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Nidotherapy for people with schizophrenia.

Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD009929.

DOI: 10.1002/14651858.CD009929.pub2.

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Nidotherapy for people with schizophrenia

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Editorial group: Cochrane Schizophrenia Group.

Publication status and date: Edited (no change to conclusions), published in Issue 5, 2013.

Citation: Chamberlain IJ, Sampson S. Nidotherapy for people with schizophrenia. *Cochrane Database of Systematic Reviews* 2013, Issue 3. Art. No.: CD009929. DOI: 10.1002/14651858.CD009929.pub2.

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ABSTRACT

Background

Nidotherapy is a therapeutic method that principally aims to modify the environment of people with schizophrenia and other serious mental illnesses, whilst working in conjunction with, or alongside other treatments. Rather than focusing on direct treatments or interventions, the aim is to help the individual identify the need for, and work to effect environmental change with the aim of minimising the impact of any form of mental disorder on the individual and society.

Objectives

To review the effects of nidotherapy added to standard care, compared with standard care or no treatment for people with schizophrenia or related disorders.

Search methods

We searched the Cochrane Schizophrenia Group Trials Register (December 2011) and supplemented this by contacting relevant study authors, handsearching nidotherapy articles and manually searching reference lists.

Selection criteria

All randomised controlled trials (RCTs) that compared nidotherapy with standard care or no treatment.

Data collection and analysis

We independently selected and quality assessed potential trials. We reliably extracted data. We calculated risk ratios (RR) and 95% confidence intervals (CI) of homogeneous dichotomous data. Scale data were only extracted from valid scales. For non-skewed continuous endpoint data, we estimated mean difference (MD) between groups. Skewed data have been presented in the Data and analyses as 'other data', with acknowledged means and standard deviations. We assessed risk of bias for the included study and used GRADE to create a 'Summary of findings' table.

Main results

We included only one study that compared nidotherapy-enhanced standard care with standard care alone (total 52 participants); this study was classified by its authors as a 'pilot study'. The duration of the included study was 18 months in total. The single study examined the short-term (up to six months) and medium-term (between six and 12 months) effects of nidotherapy-enhanced standard care versus standard care.

Nidotherapy-enhanced standard care was favoured over standard care for social functioning in both the short term (n = 50, 1 RCT, MD -2.10, 95% CI -4.66 to 0.46) and medium term (n = 37, 1 RCT, MD -1.70, 95% CI -4.60 to 1.20, *Very low quality*); however, these results did not reach statistical significance. Results concerning engagement with non-inpatient services favoured the intervention group in both the short term (n = 50, 1 RCT, MD 2.00, 95% CI 0.13 to 3.87) and medium term (n = 37, 1 RCT, MD 1.70, 95% CI -0.09 to 3.49), with statistical significance evident in the short term, but not in the medium term. Results of people leaving the study early favoured the intervention in the short term (n = 52, 1 RCT, RR 0.86, 95% CI 0.06 to 12.98), with slight favour of the control group at medium term (n = 50, 1 RCT, RR 0.99, 95% CI 0.39 to 2.54); again, these results did not reach statistical significance. Results for the adverse effects/events of death (measured by 12 months) favoured the intervention (n = 52, 1 RCT, RR 0.29, 95% CI 0.01 to 6.74, *Very low quality*) but with no statistical significance. Skewed results were available for mental state, service use, and economic outcomes, and present a mixed picture of the benefits of nidotherapy.

Authors' conclusions

Further research is needed into the possible benefits or harms of this newly-formulated therapy. Until such research is available, patients, clinicians, managers and policymakers should consider it an experimental approach.

PLAIN LANGUAGE SUMMARY

Nidotherapy for schizophrenia

Nidotherapy (from the Latin '*nidus*' or 'nest') aims at identifying the need for and making changes to a person's environment and surroundings. It works alongside other treatments to make improvements to a person's well being, housing, money management, personal relationships, work and other factors. The aim of nidotherapy is not to change the person (whereas other psychological therapies often aim to make changes in an individual's behaviour, emotions and thinking) but to create a better 'fit' between the environment and the individual. As a consequence the individual may improve, but this is not a direct result of treatment but because a more harmonious relationship has been created with the environment. Benefits of nidotherapy may include improvements in people's relationships, self-esteem, taking their medication, mental health and generally creating a better life situation. If environmental factors or someone's surroundings are at all responsible for causing illness and relapse, then nidotherapists and people with schizophrenia can identify these factors together to try and reduce the number and severity of relapses.

This review includes one small pilot study with 52 participants. The study compared nidotherapy with standard care versus standard care alone and lasted 18 months. Findings suggest some limited evidence that those who received nidotherapy might experience a slight improvement in social functioning or personal relationships, mental state and may spend less time as inpatients in hospital over the course of 12 months, but there is no information concerning the appropriateness of this for the individual. However, these limited findings need to be treated with considerable caution. The degree of any possible improvements that come from taking part in nidotherapy remain unclear due to the single study's small sample size, incomplete evidence and risk of bias. No evidence is available on the effect of nidotherapy on general functioning, quality of life, taking medication, satisfaction with treatment, employment status or adverse effects. Further research is required to fill this gap in knowledge about the effectiveness, benefits and possible hazards of nidotherapy. Until such a time, people with mental health problems, health professionals, managers and policymakers should consider this new therapy an experimental one.

This summary has been written by a consumer Ben Gray (Benjamin Gray, Service User and Service User Expert, Rethink Mental Illness. Email: ben.gray@rethink.org).

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

NIDOTHERAPY-ENHANCED STANDARD CARE compared to STANDARD CARE for people with schizophrenia						
Patient or population: patients with people with schizophrenia Settings: Intervention: NIDOTHERAPY-ENHANCED STANDARD CARE Comparison: STANDARD CARE						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	STANDARD CARE	NIDOTHERAPY-ENHANCED STANDARD CARE				
Functioning - specific - social - change in average score - medium term (6-12 months) Social Functioning Questionnaire - Key Worker (SFQ-KW) . Scale from: 0 to 24. Follow-up: 12 months		The mean functioning - specific - social - change in average score - medium term (6-12 months) in the intervention groups was 1.7 lower (4.6 lower to 1.2 higher)		37 (1 study)	⊕○○○ very low ^{1,2,3}	
Functioning - general - no important change - medium term (6-12 months) - not measured	See comment	See comment	Not estimable	-	See comment	No study reported this outcome
Mental state - no important change - medium term (6 - 12 months) Brief Psychiatric Rat-	The mean mental state - no important change - medium term (6 - 12 months) in the control groups was	The mean mental state - no important change - medium term (6 - 12 months) in the intervention groups was		37 (1 study)	⊕⊕○○ low ²	Highly skewed data - mental state average scores reported in 'Data and Analy-

ing Scale (BPRS). Scale from: 0 to 96. Follow-up: 12 months	0	0 higher (0 to 0 higher) ⁴				sis' - short term (< 6 months) medium term (6-12 months)
Quality of life - no important change - medium term (6-12 months) - not measured	See comment	See comment	Not estimable	-	See comment	No study reported this outcome
Satisfaction with treatment	Study population		Not estimable	0 (0)	See comment	No study reported this outcome
	See comment	See comment				
	Moderate					
Economic outcomes - total costs (12 months) NHS Reference Costs and unit costs Follow-up: 12 months		The mean economic outcomes - total costs (12 months) in the intervention groups was 0 higher (0 to 0 higher) ⁴		0 (1 study)	⊕⊕○○ low ^{2,5}	Highly skewed data - economic outcomes over 12 months reported in 'Data and Analysis' - direct costs; indirect costs; total costs
Adverse effects - specific - death Number of individual deaths of participants Follow-up: 12 months	Low ⁶		RR 0.29 (0.01 to 6.74)	52 (1 study)	⊕○○○ very low ^{2,7,8}	
	10 per 1000	3 per 1000 (0 to 67)				
	Moderate ⁶					
	50 per 1000	14 per 1000 (0 to 337)				
	High ⁶					

	100 per 1000	29 per 1000 (1 to 674)	
<p>*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).</p> <p>CI: Confidence interval; RR: Risk ratio;</p>			
<p>GRADE Working Group grades of evidence</p> <p>High quality: Further research is very unlikely to change our confidence in the estimate of effect.</p> <p>Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</p> <p>Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</p> <p>Very low quality: We are very uncertain about the estimate.</p>			
<p>¹ Risk of bias: rated 'serious' - co-author of study developed the SFQ scale.</p> <p>² Imprecision: rated 'serious' - only one study reported results on this outcome</p> <p>³ Publication bias: rated 'strongly suspected' - SFQ patient version results mentioned but not reported</p> <p>⁴ See comment</p> <p>⁵ Indirectness: rated 'serious' - all costs presented as an average, with wide scatter of costs in both intervention and control groups</p> <p>⁶ Moderate risk equates with that of control group.</p> <p>⁷ Risk of bias: rated 'serious' - only one death recorded from control group - cause of death unknown; "homicide was suspected but no-one was charged"</p> <p>⁸ Inconsistency: rated 'very serious' - small sample size with one death; unknown facts/ causes leading to death</p>			

BACKGROUND

Description of the condition

Schizophrenia is known to have a lifetime prevalence of between 0.4% and 1.4% (Cannon 1996). The term was first used in print in 1908 by the Swiss psychiatrist Paul Eugen Bleuler to refer to a state in which there is demonstrable 'splitting' of the 'psychic functions' (Bleuler 1908). More recently, it is understood to represent a heterogeneous range of clinical manifestations involving disorders of thought and perception (delusions, hallucinations, thought-form and thought-flow disturbances), emotional disorders (altered affect, excitation, depression), as well as motor, volitional and anxiety disorders. Generally, it is a chronic condition with periodic acute episodes of more intense disturbance, the latter often involving so-called 'positive' symptoms betraying an abnormal mental process (for example hallucinations) and the former involving 'negative' symptoms suggestive of loss of normal function (for example depression). Problems can be exacerbated for those with the diagnosis since much misunderstanding surrounds it; a situation often worsened by sensationalised media coverage of some cases. There are many therapeutic approaches to the treatment of schizophrenia; medications and individual or group therapies are commonly used, and research is ongoing into supportive therapies involving the arts (NICE).

