
IQ - Intelligence Quotient
N - Number of people in the study
Diagnostic tools:
DSM-III-R - Diagnostic and Statistical Manual of Diseases, third revision, revised.
Rating scales:
DAI - Drug Attitude Inventory
SAI - Schedule for the Assessment of Insight
PANSS - Positive and Negative Syndrome Scale
GAF - Global Assessment of Functioning
QLS - Heinrich's Quality of Life Scale

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

Study	Reason for exclusion
Barrowclough 2001	Allocation: randomised. Participants: people with schizophrenia. Interventions: routine care versus motivational nterviewing, CBT and family/caregiver intervention, not simply compliance therapy.
Kemp 1996	Allocation: randomised. Participants: people with schizophrenia, related psychotic disorders and primary affective disorder, unclear how many suffered from schizophrenia.
Spooren 1998	Allocation: randomised. Participants: people with schizophrenia, substance misuse disorders, mood disorder and adjustment disorder, unclear how many suffered from schizophrenia.

DATA AND ANALYSES

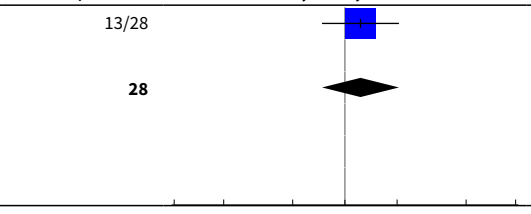
Comparison 1. COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Attitudes to treatment: 1. Non-compliance with medication - by 1 year	1	56	Risk Ratio (M-H, Fixed, 95% CI)	1.23 [0.74, 2.05]

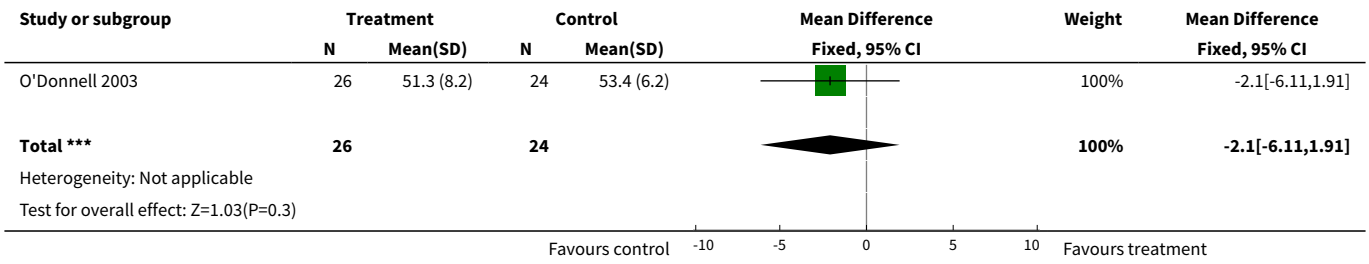
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
2 Attitudes to treatment: 2. Average endpoint score - by 1 year (DAI, high = poor)	1	50	Mean Difference (IV, Fixed, 95% CI)	-2.10 [-6.11, 1.91]
3 Death - by 1 year	1	56	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 70.64]
4 Leaving the study early for any reason - by 1 year	1	56	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.10, 2.51]
5 Mental state: Average endpoint score - by 1 year (PANSS, high = poor)	1	50	Mean Difference (IV, Fixed, 95% CI)	6.10 [-4.54, 16.74]
6 Insight: Average endpoint score - by 1 year (Schedule for the Assessment of Insight, high = poor)	1	50	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-2.43, 1.43]
7 Global functioning: Average endpoint score - by 1 year (GAF, high = poor)	1	50	Mean Difference (IV, Fixed, 95% CI)	-4.20 [-16.42, 8.02]
8 Quality of life: Average endpoint score - by 1 year (QLS, high = poor)	1	50	Mean Difference (IV, Fixed, 95% CI)	-3.40 [-16.25, 9.45]
8.1 Quality of life scale	1	50	Mean Difference (IV, Fixed, 95% CI)	-3.40 [-16.25, 9.45]
9 Service use: Inpatient bed occupancy (high = poor, skewed data)			Other data	No numeric data
9.1 one year follow up			Other data	No numeric data
9.2 two year follow up			Other data	No numeric data

Analysis 1.1. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 1 Attitudes to treatment: 1. Non-compliance with medication - by 1 year.

