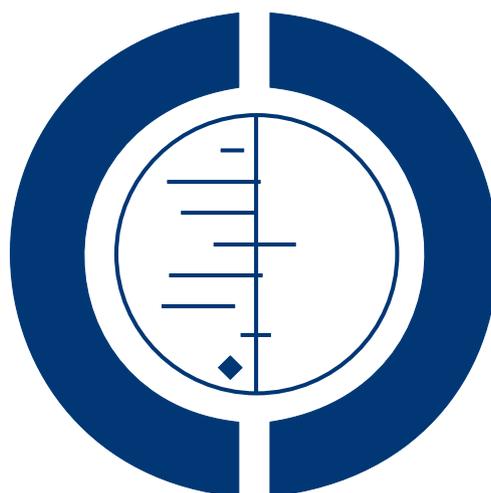


# Physical health care monitoring for people with serious mental illness (Review)

Tosh G, Clifton AV, Xia J, White MM



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[Intervention Review]

# Physical health care monitoring for people with serious mental illness

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## ABSTRACT

### Background

Current guidance suggests that we should monitor the physical health of people with serious mental illness, and there has been a significant financial investment over recent years to provide this.

### Objectives

To assess the effectiveness of physical health monitoring, compared with standard care for people with serious mental illness.

### Search methods

We searched the Cochrane Schizophrenia Group Trials Register (October 2009, update in October 2012), which is based on regular searches of CINAHL, EMBASE, MEDLINE and PsycINFO.

### Selection criteria

All randomised clinical trials focusing on physical health monitoring versus standard care, or comparing i) self monitoring versus monitoring by a healthcare professional; ii) simple versus complex monitoring; iii) specific versus non-specific checks; iv) once only versus regular checks; or v) different guidance materials.

### Data collection and analysis

Initially, review authors (GT, AC, SM) independently screened the search results and identified three studies as possibly fulfilling the review's criteria. On examination, however, all three were subsequently excluded. Forty-two additional citations were identified in October 2012 and screened by two review authors (JX and MW), 11 of which underwent full screening.

### Main results

No relevant randomised trials which assess the effectiveness of physical health monitoring in people with serious mental illness have been completed. We identified one ongoing study.

### **Authors' conclusions**

There is still no evidence from randomised trials to support or refute current guidance and practice. Guidance and practice are based on expert consensus, clinical experience and good intentions rather than high quality evidence.

## **PLAIN LANGUAGE SUMMARY**

### **Physical health care monitoring for people with serious mental illness**

People with mental health problems often have complex and long-term difficulties with their physical health such as weight gain, smoking and heart problems. They sometimes do not take care of themselves, have inactive lifestyles and may not be able to cope with daily life or work. People with mental health problems have higher rates of diabetes, lung disease, cancer, heart problems, HIV/Aids and other infectious diseases.

Physical health care monitoring can take a variety of forms from simple checks carried out by the person themselves to complex specific health checks carried out by health professionals. Monitoring helps identify current health problems and also anticipate future health problems.

In August 2006 the United Kingdom's Department of Health issued guidance on how to provide better care for the physical health needs of people with serious mental illness. Spearhead Trusts, the Royal College of Psychiatrists, the National Institute for Clinical Excellence and other organisations all promoted the use of physical health care monitoring for people with mental health problems.

This review intended to find evidence to support this guidance. The authors' conclude that current guidance and practice on physical health monitoring lacks a firm basis in research and there is little evidence to support this growing trend. They based their conclusions on results from a search carried out for trials in 2012 which found no relevant randomised studies. Current monitoring is mainly based on the agreement of experts, medical experience and good intentions. This does not mean that physical health monitoring is invalid, wrong or not of benefit to the physical health of people with severe mental illness, only that there is as yet no definite proof. Physical health care monitoring has the potential and promise to improve quality of life and help people with mental health problems live longer, but at this stage the information is uncertain and the research evidence unclear.