The influence of personal surroundings on mental health has long been considered. Thomas Main and Maxwell Jones were early pioneers in the domain of the 'therapeutic community', a term first used by Main in 1946 to describe a new ethos and practice of 'democratic' care for psychiatric inpatients in which the patient plays a central role in his/her own recovery and to some extent, that of fellow patients (Main 1946). Encouragement towards acceptance of this responsibility was recognised as an important strand of management or recovery, and its use marked a move away from older, more authoritarian models of care. Reliance on enforced sequestration and treatment was thus in many cases supplanted by a greater use of group psychological and psychotherapeutic treatment, supplemented by more judicious use of medication. During the 20th century, the advent of effective anti-psychotic drugs improved symptom control, and facilitated this general trend (Turner 2007). Maxwell Jones and others went on to develop a form of psychotherapy known as 'milieu therapy' within the setting of the therapeutic community in which patients join a group for up to 18 months and engage actively in their own care and that of other patients (Thomson 1986). A great number of therapeutic communities began to flourish worldwide from the 1960s. In the USA their use is particularly notable in the correctional or addiction-recovery setting.

The format of therapeutic community services varies across the UK, but in many areas they are supplemented with out-of-hours telephone or text networks affording users of mental health services greater access to support at times of need, from other service

users or staff. To accommodate the needs of people across a wide geographical area, successful pilots have been undertaken in the context of supporting those with personality disorders, exploring the use of Internet chat rooms (NIMH 2003; Rigby 2008).

In keeping with a climate in which psychiatric treatments are increasingly obliged to take place in outpatient or community settings, 'assertive outreach' became a prominent model for community mental health provision in the UK in 2000. Based on an American model, assertive outreach aims to assist users of mental health services to develop sustainable skills for community living 'by providing them with more intensive support in obtaining the material necessities of life and by placing a greater emphasis on social functioning and quality of life rather than symptoms' (Kent 2005). Supplementary to the assertive outreach model of care is a UK-wide network of therapeutic communities (the Community of Communities, ratified by The Royal College of Psychiatrists), described by the Association of Therapeutic Communities as 'psychologically informed planned environments [...] places where the social relationships, structure of the day and different activities together are all deliberately designed to help people's health and well-being' and which may be run on an inpatient or day-attendance basis.

Against this backdrop, in which the intensive provision of community care seeks to minimize inpatient episodes and create sustainable models of rehabilitation and living, Tyrer has recently developed the concept of 'nidotherapy', a tool specifically designed to assess and optimise the personal, physical, social and economic environment of people with mental health issues (Tyrer 2005a), particularly in those cases where it is felt that personal psychiatric treatment is currently static. In keeping with the assertive outreach model, nidotherapy is also concerned with improving social function and hence general and psychiatric well-being.

Description of the intervention

Nidotherapy is a therapeutic discipline based on the central goal of improving outcomes for the user of mental health services by altering their environment rather than by means of direct treatments or interventions (Tyrer 2003).

Early work with nidotherapy involved assisting those people diagnosed with personality disorders, especially those classified as Type R (treatment-resisting) (Tyrer 2002). However, its use has been widened to include those with other psychiatric disorders including schizophrenia and related disorders (Tyrer 2007).

Nidotherapy is based on five main principles (Tyrer 2005a).

- Collateral collocation (seeing the environment from the point of view of the person with schizophrenia)
- Formulation of realistic environmental targets
- Improvement of social function
- Personal adaptation and control
- Wider environmental integration and arbitrage

These underpin an active process involving five phases.

- Identification of the boundaries of the therapy
- Full environmental analysis
- Implementation of common nidopathway
- Monitoring of progress
- Resetting of nidopathway and completion

As set out in the phases above, a collaborative approach is used to make an assessment of the physical, emotional and social environment of the person; a ready and willing arbiter is considered essential in order to resolve any conflict in this process. On the basis of the assessment, realistic targets are decided upon in order to adjust the environment and thus to bring about improvement in the social functioning of the individual. Target attainment must be regularly monitored in order to provide useful feedback, encouragement, and to revise targets as necessary according to any difficulties encountered (Tyrer 2005a).

How the intervention might work

Nidotherapy concentrates on identifying the need for, and working to effect, environmental change. It seeks to work in conjunction with, or alongside, other treatments in order to achieve a sustainable and monitored improvement in well-being; housing, financial management, relationships and work may be among the factors considered. This may bring secondary benefits in terms of general social functioning, self-esteem, treatment adherence, and mental health, depending on the problems tackled by nidotherapy. The nidotherapist may play a previously unfulfilled role as a social or patient advocate. If environmental factors are at all responsible for precipitation of relapse in chronic conditions, then addressing these factors could help to reduce the number or severity of relapses.

The approach is recommended when the person is not in a state of mental or emotional change due to alterations in treatment or other life circumstances. S/he may or may not accept nidotherapy as an alternative to repeated changes in conventional treatment - particularly if this is perceived to have failed.

Why it is important to do this review

Nidotherapy is a relatively new formalisation of key principles in holistic care. It has a small amount of non-trial literature, including a book, and paid courses exist for the training of nidotherapists. It is unclear as yet how widespread the current adoption of nidotherapy is. It is also unclear how likely it is to provide the intended benefits, or if there are any associated risks. In this review, we sought to examine published data on nidotherapy and to make recommendations for future research into this emerging discipline.

We searched existing Cochrane systematic reviews to ensure that our review did not overlap significantly with them. Other reviews exist that cover the work of community mental health teams

(CMHTs) (Malone 2007), intensive case management (incorporating 'assertive community treatment') (Dieterich 2010), family intervention (Pharoah 2010) and supported housing (Chilvers 2006). A qualitative study has been undertaken by Spencer *et al* to investigate the benefit of nidotherapy in managing mental illness and personality disorder (Spencer 2010).

Nidotherapy merits a dedicated systematic review as an approach that seeks to achieve systematic manipulation of the physical and social environment in order to help persons with persistent or permanent mental disorder achieve a 'better fit' (Tyrer 2005a), whereas, other psychosocial interventions 'aim to target symptom reduction or changes of an individual's affect, behaviour or cognition' (Veale 2010).

OBJECTIVES

To determine whether nidotherapy is of benefit for adults, however defined, with schizophrenia or related disorders.

METHODS

Criteria for considering studies for this review

Types of studies

All relevant randomised controlled trials. If we had included trials that were described in such a way as to imply randomisation, we would have included such trials in a sensitivity analysis (see [Sensitivity analysis](#)). Had their inclusion not resulted in a substantive difference, they would have remained in the analyses. Had their inclusion resulted in statistically significant differences, we would not have added the data from these lower quality studies to the results of the better trials, but would have presented such data within a subcategory. We intended to exclude quasi-randomised studies, such as those allocating by alternate days of the week. Where people were given additional treatments within nidotherapy, we would only have included the data if the adjunct treatments were evenly distributed between groups and only the nidotherapy group was randomised.

Types of participants

Adults, however defined, with schizophrenia or related disorders, including schizophreniform disorder, schizoaffective disorder and delusional disorder, again, by any means of diagnosis.

We were interested in making sure that information is as relevant to the current care of people with schizophrenia as possible so proposed to clearly highlight the current clinical state (acute,

early post-acute, partial remission, remission) as well as the stage (prodromal, first episode, early illness, persistent) and whether the studies primarily focused on people with particular problems (for example, negative symptoms, treatment-resistant illnesses).

Types of interventions

1. Nidotherapy, either alone or in combination with any standard treatment or care. Nidotherapy is defined as 'a treatment that systematically adjusts the environment to suit the needs of a person with a chronic mental illness' (Tyler 2005a) and is based on five main principles.

- Collateral collocation (seeing the environment from the point of view of the person with schizophrenia)
- Formulation of realistic environmental targets
- Improvement of social function
- Personal adaptation and control
- Wider environmental integration and arbitrage

2. Any standard treatment or care, or no treatment. For the purposes of this review, we chose to define 'standard treatment or care' as the normal level of psychiatric treatment or care offered in the region from which the trial population was drawn.

Types of outcome measures

All outcomes have been divided into short term (less than six months), medium term (six to 12 months) and long term (over one year).

Primary outcomes

1. Functioning

1.1 Specific - social

- 1.1.1 Clinically significant change in overall social functioning
- 1.1.2 Clinically significant change in specific aspect of social functioning- as defined by trial authors

Secondary outcomes

1. Functioning

1.1 Specific - social

- 1.1.3 Any change in social functioning - as defined by trial authors
- 1.1.4 Important change in social functioning
- 1.1.5 Average change/endpoint scores

1.2 General

- 1.2.1 Clinically significant change in any other aspect of general functioning - as defined by trial authors
- 1.2.2 Any change in any other aspect of general functioning - as defined by trial authors
- 1.2.3 Important change in any other aspect of general functioning
- 1.2.4 Average change/endpoint scores

2. Mental state

2.1 General

- 2.1.1 Clinically significant change in general mental state - as defined by trial authors
- 2.1.2 Any change in general mental state - as defined by trial authors
- 2.1.3 Important change in general mental state
- 2.1.4 Average change/endpoint scores

2.2 Positive symptoms

- 2.2.1 Clinically significant change in positive symptoms - as defined by trial authors
- 2.2.2 Any change in positive symptoms - as defined by trial authors
- 2.2.3 Important change in positive symptoms
- 2.2.4 Average change/endpoint scores

2.3 Negative symptoms

- 2.3.1 Clinically significant change in negative symptoms - as defined by trial authors
- 2.3.2 Any change in negative symptoms - as defined by trial authors
- 2.3.3 Important change in negative symptoms
- 2.3.4 Average change/endpoint scores