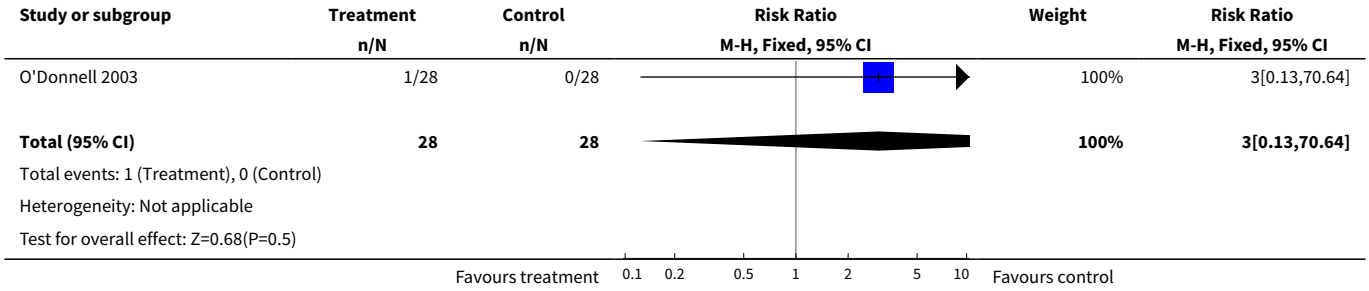
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
O'Donnell 2003	16/28	13/28		100%	1.23[0.74,2.05]
Total (95% CI)	**28**	**28**		**100%**	**1.23[0.74,2.05]**
Total events: 16 (Treatment), 13 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.8(P=0.43)					



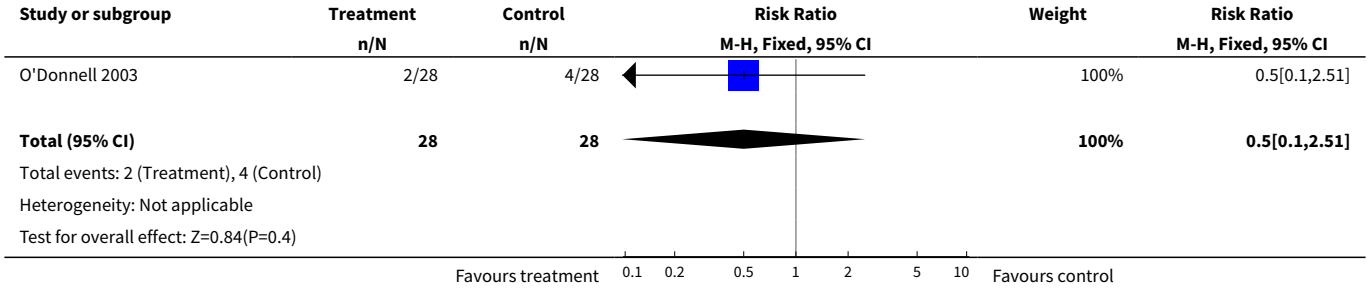
Analysis 1.2. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 2 Attitudes to treatment: 2. Average endpoint score - by 1 year (DAI, high = poor).



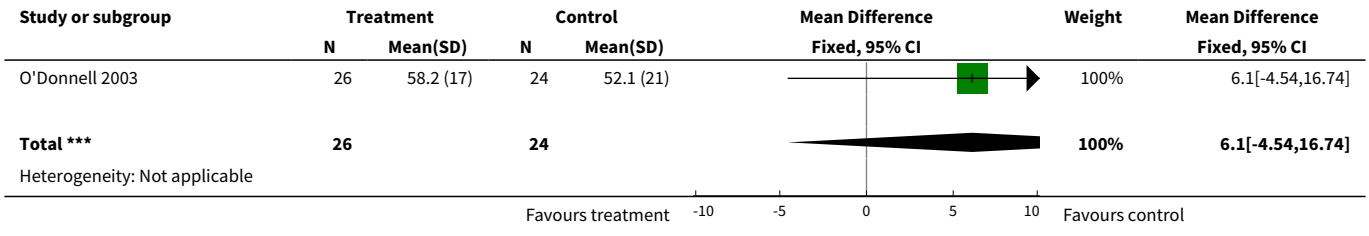
Analysis 1.3. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 3 Death - by 1 year.