This summary has been written by a consumer, Benjamin Gray, from Rethink Mental Illness. Email: [ben.gray@rethink.org](mailto:ben.gray@rethink.org)

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

| Physical health monitoring compared to no monitoring for people with serious mental illness   |  |                            |                          |                              |                                 |   |
|---|--|----------------------------|--------------------------|------------------------------|---------------------------------|---|
| <b>Patient or population:</b> patients with people with serious mental illness<br><b>Settings:</b><br><b>Intervention:</b> physical health monitoring<br><b>Comparison:</b> no monitoring |  |                            |                          |                              |                                 |   |
| Outcomes  | Illustrative comparative risks* (95% CI) |                            | Relative effect (95% CI) | No of Participants (studies) | Quality of the evidence (GRADE) | Comments  |
|   | Assumed risk                             | Corresponding risk         |                          |                              |                                 |   |
|   | No monitoring                            | Physical health monitoring |                          |                              |                                 |   |
| <b>Physical health</b> - failure to identify a disease state and provide appropriate treatment  | See comment                              | See comment                | Not estimable            | 0 (0)                        | See comment                     | We did not identify any trial-based data for any outcome. |
| <b>Physical health</b> - failure to effectively manage a known disease state  |  |                            |                          |                              |                                 |   |
| <b>Quality of life:</b> Loss of activities of Daily Living (ADL) skills   |  |                            |                          |                              |                                 |   |
| <b>Adverse event</b> - clinically important adverse effect  |  |                            |                          |                              |                                 |   |
| <b>Adverse event</b> - death  |  |                            |                          |                              |                                 |   |
| <b>Economic</b> - increase costs of care  |  |                            |                          |                              |                                 |   |

**Social** - social isolation as a result of preventable incapacity

## BACKGROUND

### Description of the condition

The definition of severe mental illness with the widest consensus is that of the National Institute of Mental Health (NIMH) (Schinnar 1990) and is based on diagnosis, duration and disability (NIMH 1987). People with serious mental illness have conditions such as schizophrenia or bipolar disorder, over a protracted period of time and resulting in erosion of functioning in day to day life. A European survey put the total population-based annual prevalence of serious mental illness at approximately two per 1000 (Ruggeri 2000). As a consequence of their illness, people with serious mental illness have a significantly reduced life expectancy for a variety of reasons including poor self care, adverse health behaviours (smoking, sedentary lifestyle) and negative effects from psychotropic medications (weight gain, metabolic syndrome) (Robson 2007). In schizophrenia, for example, life expectancy is reduced by around 10 years (Newman 1991). A recent publication has shown that people with schizophrenia have a threefold increase in mortality compared with the general population of England and Wales, and that approximately 81% of that increase is from natural causes, especially cardiovascular disease (Brown 2010). There is historical evidence that sufferers from serious mental illness also have increased rates of infectious diseases (including HIV) (Cournos 2005), non-insulin dependent diabetes, respiratory disease and cancer (Dixon 1999; Robson 2007). Despite this, evidence says that there exists a lack of physical health monitoring in people with serious mental illness in both the primary care (Burns 1998) and in the secondary care setting (Paton 2004).

### Description of the intervention

Physical health monitoring can take many forms, and these forms are highly divergent and dependent on environmental and socio-economic factors. In some instances monitoring is indicated for a specific group of people because of demographic risk factors; one such population is those suffering from serious mental illness (Robson 2007). People with illnesses such as schizophrenia are at greater risk for a number of conditions. This is compounded by the fact that they are less likely to seek medical advice and more likely to be exposed to medications with potentially negative health consequences (Weinmann 2009). People with serious mental illnesses should stand to benefit greatly from a programme of well organised and regular physical health monitoring. Monitoring differs from promotion in that its principle aim is to obtain information which can then be acted on to treat or prevent a physical health problem. Promotion, on the other hand, is the provision of information and encouragement to people in the hope that they will act to avoid deterioration of current health or development of future health problems. The effects of physical

health promotion or advice for people with serious mental illness is evaluated in another future review in this series: 'Physical health advice for people with serious mental illness'.