3. Quality of life

3.1 General quality of life

- 3.1.1 Clinically significant change in general quality of life - as defined by trial authors
- 3.1.2 Any change in quality of life - as defined by trial authors
- 3.1.3 Important change in quality of life
- 3.1.4 Average change/endpoint scores

3.2 Physical health

- 3.2.1 Clinically significant change in physical health - as defined by trial authors
- 3.2.2 Any change in physical health - as defined by trial authors
- 3.2.3 Important change in physical health
- 3.2.4 Average change/endpoint scores

3.3 Sexual health

- 3.3.1 Clinically significant change in sexual health - as defined by trial authors
- 3.3.2 Any change in sexual health - as defined by trial authors
- 3.3.3 Important change in sexual health
- 3.3.4 Average change/endpoint scores

4. Service outcomes

4.1 Level of medication use

- 4.1.1 Increase in medication use
- 4.1.2 Decrease in medication use
- 4.1.3 Important change in medication use
- 4.1.4 Average change/endpoint scores

4.2 Change in medication

- 4.2.1 Change in type of medication used
- 4.2.2 Important change in type of medication used

4.3 Engagement with non-inpatient services

- 4.3.1 Increase in engagement with non-inpatient services
- 4.3.2 Decrease in engagement with non-inpatient services
- 4.3.3 Important change in engagement with non-inpatient services
- 4.3.4 Average change/endpoint scores

4.4 Change in type of non-inpatient services

- 4.4.1 Change in type of non-inpatient services used
- 4.4.2 Important change in type of non-inpatient services used

4.5 Hospitalisation

- 4.5.1 Time to hospitalisation
- 4.5.2 Number of inpatient episodes
- 4.5.3 Duration of inpatient episodes
- 4.5.4 Average change scores

5. Satisfaction with treatment

- 5.1 Important change in satisfaction with treatment - as defined by trial authors
- 5.2 Any change in satisfaction with treatment - as defined by trial authors
- 5.3 Important change in satisfaction
- 5.4 Average change/endpoint scores

6. Employment status

- 6.1 Positive change (however defined) in employment status
- 6.2 Negative change (however defined) in employment status
- 6.3 Important change in employment status

7. Economic outcomes

- 7.1 Direct costs - as defined by trial authors
- 7.2 Indirect costs - as defined by trial authors
- 7.3 Cost-effectiveness - as defined by trial authors

8. Leaving the study early

- 8.1 Issues relating to nidothrapy
- 8.2 Issues not relating to nidothrapy

9. Adverse effects/events

- 9.1 Risks of therapy
- 9.2 Death
- 9.3 Other adverse effects/events

10. 'Summary of findings' tables

We used the GRADE approach to interpret findings ([Schünemann 2008](#)) and used GRADE profiler ([GRADEPRO](#)) to import data from RevMan 5 ([Review Manager](#)) to create 'Summary of findings' tables. These tables provide outcome-specific information concerning the overall quality of evidence from each included study in the comparison, the magnitude of effect of the interventions examined, and the sum of available data on all outcomes we rated as important to patient care and decision making. We selected the following main outcomes for inclusion in the '[Summary of findings for the main comparison](#)'.

1. Social functioning
2. General functioning
3. Mental state
4. Quality of life
5. Satisfaction with treatment
6. Economic outcomes
7. Adverse effects/events

Search methods for identification of studies

Electronic searches

Cochrane Schizophrenia Group Trials Register

The Trials Search Co-ordinator of the Cochrane Schizophrenia Group searched the register (14 December 2011) using the phrase: [*nidoththerapy* in title, abstract and index terms of REFERENCE or interventions of STUDY]

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

Searching other resources

1. Reference searching

We inspected the references of the one included study for further relevant studies.

2. Personal contact

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

Data collection and analysis

Selection of studies

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

Data extraction and management

1. Extraction

Review authors IJC and SS extracted data from the single included study. Had there been several included studies, CEA would have independently extracted data from a random sample of these studies, comprising 10% of the total, to ensure reliability. Again, any disagreement would have been discussed, decisions documented

and, if necessary, authors of studies contacted for clarification. With any remaining problems, CEA would have helped to clarify issues and any final decisions would have been documented. Data presented only in graphs and figures were extracted whenever possible, but included only if both review authors independently had the same result. We contacted authors through an open-ended request in order to obtain missing information or for clarification whenever necessary. If we had included multi-centre studies, where possible, we would have extracted data relevant to each component centre separately.

2. Management

2.1 Forms

We extracted data onto standard, simple forms.

2.2 Scale-derived data

We included continuous data from rating scales only if:

- a. the psychometric properties of the measuring instrument had been described in a peer-reviewed journal ([Marshall 2000](#)); and
- b. the measuring instrument had not been written or modified by one of the trialists for that particular trial.

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

2.3 Endpoint versus change data

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

2.4 Skewed data

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

- a) standard deviations (SDs) and means are reported in the paper or obtainable from the authors;
- b) when a scale starts from the finite number zero, the SD, when multiplied by two, is less than the mean (as otherwise the mean is

unlikely to be an appropriate measure of the centre of the distribution, (Altman 1996);

c) if a scale started from a positive value (such as the Positive and Negative Syndrome Scale (PANSS) (Kay 1986) which can have values from 30 to 210), the calculation described above was modified to take the scale starting point into account. In these cases skew is present if $2\text{ SD} > (S - S_{\min})$, where S is the mean score and $S_{\min}$ is the minimum score. Endpoint scores on scales often have a finite start and end point and these rules can be applied. When continuous data are presented on a scale that includes a possibility of negative values (such as change data), it is difficult to tell whether data are skewed or not. We entered skewed endpoint data from studies of less than 200 participants as 'other data' within the [Data and analyses](#) section rather than into a statistical analysis. Skewed data pose less of a problem when looking at means if the sample size is large and were entered into syntheses.

2.5 Common measure

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

2.6 Conversion of continuous to binary

Where possible, efforts were made to convert outcome measures to dichotomous data. This can be done by identifying cut-off points on rating scales and dividing participants accordingly into 'clinically improved' or 'not clinically improved'. It is generally assumed that if there is a 50% reduction in a scale-derived score such as the Brief Psychiatric Rating Scale (BPRS, Overall 1962) or the PANSS (Kay 1986), this could be considered as a clinically significant response (Leucht 2005; Leucht 2005a). If data based on these thresholds were not available, we used the primary cut-off presented by the original authors.

2.7 Direction of graphs

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

Assessment of risk of bias in included studies

Review authors IJC and SS worked independently to assess risk of bias by using criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to assess trial quality. This set of criteria is based on evidence of associations between overestimate of effect and high risk of bias of the article

such as sequence generation, allocation concealment, blinding, incomplete outcome data and selective reporting.

If the raters disagreed, the final rating was made by consensus, with the involvement of another member of the review group. Where inadequate details of randomisation and other characteristics of trials were provided, we contacted authors of the studies to obtain further information. Non-concurrence in quality assessment would have been reported, but any disputes as to which category a trial was to be allocated were resolved by discussion.

The level of risk of bias was noted in both the text of the review and in the [Summary of findings for the main comparison](#)

Measures of treatment effect

1. Binary data

For binary outcomes we calculated a standard estimation of the risk ratio (RR) and its 95% confidence interval (CI). It has been shown that RR is more intuitive (Boissel 1999) than odds ratios and that odds ratios tend to be interpreted as RR by clinicians (Deeks 2000).

2. Continuous data

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

Unit of analysis issues

1. Cluster trials

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

If clustering had not been accounted for in primary studies, we would have presented data in a table, with a (*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review, we will seek to contact first authors of studies to obtain intra-class correlation coefficients (ICCs) for their clustered data and to adjust for this by using accepted methods (Gulliford 1999). Had clustering been incorporated into the analysis of primary studies, we would have presented these data

as if from a non-cluster randomised study, but adjusted for the clustering effect.

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

If cluster studies were appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies would have been possible using the generic inverse variance technique.

2. Cross-over trials

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

3. Studies with multiple treatment groups

We planned that if a study involved more than two treatment arms, if relevant, the additional treatment arms would have been presented in the comparisons. If data were binary these would simply have been added and combined within the two-by-two table. If data were continuous, we would have combined the data following the formula in section 7.7.3.8 (Combining groups) of the *Cochrane Handbook for Systematic Reviews of Interventions*. Where the additional treatment arms were not relevant, these data would not have been reproduced.

Dealing with missing data

1. Overall loss of credibility

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

2. Binary

In the case where attrition for a binary outcome was between 0% and 50% and where these data were not clearly described, we intended to present data on a 'once-randomised-always-analyse' basis (an intention-to-treat analysis). Those leaving the study early are all assumed to have the same rates of negative outcome as those who completed, with the exception of the outcome of death and adverse effects. A sensitivity analysis would have been undertaken to test how prone the primary outcomes were to change when 'completer' data only were compared with the intention-to-treat analysis using the above assumptions.

3. Continuous

3.1 Attrition

In the case where attrition for a continuous outcome was between 0% and 50% and completer-only data were reported, we reproduced these.

3.2 Standard deviations

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

3.3 Last observation carried forward

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

Assessment of heterogeneity

1. Clinical heterogeneity

We planned to consider all included studies initially, without seeing comparison data, to judge clinical heterogeneity. We would simply have inspected all studies for clearly outlying people or situations which we had not predicted would arise. Had such situations or participant groups arisen, these would have been fully discussed.

2. Methodological heterogeneity

We intended to consider all included studies initially, without seeing comparison data, to judge methodological heterogeneity. We would simply have inspected all studies for clearly outlying methods which we had not predicted would arise. Had such methodological outliers arisen these would have been fully discussed.

3. Statistical heterogeneity

3.1 Visual inspection

We planned to visually inspect graphs to investigate the possibility of statistical heterogeneity.

3.2 Employing the I^2 statistic

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

Assessment of reporting biases

1. Protocol versus full study

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results. These are described in section 10.1 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We located the protocol to the included randomised trial and compared the outcomes in the protocol to those in the published report.