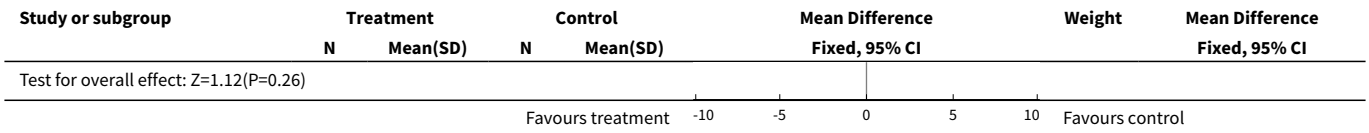


Analysis 1.4. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 4 Leaving the study early for any reason - by 1 year.

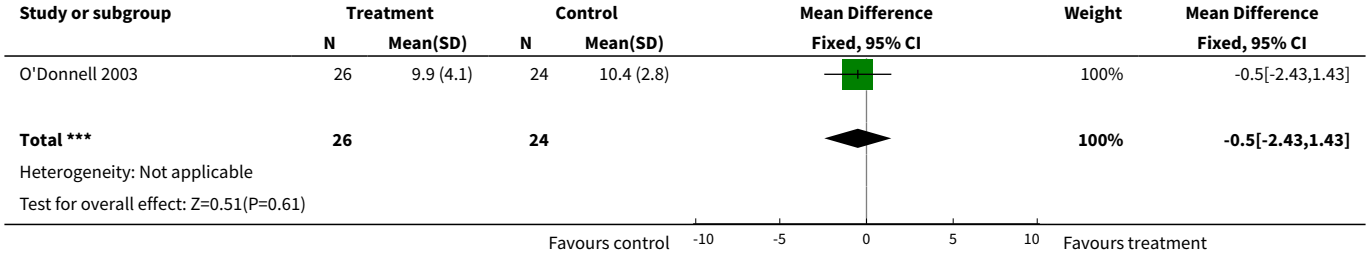


Analysis 1.5. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 5 Mental state: Average endpoint score - by 1 year (PANSS, high = poor).