2. Funnel plot

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). Again, these are described in Section 10 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We are aware that funnel plots may be useful in investigating reporting biases but are of limited power to detect small-study effects. We did not use funnel plots for outcomes (since there was only one included study). In future versions of this review, where funnel plots are possible, we will seek statistical advice in their interpretation.

Data synthesis

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

Subgroup analysis and investigation of heterogeneity

1. Subgroup analyses

There are no subgroup analyses.

2. Investigation of heterogeneity

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

We planned that if unanticipated clinical or methodological heterogeneity were obvious, we would simply state hypotheses regarding these for future reviews or versions of this review. We did not anticipate undertaking analyses relating to these.

Sensitivity analysis

1. Implication of randomisation

If sufficient trials had been included, we would have included trials in a sensitivity analysis if they were described in some way as to imply randomisation. For the primary outcomes, we would have included these studies and if there was no substantive difference when the implied randomised studies were added to those with better description of randomisation, then all data would have been employed from these studies.

2. Assumptions for lost binary data

Where assumptions had to be made regarding people lost to follow-up (see [Dealing with missing data](#)), we compared the findings of the primary outcomes when we used our assumption compared with completer data only. If there was a substantial difference, we reported results and discussed them but continued to employ our assumption.

Where assumptions had to be made regarding missing SDs data (see [Dealing with missing data](#)), we compared the findings on primary outcomes when we used our assumption compared with completer data only. A sensitivity analysis would have been undertaken to test how prone results were to change when 'completer' data only were compared with the imputed data using the above assumption. We planned that if there was a substantial difference, we would report results and discuss them but continue to employ our assumption.

3. Risk of bias

We intended to analyse the effects of excluding trials that were judged to be at high risk of bias across one or more of the domains of randomisation (implied as randomised with no further details available) allocation concealment, blinding and outcome reporting for the meta-analysis of the primary outcome. If the exclusion of

trials at high risk of bias did not substantially alter the direction of effect or the precision of the effect estimates, then data from these trials were to be included in the analysis

4. Imputed values

We also intended to undertake a sensitivity analysis to assess the effects of including data from trials where we used imputed values for ICC in calculating the design effect in cluster randomised trials. If substantial differences were noted in the direction or precision of effect estimates in any of the sensitivity analyses listed above, we would not have pooled data from the excluded trials with the other trials contributing to the outcome, but instead presented them separately.

5. Fixed and random effects

If possible, all data would have been synthesised for a sensitivity analysis using a fixed-effect model, however, we would also have synthesised data for the primary outcome using a random-effects model to evaluate whether this altered the significance of the results.

RESULTS

Description of studies

See: [Characteristics of included studies](#).

Results of the search

The original search identified three potentially relevant studies. After excluding duplicates, one study was inspected closely and ultimately included in the analysis ([Figure 1](#)).

Figure 1. Study flow diagram (all searches)

Included studies

We included only one study that compared nidothrapy-enhanced standard care with standard care alone ([Ranger 2009](#)), classified by its authors as a 'pilot study'. The characteristics of this study are described below (See: [Characteristics of included studies](#)).

1. Length of trial

The duration of the included study ([Ranger 2009](#)) was 18 months in total. The single study examined the short-term (up to six months) and medium term (between six and 12 months) effects of nidothrapy-enhanced standard care versus standard treatment or care. The use of psychiatric beds was measured over a 12-month period, with change from baseline in use of other health service resources, psychiatric symptoms, social functioning and engagement with services measured at six and 12 months.

2. Participants

The included study reported on a total of 52 participants. They predominantly had primary diagnoses of schizophrenia (n = 30) with others experiencing severe mental illness and comorbid personality disturbance, including schizoaffective disorder (n = 10); bipolar disorder (n = 5) and borderline personality disorder (n = 5). Of the participants, 49 had 'differing degrees of severity of full personality disorder' of which 39 participants had Type R (treatment-resisting) personalities; three participants had 'personality difficulty'. Thirty-six participants were drug or alcohol dependent. Included in the trial were 35 men and 17 women; age was not reported.

Racial origin was recorded as white participants n = 31; Black African or Caribbean (n = 12); other (n = 9) - distribution was similar in the two groups.

3. Setting

The included study population was drawn from those receiving assertive community outreach care in central London.

4. Study size

In the included study, there was a sample size of 52; however, the number randomised was not reported (see: [Characteristics of included studies](#)).

5. Interventions

In the included study, the intervention group (those allocated to nidothrapy-enhanced assertive treatment) received up to 15 sessions of nidothrapy (a mean of 20 hours) from two nidotherapists following a standard format (see [Description of the intervention](#) and [Tyrer 2005a](#)).

6. Outcomes

This section describes the outcomes used in the included studies, categorised according to the list of relevant outcomes in the [Methods](#) section and [Summary of findings for the main comparison](#).

6.1 Social functioning

Social Functioning Questionnaire (SFQ) ([Tyrer 2005b](#)).

The SFQ is an adaptation of the Social Function Schedule ([Remington 1979](#)) in the form of an eight-item self-report questionnaire comprising several assertions concerning social functioning. Respondents score between zero and three points in each section, having rated their level of agreement with the assertions. A lower score indicates a better situation in terms of social functioning. Mention is made in the one included study ([Ranger 2009](#)) and in [Tyrer 2005b](#) of differing versions of the SFQ, namely the SFQ subject version and SFQ-KW (SFQ key worker version). [Ranger 2009](#) only reports results from the SFQ-KW.

6.2 General functioning

The included study did not report this outcome.

6.3 Mental state

Brief Psychiatric Rating Scale (BPRS) ([Overall 1962](#)).

The BPRS is a 16-item self-report questionnaire measuring severity of psychiatric symptomatology on a seven-point scale where one equals 'not present' and seven equals 'extremely severe'; thus a total score of 112 is possible, with a lower score representing a better mental state.

6.4 Quality of life

The included study did not report this outcome.

6.5 Service outcomes

The included study reports results from the Engagement and Acceptance Scale (EAS). The review authors understand that the study authors refer to an adaptation of the Homeless Engagement and Acceptance Scale (HEAS) (both scales are explained in [Park 2002](#)). The EAS is a four-point keyworker-completed assessment of the patient's level of engagement with and acceptance of service provision in which a score of up to 15 points may be obtained. A higher score indicates better levels of engagement and acceptance.

6.6 Satisfaction with treatment

The included study did not report this outcome.

6.7 Employment status

The included study did not report this outcome.

6.8 Economic outcomes

Service costs using NHS Reference Costs and unit costs over 12 months ([Department of Health 2005](#)) and the Secure Facilities Service Use Schedule (SFSUS) ([Barrett 2007](#)).

Unit costs were applied to each service. Hospital services were costed using NHS Reference Costs, with published unit costs applied to community health and social services, medication, and criminal justice services ([Ranger 2009](#)). Service costs were assessed using the SFSUS, which covered every possible service contact for those with severe mental illness in secure facilities and in the community ([Ranger 2009](#)).

6.9 Leaving the study early

Number of individuals leaving the study early over the course of 12 months.

6.10 Adverse effects/events

Number of individual deaths of participants over the course of 12 months.

Excluded studies

None.

Ongoing studies

There are no known ongoing studies at the time of writing this review. Through email contact with Peter Tyrer, the review authors understand that there are two planned studies awaiting funding. One of these studies has passed the first stage of the funding process, and will focus on the use of nidothrapy in comorbid psychosis (predominantly schizophrenia) and substance misuse. Details are as yet unavailable for the other planned study.

Awaiting assessment

There are no studies awaiting assessment at the time of writing this review.

Risk of bias in included studies

For a graphical representation of the risk of bias in the single included study see [Figure 2](#) and also the 'Risk of bias' table in [Characteristics of included studies](#). The review authors were able to assess three aspects of the included study as carrying a low risk of bias, but four aspects as having unclear or high risk of bias.

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

Allocation

The method of allocation was stated in the text of the included study to be “randomly allocated by an independent statistician using a random numbers design with no stratification of groups, to either nidothrapy or control groups”. The study authors went on to state that “patients were assessed at baseline and at 6 and 12 months by MR and KI who remained blind of trial allocation”. The review authors therefore elected to consider this a low risk of bias.

Blinding

In an intervention of this nature it is impossible for the patients to be blind to trial allocation during therapy, therefore, since the

assessors were kept blind of trial allocation, the trial can be considered single-blind, although this is not explicitly stated in the report and the method of ensuring this is unclear. It was however stated that “patients were assessed at baseline and at 6 and 12 months by MR and KI who *remained* blind of trial allocation”. MR was external to the team at the time of patient assessment, and was not made aware of the form of management each participant received; she was, however, informed of the general nature of the study. It is not explicitly stated whether or not all the assessors were blind to trial hypotheses, although this seems unlikely given that one of the assessors was the lead author of the study. The review authors therefore elected to consider this a low to unclear risk of bias.

Incomplete outcome data

The included study reported 52 patients randomised from 57 eligible people. A CONSORT diagram of selection of patients and their pathway through the trial is provided in the study report, however, the figures in the diagram and the text are not entirely consistent. Of 24 patients allocated to the control arm, one was lost to follow-up at six months but accounted for (death). Twenty-three are followed up at six months, of which five are lost to follow-up by 12 months (accounted for, with four refusals (no explanation reported) and one change of address). However, only 17 patients are reported to be in the 12-month follow-up group rather than the expected 18. Of 28 allocated to the treatment arm, one was lost to follow-up at six months (accounted for, having refused to continue, but with no explanation as to why). After follow-up at six months of 27 patients, a further six losses to follow-up at 12 months were accounted for by five unexplained refusals and one uncontactable patient. However, only 20 patients are reported to be in the 12-month follow-up rather than the expected 21.

This means that the expected total of patients having 12-month follow-up should be 39, but is reported as 37. The review authors made contact with the trial authors in order to clarify this information; we were notified that a seventh participant had been omitted from the trial report, at the admitted error of the trial authors. Again, in the control group, another seventh participant had been omitted from the trial report; one additional participant who was not accounted for between six to 12 months. This participant did not refuse but had moved to a different area; the trial authors had been unable to contact this person successfully. These clarifications mean that the reported total number of participants at 37 is correct; however, due to the element of poor reporting, the review authors recommend extreme caution when interpreting these data.

Furthermore, the text of the study states that “service use data at 12 months follow-up was available for 48 patients”, where 37 are reported - the reason for which is not stated. The trial authors stated through personal correspondence that each of the 52 participants originally randomised gave permission at baseline to have their data examined even though they may have subsequently refused clinical interview. However, four out of the total 15 participants who left the study early had moved away from the area in which the trial was taking place (two to locations abroad and two others to places where the trial authors were not able to access the data for local ethical reasons). Since permission to assess participants in other areas was not given in the trial author’s original submission, these four participants were excluded from the results of ‘service outcomes’.

For the study authors’ primary outcome at one year and 18 months (duration of inpatient admissions), the study reported on 47 patients. The footnote to the CONSORT diagram reads as follows: “Five patients did not have data recorded on service use over the 12-month period. The patient in the control group who died after two months did not have his data included (except for admission)

and seven patients left the immediate area (one of them to Ireland) and so exact service use not available”.

In terms of the results for secondary study outcomes of clinical symptoms, social functioning and engagement with services, the number in each arm is seen to alter, in some cases upwards, between baseline and six and 12 months. This is not explained in the study text.

The review authors therefore elected to consider this a high risk of bias.

Selective reporting

The Social Functioning Questionnaire (SFQ) has at least two versions known to the review authors: the patient version and the key worker version. The included study methods section indicates that both of these will be used in assessing the patients. In the event, only SFQ-KW results were reported, with the following footnote in the study: “The patient version of the SFQ is not shown; this showed similar findings to the SFQ-KW version but had smaller numbers”.

The review authors therefore elected to consider this a high risk of bias.

In addition, while this did not contribute to the review authors’ assessment of high risk of reporting bias, the authors of the included study did not mention in their methods section the use of the EAS assessment tool, from which they later reported results.

Other potential sources of bias

A co-author of the included study is the main developer and “product champion” of the nidotherapy intervention. The same co-author developed the Social Function Schedule (Remington 1979), from which the SFQ scale is derived (Tyrrer 2005b) and developed the HEAS (Homeless Acceptance and Assessment Scale) from which the EAS (Engagement and Acceptance Scale) (Park 2002) is derived.

While the scales mentioned were unlikely to have been developed with the included study in mind, the review authors elected to consider this an unclear risk of bias.

Effects of interventions

See: [Summary of findings for the main comparison NIDOTHERAPY-ENHANCED STANDARD CARE compared with STANDARD CARE for people with schizophrenia](#)

The review contains one included study (Ranger 2009) hence no meta-analyses were possible. The included study allows for one comparison: nidotherapy-enhanced standard care (the ‘intervention treatment’ referred to below) versus standard care, where ‘standard care’ refers to assertive community outreach treatment. Outcomes are presented below in the order in which they are listed in

the [Types of outcome measures](#) section. Outcomes are measured at short term (<6 months) and medium term (6 - 12 months).

Comparison 1: NIDOTHERAPY-ENHANCED STANDARD CARE versus STANDARD CARE

1. Functioning

1.1 Social functioning

Social functioning was measured in the included study using the SFQ-KW. The results at short and medium term favoured the intervention treatment (short term $n = 50$, 1 RCT, mean difference (MD) -2.10, 95% confidence interval (CI) -4.66 to 0.46, medium term $n = 37$, 1 RCT, MD -1.70, 95% CI -4.60 to 1.20), results which did not reach statistical significance ([Analysis 1.1](#))

2. Mental state

Mental state was measured in the included study using the BPRS. The data concerning this outcome at short and medium term were skewed and are best considered by viewing [Analysis 1.2](#).

3. Service outcomes

3.1 Engagement with non-inpatient services

Engagement with non-inpatient services was measured in the included study using the EAS. The results at short and medium term favoured the intervention treatment (short term $n = 50$, 1 RCT, MD 2.00, 95% CI 0.13 to 3.87, medium term $n = 37$, 1 RCT, MD 1.70, 95% CI -0.09 to 3.49). Statistical significance is evident in the short-term results, but not in the medium term ([Analysis 1.3](#))

3.2 Use of services

Results were available for use of a large number of non-inpatient services by 12 months (i.e. to medium term). These data are all skewed and best considered by viewing [Analysis 1.4](#).

3.3 Hospitalisation

Mean duration of inpatient stay and number of inpatient nights were measured by 12 months (i.e. to medium term). These data are all skewed and best considered by viewing [Analysis 1.5](#).

4. Economic outcomes

4.1 Direct costs

Overall costs to the healthcare system by 12 months (i.e. to medium term) were reported, and also divided into community, hospital and medication costs. These data are all skewed and best considered by viewing [Analysis 1.6](#).

4.2 Indirect costs

These results comprise costs to the social and voluntary sector, and to the criminal justice system by 12 months (i.e. to medium term). These data are all skewed and best considered by viewing [Analysis 1.7](#).

4.3 Total costs

These results are a combination of direct and indirect costs by 12 months (i.e. to medium term). These data are all skewed and best considered by viewing [Analysis 1.8](#).

5. Leaving the study early

This outcome was measured in the included study. The results at short term favoured the intervention treatment ($n = 52$, 1 RCT, risk ratio (RR) 0.86, 95% CI 0.06 to 12.98). At medium term, the results very slightly favoured the control group ($n = 50$, 1 RCT, RR 0.99, 95% CI 0.39 to 2.54). Neither of these results reached statistical significance ([Analysis 1.9](#)).

6. Adverse effects/events

6.1 Death

One death, at two months after randomisation, in the control arm of the included study meant that the results for this outcome favoured the nidotherapy group. The results for this outcome by 12 months (i.e. to medium term) are $n = 52$, 1 RCT, RR 0.29, 95% CI 0.01 to 6.74. The difference here did not reach statistical significance ([Analysis 1.10](#)).

DISCUSSION

Summary of main results

Comparison 1: NIDOTHERAPY-ENHANCED STANDARD CARE versus STANDARD CARE

The authors of the included study (Ranger 2009) mention in the text that it is a pilot study on a new intervention. This is reflected in the fact that the number of participants is small, and the results of the one included study of this review should clearly be considered in this light.

1. Functioning

1.1 Social functioning

Results from the SFQ-KW (social functioning questionnaire - key-worker version) indicate that nidothrapy is more effective than control at both short and medium term in improving social functioning; mean differences of -2.10 and -1.70 in favour of the nidothrapy group (from a scale with a maximum score of 24) however need consideration to clarify their real-life significance. The trial authors did not discuss this.

In addition, the trial authors did not disclose the results they obtained from use of the SFQ-patient version, which we have noted as a high risk of bias (see [Characteristics of included studies](#) and [Summary of findings for the main comparison](#)).

2. Mental state

Mental state, measured using the validated BPRS tool, appears to be improved at short and medium term in the nidothrapy group, with the difference slightly more marked at medium term. These results have large standard deviations, are skewed, and are presented in a table. Again, the real-life significance of these changes in score needs to be considered.

3. Service outcomes

3.1 Engagement with non-inpatient services

Engagement with non-inpatient services was measured in the included study using the EAS. The results at short and medium term favoured the control group. Statistical significance is evident in the short-term results, but not in the medium term. This could reasonably be interpreted as indicating a positive effect of nidothrapy in terms of good functional communication between patients and service providers, but data from larger studies will be needed to confirm this.

3.2 Use of services

Evidently the numbers of participants in the arms of the included study are small, and for these outcomes standard deviations are large and results are skewed; larger sample sizes may lend weight to apparently positive or negative effects of nidothrapy in terms of these outcomes. Furthermore, these results need to be interpreted

with caution, since value judgements are possible concerning exactly what each use of a given service means. Increased numbers of home help contacts in the nidothrapy group, for example, may represent a less equivocal improvement for that patient group than an increased number of contacts with an out-of-hours psychiatrist. In addition, inferences may be drawn about the benefit of increased contacts for the providers of the services themselves, if for example, their caseloads are stretched.

With this caveat in mind, one arguable view is that it would be 'better' for a given patient to increase use of the following services:

- district nurse/health visitor contacts (results favour nidothrapy);
- home help contacts (results favour nidothrapy);
- community psychiatric nurse contacts (results favour nidothrapy);
- community psychologist contacts (results favour nidothrapy);
- social worker contacts (results favour nidothrapy);
- day-care days (results favour nidothrapy);
- service-provided accommodation nights (results favour nidothrapy);
- support worker contacts (results favour control);
- clozapine clinic contacts (results favour control);
- drug/alcohol worker contacts (results favour control);

and that it would be 'worse' for a given patient to increase use of the following services:

- out-of-hours psychiatrist contacts (results favour control);
- A&E admissions (results favour control);
- prison (results favour control).

This interpretation of the skewed results presented in the included study allows the inference to be drawn that nidothrapy can promote beneficial contact with district nurses/health visitors, home help services, community psychiatric nurses, community psychologists, and social workers, and use of day-care facilities and service-provided accommodation, and in avoiding out-of-hours psychiatrist calls, A&E admissions and prison. On the other hand, nidothrapy does not appear superior to control in promoting contact with support workers, clozapine clinics or drug/alcohol workers.

It should be reiterated that the numbers of participants in the included study were very small, and just as the trial authors did not discuss the absolute significance of an increase or decrease in each service use, so a thoughtful interpretation of the results for use of each service is recommended by the review authors.