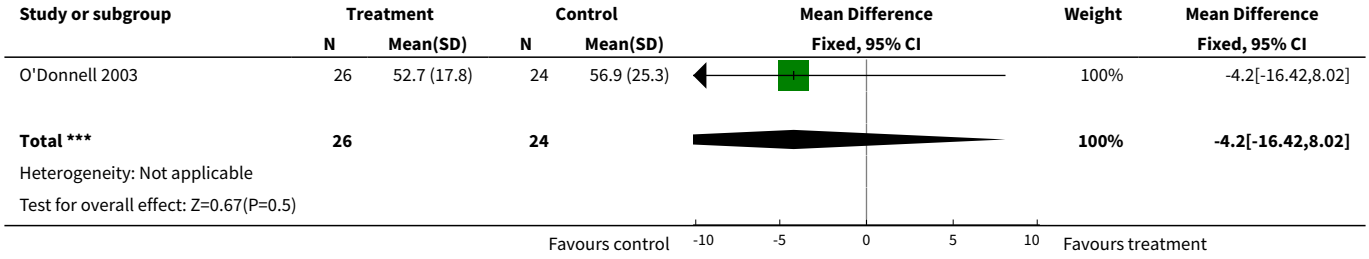




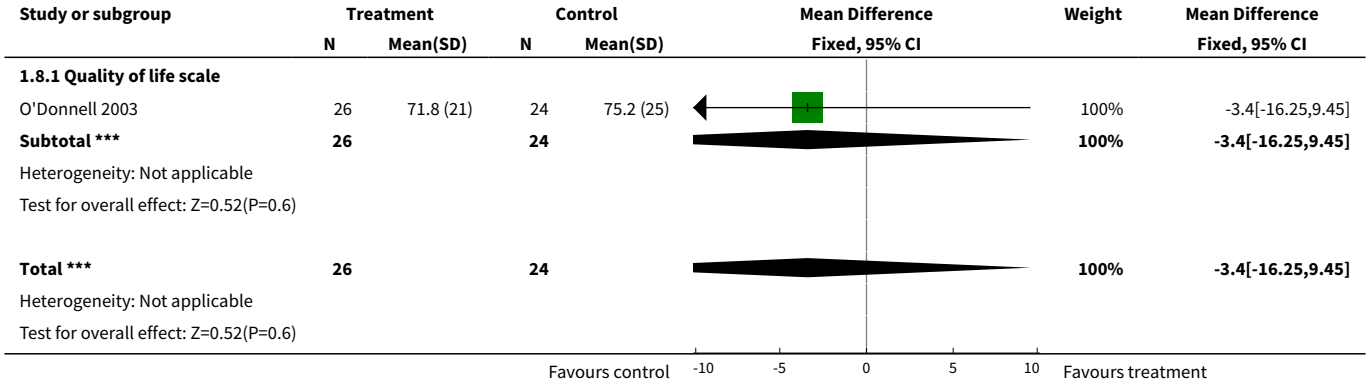
Analysis 1.6. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 6 Insight: Average endpoint score - by 1 year (Schedule for the Assessment of Insight, high = poor).



Analysis 1.7. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 7 Global functioning: Average endpoint score - by 1 year (GAF, high = poor).



Analysis 1.8. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 8 Quality of life: Average endpoint score - by 1 year (QLS, high = poor).



Analysis 1.9. Comparison 1 COMPLIANCE THERAPY versus NON-SPECIFIC COUNSELLING, Outcome 9 Service use: Inpatient bed occupancy (high = poor, skewed data).

Service use: Inpatient bed occupancy (high = poor, skewed data)				
Study	**Intervention**	**N**	**Mean (days)**	**SD**
one year follow up				
O'Donnell 2003	Compliance therapy	26	26	45
O'Donnell 2003	Non-specific counselling	24	33	57
two year follow up				
O'Donnell 2003	Compliance therapy	26	43	60
O'Donnell 2003	Non-specific counselling	24	50	70

ADDITIONAL TABLES

Table 1. PICO table

Methods	Participants	Interventions	Outcomes	Notes
Allocation: randomised, concealment clear. Blindness: patients and therapists not blind, assessors blind. Duration: 2 years. Setting: in hospital at start of study, community follow up.	Diagnosis: people with schizophrenia or related disorders. N=300.* Age: working age adults. Sex: men & women. History: people in their first episode reported separately.	1. Compliance therapy: administered according to manual of Kemp and David, given over 5 sessions of 30-60 minutes. N=150. 2. Non-specific' counseling: delivered over 5 sessions of 30-60 minutes duration. N=150.	Service use: bed occupancy (primary outcome). Compliance: clinical interview. Other routinely recorded measures of mental state, quality of life, general functioning, adverse effects and service use.	* Powered to be reasonably confident of finding a 10% difference between groups for the primary outcome.

WHAT'S NEW

Date	Event	Description
22 October 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

Andrew McIntosh - initiation of the review, protocol production, searching, data extraction, analysis, data interpretation and writing the final report.

Louise Conlon - searching and writing the final report.

Stephen Lawrie - protocol production, searching, data interpretation and writing the final report.

Andrew Stanfield - searching, data extraction, data interpretation and writing the final report.

DECLARATIONS OF INTEREST

SL has been paid for speaking about critical appraisal by employees of the manufacturers of olanzapine, quetiapine, risperidone, and ziprasidone, and has been paid to speak about the management of schizophrenia by employees of the manufacturers of amisulpiride, olanzapine, risperidone, and clozapine.

SOURCES OF SUPPORT

Internal sources

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- National University of Ireland, Ireland.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Patient Compliance; Antipsychotic Agents [*therapeutic use]; Confidence Intervals; Recurrence; Risk; Schizophrenia [*drug therapy]

MeSH check words

Humans