3.3 Hospitalisation

Despite the large standard deviations and the skew of the data, it is clear that the mean number of inpatient nights (in any admission) and the mean duration in nights of inpatient stay are considerably reduced in the nidothrapy group compared with

control. Larger sample sizes in future studies will be welcomed to confirm and strengthen this result. This may well represent a benefit of nidothrapy treatment, but it is important to clarify to whom. Evidently inpatient costs and total costs per patient (detailed elsewhere in the results) could be reduced, but further research is needed, for example, to ascertain if this level of saving is tenable over subsequent years for a given patient. It is conceivable that inpatient costs could be reduced in the short term as a result of patient empowerment to resist inpatient treatment, but this may have a later cost effect if such treatment were to have had a greater clinical benefit.

4. Economic outcomes

4.1 Direct costs

Skewed data from a small number of participants in the included study show an increase in community healthcare costs and a very modest increase in medication costs in the nidothrapy group over 12 months. In contrast, the hospital costs are reduced, as are the total direct costs (i.e. to the healthcare system). This may well represent a benefit of nidothrapy treatment, especially if the increased costs for community healthcare services and medication represent a real-world increase in successful engagement by patients with appropriate and beneficial services, and a willingness to work towards optimisation of medication as a 'fringe benefit' of therapy. The counterpoint to this may be to consider the possible meaning or future implication of reduced inpatient bed use at the level of the individual patient, notwithstanding the short-term cost saving.

4.2 Indirect costs

Skewed data from a small number of participants in the included study show an increase in community and accommodation costs provided by the social and voluntary sector in the nidothrapy group over 12 months.

This may well be a natural and acceptable corollary of nidothrapy treatment, especially if the costs represent a real-world increase in successful engagement by patients with appropriate and beneficial services. The counterpoint to this may be to consider the likely length of community service provision, acceptability of increased community costs to the commissioners of such services, as well as the possible meaning or future implication of reduced inpatient bed use at the level of the individual patient, notwithstanding the short-term cost saving, as per the direct costs above.

Skewed data are also available from the included study concerning costs to the criminal justice system. These data appear to strongly favour the control group in terms of this outcome. Given the small sample size and the lack of any background information about how the reported costs were incurred, extreme caution should be

used before assuming these data to represent an adverse effect of nidothrapy.

4.3 Total costs

Skewed data from a small number of participants in the included study show a decrease in total costs (the sum of direct and indirect costs) in the nidothrapy group over 12 months. Caution should however be used in interpreting them; see section 4.1 and 4.2 above for some suggestions on this. Overall, this may well represent a benefit of nidothrapy treatment, and further research into this outcome is welcomed to potentially strengthen the results.

5. Leaving the study early

These results, from a small number of participants in the included study, are difficult to interpret meaningfully as incomplete information was given in the paper as to why those who left the study early did so. In the nidothrapy group, one patient was reported as becoming 'uncontactable', while six were listed as having dropped out ('refused') over the course of 12 months with no reasoning reported. After contacting the trial authors to clarify this information, we were informed that the one 'uncontactable' participant had refused to be seen by an independent assessor but did not give a reason why, and the remaining six had merely 'refused'. However, we were informed that a further seventh participant had been omitted from the trial report, at the admitted error of the trial authors; this seventh participant had agreed to assessment but avoided being seen by the trial authors, and so in the end was not assessed. In the control group, one patient died under suspicious circumstances, and another moved from the area, while four were listed as having dropped out ('refused') over the course of 12 months with no reasoning reported. Again, contact with the trial authors revealed that there was another seventh participant omitted from the trial report; one additional participant who was not accounted for between six to 12 months. This participant did not refuse but had moved to a different area; the trial authors were unfortunately unable to contact them successfully. Both of these omissions of fact slightly affect the data inputted and subsequent outcome in [Data and analyses](#).

6. Adverse effects/events

6.1 Death

These results, from a small number of participants in the included study, would appear to demonstrate a non-significant benefit of nidothrapy as regards this outcome. However, the one death reported (included also in 'Leaving the study early', above) was under suspicious circumstances and cannot reasonably be used to infer anything about the risk of death when nidothrapy is not provided.

Overall completeness and applicability of evidence

1. Completeness

The included study reported on most of the outcomes specified in the review. The study did not report on outcome 1.2 'General functioning', outcome 3 'Quality of life', outcome 5 'Satisfaction with treatment', or outcome 6 'Employment status'. The review authors feel that, bearing in mind the nature of the intervention, level of general functioning and quality of life are outcomes of particular interest to people who are likely to derive maximum benefit from it.

The primary outcome in the included study concerned cost-effectiveness, a commissioning-oriented outcome. While the results of the trial appear to demonstrate a cost benefit of nidotherapy, this requires further research over the longer term, and needs to be balanced by more research into patient-centred outcomes. Well-chosen patient-centred outcomes were explored by the included study, but the clinical significance of change in average scores, even on validated scales, needs to be considered and discussed.

One of the review outcomes concerned 'Adverse effects/events'. While the included study did report on deaths, no consideration was given to any other potential adverse effects of nidotherapy. The review authors would welcome a discussion within future trials of the possible harm to patients of, for instance, a sharp reduction in time spent as inpatients if in fact this environment were objectively the correct one for them.

On the whole, the evidence available is relevant for this review question. However, as acknowledged by the trial authors, [Ranger 2009](#) is a pilot study with a very small number of participants. Further higher-powered trials are indicated to explore the potential benefits and adverse effects of nidotherapy. In addition, some data may be missing from the included study (see [Quality of the evidence](#) below)

2. Applicability

The included study investigated patients with schizophrenia and a range of other mental health issues. Participants were mixed in gender and ethnic origin, though age range was not specified in the trial report. The included trial was conducted in a central, densely-populated urban area in the UK. This has implications in terms of applicability of trial results; if beneficial environmental changes are to be made, are such options more or less available in this type of area than in other areas of the UK or worldwide?

In terms of interventions, nidotherapy as a new therapy is tightly defined (see [Description of the intervention](#)) and does not replace but works alongside other treatments. As such, the appropriate intervention treatment (nidotherapy-enhanced assertive community care) was investigated in the included trial. It was also clearly appropriate to use assertive community care alone as the control.

Nidotherapy is a newly-formulated therapeutic method, and as such this raises issues concerning the likely methods for the format of training, its provision and accreditation. Although reference is made in the included study to background literature which gives a very clear explanation of the principles and phases of therapy (see [Description of the intervention](#)), the review authors would welcome discussion of how the trial authors and others envisage nidotherapy being established in the context of current practice.

Quality of the evidence

The review included only one small study of 52 participants, not all of whom were included in the results for every outcome. The trial authors clearly state that this is a pilot study, and the review authors have received information that there are at least two further trials planned of the effectiveness of nidotherapy.

The design of the included trial appears good and the randomisation process is described. The trial authors reported on their stated outcomes, and make full acknowledgement of the limitations of their own trial, including the observation that initial trials of new interventions can suffer positive bias.

However, the quality of the reporting was not high. The age range of the participants was not stated, and social functioning results from the SFQ-patient version were not provided (the trial authors provide a footnote stating that the latter version 'showed similar findings to the SFQ-KW but had smaller numbers'. A CONSORT diagram provided in the included study paper details patient selection and their pathway through the trial. This is helpful but numbers appear inconsistent - the review authors therefore sought clarification on this from the trial authors.

We received clarification concerning the number of participants leaving the study early - this is detailed in [Summary of main results](#) under 'Leaving the study early'. Concerning missing data on service use, the trial author's clarification is detailed in the section [Incomplete outcome data \(attrition bias\)](#).

In the [Summary of findings for the main comparison](#), we downgraded the evidence on the outcome 'social functioning' to 'very low' due to possible authorship bias (a trial author having developed the SFQ scale), small sample size, and potential publication bias (withholding of the SFQ-patient version results). We graded the evidence for the outcome 'mental state' as 'low' due to small sample size and the skew of the presented data. Economic outcome evidence was graded as 'low' due to small sample size, skewed data, and the fact that all costs were presented as an average, with a wide scatter of costs in both the intervention and control groups. Evidence concerning adverse effects/events was graded as 'very low' due to the uncertain connection of the one death reported in the study to any aspect of the active or control interventions.

Potential biases in the review process

The review authors worked hard to ensure that studies were selected, and data were extracted and analysed independently, as set out in the protocol for the review. The latter was difficult to completely adhere to given the numerical inconsistencies in part of the reported data.

The trials search process was a thorough one. The review authors are aware that the search strategy was narrow; this was a deliberate decision to identify trials on those interventions labelled as 'nidotherapy' and which therefore complied totally with the definition of the therapy (see [Description of the intervention](#)). A lead author of the included study was contacted to obtain details of ongoing or unpublished studies (see [Quality of the evidence](#)) but there remains a small possibility that other unpublished trials of the intervention exist which the review authors do not currently have access to. This means that the review authors may unwittingly be perpetuating a publication bias. It may be that trials exist on intervention packages that include the essential elements of nidotherapy but which are not packaged and delivered as such (see [Implications for research](#) below).

Some data reported by the included study were skewed. Without access to individual patient data, it is difficult to present these reported data in a meaningful way, or likewise to comment upon them with certainty.

Agreements and disagreements with other studies or reviews

The review authors are not aware of any other systematic reviews of this topic. We have made reference to previously published non-systematic review literature on the topic (see [Additional references](#)).

AUTHORS' CONCLUSIONS

Implications for practice

1. For people with schizophrenia

As a patient with schizophrenia, one would wish to ascertain from available evidence both the likely benefits and likely harms of nidotherapy as a new adjunctive therapeutic method. From the available evidence included in this review, it is not possible to draw strong conclusions as to the ability of nidotherapy to provide the intended benefits to the patient. Data concerning social functioning and mental state show only small, non-significant improvements using nidotherapy. It is possible that patients may, to their benefit, better engage with non-inpatient services. No evidence is available to assess the effect of nidotherapy on general functioning, quality of life, medication use, satisfaction with treatment,

or employment status. Patients receiving nidotherapy may spend less time as inpatients over the course of 12 months; no evidence appears to exist concerning the appropriateness of this for the individual patient.

No data are available on the reasons for participants leaving the study early; this reflects a general lack of evidence on potential adverse effects of therapy.

Until further evidence is available concerning the potential range and extent of both benefits and harms of nidotherapy, patients should consider it an experimental therapy.

2. For clinicians

While nidotherapy may offer some potential benefits to patients in terms of improved social functioning, mental state, and reduced hospitalisation, this should be interpreted with caution on an individual patient basis, and clinical judgement exercised as to the suitability of a patient for nidotherapy. Some evidence (from a small sample population, but reaching statistical significance) exists to suggest that patients receiving nidotherapy may better engage with non-inpatient services. Little evidence exists concerning the potential adverse effects of therapy.

It is not clear at this stage what benefits are provided by nidotherapy over and above those provided by comprehensive, well-judged current practice in which relevant environmental factors are considered. The extent to which this occurs in practice should be judged by clinicians themselves.

Until further evidence is available concerning the potential range and extent of both benefits and harms of nidotherapy, clinicians should consider it an experimental therapy.

3. For managers/policymakers

Some cost reductions are apparently demonstrated over a 12-month period by the evidence presented in this review, mainly in terms of reduced inpatient bed use. This however, requires further research in order to place this saving in the context of possible longer-term reliance on nidotherapy, and the cost of any as-yet unexplored adverse effects. It is not clear as yet how nidotherapy could be implemented in the context of current practice, or how applicable the therapy could be over a wider geographical or cultural range.

Until further evidence is available concerning the potential range and extent of both benefits and harms of nidotherapy, managers and policymakers should consider it an experimental therapy.

Implications for research

1. General

Further research is required to clarify the apparent positive effects of nidothrapy and to assess potential risks/harms. Future trials should improve the quality and completeness of data reporting.

2. Specific

As a newly-formulated therapeutic tool to consider patient needs in a holistic and ongoing way, nidothrapy embodies an approach that is intuitively 'correct' in that some elements of the package are likely to be routinely, if not systematically, addressed by clinicians and support workers in current practice. Since current available evidence offers little support for the effectiveness of these practices when packaged and delivered as nidothrapy, more well-designed, conducted and reported randomised studies investigating the efficacy of nidothrapy are needed.

The review authors suggest that future research into the effectiveness of nidothrapy addresses the important patient-oriented outcomes of general functioning levels, quality of life, and adverse effects. It may be fruitful to consider a review involving a search strategy to identify trials involving some or all of the key elements of nidothrapy, but where they are not packaged and delivered as such, in order to try to assess the value of the format itself.

Continuous data should be reported with means, standard deviations and number of participants. Endpoint scores should always be used when reporting data derived from scales.

The review authors, by no means experienced in trial design or execution, have nevertheless produced a suggested outline design for future trials (see Table 1).

ACKNOWLEDGEMENTS

The authors thank Professor Clive E Adams (CEA) for input as noted in the text of the protocol, and the staff of the Cochrane Schizophrenia Group editorial base for their support in the writing of the protocol.

We would also like to thank the Trials Search Co-ordinator of the Cochrane Schizophrenia Group, Samantha Roberts who developed and ran the search and Ben Gray who wrote the Plain Language Summary.

The Cochrane Schizophrenia Group Editorial Base in Nottingham produces and maintains standard text for use in the Methods section of their reviews. We have used this text as the basis of what appears here and adapted it as required.

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- * Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

Ranger 2009

Methods	<p>Allocation: randomised¹.</p> <p>Blindness: patients assessed by two researchers blind to trial allocation².</p> <p>Design: 'simple parallel design with two treatment arms'.</p> <p>Duration: 18 months.</p>
Participants	<p>Diagnosis: primary diagnoses of: schizophrenia (n = 30); schizoaffective disorder (n = 10); bipolar disorder (n = 5); borderline personality disorder (n = 5). 49 participants had 'differing degrees of severity of full personality disorder' of which 39 participants had Type R personalities; 3 participants had 'personality difficulty'. 36 participants were drug or alcohol dependent</p> <p>N = 52*.</p> <p>Age: not reported.</p> <p>Sex: 35M, 17F.</p> <p>Racial origin: White (n = 31); Black African or Caribbean (n = 12); other (n = 9). Similar distribution in the two groups</p> <p>History: patients with severe mental illness and comorbid personality disturbance, recruited from the caseload of a Central London assertive outreach and rehabilitation team between August 2003 and September 2004</p> <p>Country: UK.</p> <p>Excluded: three refused consent, one judged intellectually incapable of providing consent, one considered unsuitable for assertive outreach treatment and therefore discharged</p>
Interventions	<p>1. Up to 15 sessions of nidotherapy³ added to standard assertive outreach treatment as provided by the Community (formerly Paddington) Outreach and Rehabilitation Team in central London</p> <p>2. Standard assertive outreach treatment as provided by the Community (formerly Paddington) Outreach and Rehabilitation Team in central London</p>
Outcomes	<p>Functioning: any change in social functioning (SFQ-KW) - at 6 and 12 months</p> <p>Service outcome: Engagement with non-inpatient services: average change/endpoint scores (EAS) - at 6 and 12 months, prison nights, number of A&E attendances; number of police contacts - at 12 months</p> <p>Leaving the study early.</p> <p>Adverse effects/events: death.</p> <p>Unable to use:</p> <p>Service outcomes: other engagement with non-inpatient services⁴; hospitalisation: number of nights as inpatient, duration of inpatient episodes - at 12 months (skewed data)</p> <p>Mental state: any change in general mental state (BPRS) - at 6 and 12 months (skewed data)</p> <p>Economic outcomes: direct costs; cost-effectiveness - at 12 months (skewed data).</p>

Notes	<p>FOOTNOTES:</p> <ol style="list-style-type: none"> 1. 'randomly allocated by an independent statistician using a random numbers design with no stratification of groups' 2. 'maintenance of blinding was aided because the main nidotherapists also had responsibilities as support workers in the team, thus knowledge of their involvement did not disclose the nature of their intervention' 3. Nidotherapy received 'from two nidotherapists following a standard format' (Tyrer 2005a): <ul style="list-style-type: none"> • Identification of the boundaries of the therapy • Full environmental analysis • Implementation of common nidopathway • Monitoring of progress • Resetting of nidopathway and completion <p>*number randomised not reported. one patient died in suspicious circumstances two months after randomisation, one patient refused to continue</p> 4. Engagement with non-inpatient services: service-provided accommodation nights; day care days; number of CPN contacts; number of community psychiatrist contacts; number of community psychologist contacts; number of drug/alcohol worker contacts; number of health visitor/DN contacts; number of social worker contacts; number of support worker contacts; number of home help contacts; number of OOH psychiatry service attendances; number of Clozaril clinic attendances - at 12 months
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised - "randomly allocated by an independent statistician using a random numbers design with no stratification of groups, to either nidotherapy or control groups" (p129)
Allocation concealment (selection bias)	Low risk	"Patients were assessed [...] by [researchers] MR and KI who remained blind of trial allocation" (p129)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Single blind. Rater MR was external to the trial team, and was not made aware of the form of management each participant received
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The main nidotherapists also had roles as support workers in the team, thus knowledge of their involvement did not disclose the nature of their intervention" (p129). Participants and other staff were instructed in advance not to disclose any information to study assessors

Ranger 2009 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	Loss to follow-up uncertain: numbers reported in trial inconsistent
Selective reporting (reporting bias)	High risk	SFQ patient version results mentioned but not reported.
Other bias	Unclear risk	Co-author of study is developer and “product champion” of the intervention Co-author of study developed the Social Function Schedule, from which the SFQ scale is derived Co-author of study developed the HEAS (Homeless Acceptance and Assessment Scale) from which the EAS (Engagement and Acceptance Scale) is derived

A&E: Accident and Emergency

BPRS: Brief Psychiatric Rating Scale

CPN: Community Psychiatric Nurse

DN: District Nurse

OOH: out-of-hours

SFQ: Social Functioning Questionnaire

DATA AND ANALYSES

Comparison 1. NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Functioning - specific - social - change in average score (SFQ-KW, better = low)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 short term (< 6 months)	1	50	Mean Difference (IV, Fixed, 95% CI)	-2.10 [-4.66, 0.46]
1.2 medium term (6-12 months)	1	37	Mean Difference (IV, Fixed, 95% CI)	-1.70 [-4.60, 1.20]
2 Mental state: Average scores (BPRS, better = low, skewed data)			Other data	No numeric data
2.1 short term (< 6 months)			Other data	No numeric data
2.2 medium term (6-12 months)			Other data	No numeric data
3 Service outcomes: 1. Engagement with non-inpatient services - change in average score (EAS, better = high)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 short term (< 6 months)	1	50	Mean Difference (IV, Fixed, 95% CI)	2.0 [0.13, 3.87]
3.2 medium term (6-12 months)	1	37	Mean Difference (IV, Fixed, 95% CI)	1.70 [-0.09, 3.49]
4 Service outcomes: 2. Use of services - by 12 months (skewed data)			Other data	No numeric data
4.1 number of contacts - clozapine clinic			Other data	No numeric data
4.2 number of contacts - drug/alcohol worker			Other data	No numeric data
4.3 number of contacts - health visitor / district nurse			Other data	No numeric data
4.4 number of contacts - home help			Other data	No numeric data
4.5 number of contacts - out-of-hours psychiatry service			Other data	No numeric data
4.6 number of contacts: Police			Other data	No numeric data
4.7 number of contacts - psychiatric nurse (community)			Other data	No numeric data
4.8 number of contacts - psychiatrist (community)			Other data	No numeric data
4.9 number of contacts - psychologist (community)			Other data	No numeric data
4.10 number of contacts - social worker			Other data	No numeric data

4.11 number of contacts - support worker contacts			Other data	No numeric data
4.12 number of attendances: accident and emergency			Other data	No numeric data
4.13 number of days - day care			Other data	No numeric data
4.14 number of nights - service-provided accommodation			Other data	No numeric data
4.15 number of nights: prison			Other data	No numeric data
5 Service outcomes: 3. Hospitalisation - by 12 months (skewed data)			Other data	No numeric data
5.1 hospital inpatient: number of nights (any admission)			Other data	No numeric data
5.2 hospital inpatient: mean duration of stay (number of nights)			Other data	No numeric data
6 Economic outcomes: 1. Direct costs over 12-month period (skewed data)			Other data	No numeric data
6.1 healthcare: community			Other data	No numeric data
6.2 healthcare: hospital			Other data	No numeric data
6.3 healthcare: medication			Other data	No numeric data
6.4 healthcare: total healthcare costs			Other data	No numeric data
7 Economic outcomes: 2. Indirect costs over 12-month period (skewed data)			Other data	No numeric data
7.1 social and voluntary services - community			Other data	No numeric data
7.2 social and voluntary services - accommodation			Other data	No numeric data
7.3 social and voluntary services - total			Other data	No numeric data
7.4 criminal justice			Other data	No numeric data
8 Economic outcomes: 3. Total costs over 12-month period (skewed data)			Other data	No numeric data
8.1 Total costs over 12-month period			Other data	No numeric data
9 Leaving the study early (reasons unclear)	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
9.1 short term (< 6 months)	1	52	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.06, 12.98]
9.2 medium term (6-12 months)	1	50	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.39, 2.54]
10 Adverse effects/events - death	1	52	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.01, 6.74]

Analysis 1.1. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 1 Functioning - specific - social - change in average score (SFQ-KW, better = low).

Review: Nidotherapy for people with schizophrenia

Comparison: 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE

Outcome: 1 Functioning - specific - social - change in average score (SFQ-KW, better = low)

Analysis 1.2. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 2 Mental state: Average scores (BPRS, better = low, skewed data).

Mental state: Average scores (BPRS, better = low, skewed data)

Study	Intervention	Mean	SD	N
short term (< 6 months)				
Ranger 2009	Nidotherapy	27.6	9.3	25
Ranger 2009	Standard care	32.3	9.0	24
medium term (6-12 months)				
Ranger 2009	Nidotherapy	24.8	8.2	19
Ranger 2009	Standard care	29.2	11.1	18

Analysis 1.3. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 3 Service outcomes: 1. Engagement with non-inpatient services - change in average score (EAS, better = high).

Review: Nidotherapy for people with schizophrenia

Comparison: 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE

Outcome: 3 Service outcomes: 1. Engagement with non-inpatient services - change in average score (EAS, better = high)

(1) Note: graph labels reversed to reflect that high score in EAS = better

Analysis 1.4. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 4 Service outcomes: 2. Use of services - by 12 months (skewed data).

Service outcomes: 2. Use of services - by 12 months (skewed data)

Study	Intervention	Mean	SD	N
number of contacts - clozapine clinic				
Ranger 2009	Nidotherapy	1	4	26
Ranger 2009	Standard care	1	6	22
number of contacts - drug/alcohol worker				
Ranger 2009	Nidotherapy	0	0	26
Ranger 2009	Standard care	2	8	22
number of contacts - health visitor / district nurse				

Service outcomes: 2. Use of services - by 12 months (skewed data) (Continued)

Ranger 2009	Nidothetapy	4	17	26
Ranger 2009	Standard care	0	0	22
number of contacts - home help				
Ranger 2009	Nidothetapy	14	61	26
Ranger 2009	Standard care	4	12	22
number of contacts - out-of-hours psychiatry service				
Ranger 2009	Nidothetapy	1	1	26
Ranger 2009	Standard care	0	1	22
number of contacts: Police				
Ranger 2009	Nidothetapy	0	1	26
Ranger 2009	Standard care	0	0	22
number of contacts - psychiatric nurse (community)				
Ranger 2009	Nidothetapy	43	27	26
Ranger 2009	Standard care	34	26	22
number of contacts - psychiatrist (community)				
Ranger 2009	Nidothetapy	5	5	26
Ranger 2009	Standard care	4	2	22
number of contacts - psychologist (community)				
Ranger 2009	Nidothetapy	1	3	26
Ranger 2009	Standard care	0	0	22
number of contacts - social worker				
Ranger 2009	Nidothetapy	12	18	26
Ranger 2009	Standard care	9	13	22
number of contacts - support worker contacts				

Service outcomes: 2. Use of services - by 12 months (skewed data) (Continued)

Ranger 2009	Nidothorapy	7	17	26
Ranger 2009	Standard care	6	13	22
number of attendances: accident and emergency				
Ranger 2009	Nidothorapy	2	3	26
Ranger 2009	Standard care	1	1	22
number of days - day care				
Ranger 2009	Nidothorapy	20	34	26
Ranger 2009	Standard care	10	23	22
number of nights - service-provided accommodation				
Ranger 2009	Nidothorapy	132	175	26
Ranger 2009	Standard care	99	153	22
number of nights: prison				
Ranger 2009	Nidothorapy	2	8	26
Ranger 2009	Standard care	0	0	22

Analysis 1.5. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 5 Service outcomes: 3. Hospitalisation - by 12 months (skewed data).

Service outcomes: 3. Hospitalisation - by 12 months (skewed data)

Study	Intervention	Mean	SD	N
hospital inpatient: number of nights (any admission)				
Ranger 2009	Nidothorapy	73	126	26
Ranger 2009	Control	108	126	22
hospital inpatient: mean duration of stay (number of nights)				
Ranger 2009	Nidothorapy	25	52	26
Ranger 2009	Control	57	64	21

Analysis 1.6. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 6 Economic outcomes: 1. Direct costs over 12-month period (skewed data).

Economic outcomes: 1. Direct costs over 12-month period (skewed data)

Study	Intervention	Mean	SD	N
healthcare: community				
Ranger 2009	Nidoththerapy	3,024	1,593	26
Ranger 2009	Control	2,068	1,239	22
healthcare: hospital				
Ranger 2009	Nidoththerapy	15,467	28,696	26
Ranger 2009	Control	21,624	25,190	22
healthcare: medication				
Ranger 2009	Nidoththerapy	1,070	1,530	26
Ranger 2009	Control	998	810	22
healthcare: total healthcare costs				
Ranger 2009	Nidoththerapy	19,562	28,641	26
Ranger 2009	Control	24,690	25,483	22

Analysis 1.7. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 7 Economic outcomes: 2. Indirect costs over 12-month period (skewed data).

Economic outcomes: 2. Indirect costs over 12-month period (skewed data)

Study	Intervention	Mean	SD	N
social and voluntary services - community				
Ranger 2009	Nidoththerapy	1,039	1,179	26
Ranger 2009	Control	617	639	22
social and voluntary services - accommodation				
Ranger 2009	Nidoththerapy	3,014	6,325	26
Ranger 2009	Control	2,599	5,113	22

Economic outcomes: 2. Indirect costs over 12-month period (skewed data) (Continued)

social and voluntary services - total				
Ranger 2009	Nidoththerapy	4,052	6,419	26
Ranger 2009	Control	3,217	5,054	22
criminal justice				
Ranger 2009	Nidoththerapy	132	673	26
Ranger 2009	Control	1	6	22

Analysis 1.8. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 8 Economic outcomes: 3. Total costs over 12-month period (skewed data).

Economic outcomes: 3. Total costs over 12-month period (skewed data)

Study	Intervention	Mean	SD	N
Total costs over 12-month period				
Ranger 2009	Nidoththerapy	23796	29472	26
Ranger 2009	Control	27908	25033	22

Analysis 1.9. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 9 Leaving the study early (reasons unclear).

Review: Nidotherapy for people with schizophrenia

Comparison: 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE

Outcome: 9 Leaving the study early (reasons unclear)

Analysis 1.10. Comparison 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE, Outcome 10 Adverse effects/events - death.

Review: Nidotherapy for people with schizophrenia

Comparison: 1 NIDOTHERAPY-ENHANCED STANDARD CARE vs STANDARD CARE

Outcome: 10 Adverse effects/events - death

ADDITIONAL TABLES

Table 1. Suggested design of study

Methods	Participants	Interventions	Outcomes	Notes
Allocation: randomised, fully described in terms of methods of randomisation and allocation concealment Blinding: Single blind, with methods of maintenance of blinding fully described Setting: community, with extra-urban and rural populations included Duration: follow-up of at least 24 months	Diagnosis: primary diagnosis of schizophrenia or related disorders, including schizophreniform disorder, schizoaffective disorder and delusional disorder N > 400 Age: adults, with age specified in trial Sex: both	1.Nidotherapy-enhanced standard care. n = 200 2.Non-enhanced standard care. n = 200	1.Social functioning 2.General functioning 3.Mental state (clinically significant improvement, however measured) 4.Quality of life 5.Level of medication use (clinically important observations) 6.Engagement with non-inpatient services 7.Hospitalisation 8.Satisfaction with treatment 9.Employment status 10.Economic outcomes 11.Adverse effects/events including reasons for leaving the study early	Any outcomes measured using scale-derived data should be interpreted in such a way as to make clear the real-life relevance of changes in scale score

WHAT'S NEW

Date	Event	Description
17 April 2013	Amended	Spelling correction

CONTRIBUTIONS OF AUTHORS

Ian J Chamberlain - developing and writing the protocol. Identifying and selecting reports, extracting data and preparing the review.

Stephanie Sampson - developing and writing the protocol. Identifying and selecting reports, extracting data and preparing the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- The University of Nottingham, UK.
- Nottinghamshire Healthcare NHS Trust, UK.

External sources

- National Institute for Health Research (NIHR), UK.
- Cochrane Collaboration Programme Grant 2011

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None.

NOTES

None.

INDEX TERMS

Medical Subject Headings (MeSH)

*Interpersonal Relations; *Social Adjustment; *Social Environment; Personal Autonomy; Pilot Projects; Schizophrenia [*therapy]

MeSH check words

Humans