Past reviewers have suggested that "essential routine health monitoring [for people with serious mental illness] should include weight, body mass index (BMI) and waist circumference, blood pressure, lipid profiles, screening for insulin resistance and diabetes, dental checks and eye health checks" (Robson 2007). Physical health care monitoring could, therefore, range from the simplest forms of self monitoring through to more systematised self screening, to well regulated and guideline-directed monitoring of health by healthcare professionals.

### How the intervention might work

Information obtained from physical health monitoring is often the catalyst for more intensive medical input, which can be either curative, palliative or preventative. The routine employment of simple and relatively inexpensive physical health monitoring has the potential to identify current, and pre-empt future, health problems. Subsequent action could improve the quality and duration of life for sufferers of serious mental illness. Additional benefits may include a reduction in dependence on medical services. "There are potential savings to be made on prescribing and acute care budgets through prevention or early detection of serious illness in these groups of service users" (DoH 2006).

### Why it is important to do this review

In August 2006 the UK's Department of Health published a commissioning framework (DoH 2006) which, based on examples of current practice (including pilot programmes and expert advice), was intended to provide best practice guidance on the physical health needs of people with severe mental illness. In conjunction with this publication there has been significant investment in 88 English Primary Care Trusts, known as 'Spearhead' Trusts, to implement the services it suggested. In addition, a raft of guidance around physical health monitoring in psychiatry has arisen over recent years from organisations such as the Royal College of Psychiatrists (RCPsych 2009; RCPsych 2009a), the National Institute for Clinical Excellence (NICE 2006), Maudsley Prescribing Guidelines (Taylor 2009) and the Serious Mental Illness Physical Health Improvement Profile (White 2009). At no point do the current commissioning framework or guidance documents refer to evidence from randomised controlled trials or previous systematic reviews. This pathway of identifying a problem, consultation, creation of guidelines and investment to implement the guidance would appear to make good sense. We feel that at this point it would be good to assess the available evidence on the effects of physical health monitoring. This is one of a series of related reviews (Table 1).

## OBJECTIVES

To assess the effectiveness of physical health monitoring, compared with standard care for people with severe mental illness.

A secondary objective was to compare types and techniques of monitoring.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

We considered all relevant randomised controlled trials and economic evaluations conducted alongside included randomised controlled trials. We excluded studies such as those allocating participants to groups by using alternate days of the week. If we had encountered trials described in some way to suggest or imply that the study was randomised, and where the demographic details of each group's participants were similar, we would have included them and a sensitivity analysis would have been undertaken to assess the influence of the presence or absence of these data on the results.

#### Types of participants

We required that a majority of the participants should be within the age range 18 to 65 years and suffering from severe mental illness, preferably as defined by the National Institute of Mental Health (NIMH 1987) but, in the absence of that, from diagnosed illness such as schizophrenia, schizophrenia-like disorders, bipolar disorder or serious affective disorders. We did not consider substance abuse to be a severe mental illness in its own right, however we did feel that studies should remain eligible if they dealt with people with dual diagnoses, that is those with severe mental illness plus substance abuse. We would not have included studies focusing on dementia, personality disorder and mental retardation as they were not covered by our definition of severe mental disorder.

#### Types of interventions

##### 1. Physical health care monitoring

###### 1.1 General physical health care monitoring in addition to standard care

Monitoring can be any means of observation, supervision, keeping under review, measuring or testing at intervals. We defined 'physical health' as 'soundness of body' as opposed to the World

Health Organization's definition of health which includes mental and social well being (WHO 1948).

##### 1.2 Focused physical health care monitoring

Adherence to specific guidance for example as a result of an identified illness (blood sugar in diabetes) or as a result of pharmacological treatment (weight gain with an atypical antipsychotic) in addition to standard care.

##### 2. Standard care

Care in which physical health monitoring is not specifically emphasised above and beyond care that would be expected for people not suffering from severe mental illness.

##### 3. Variations in delivery

We consider that there may be important studies comparing different types of monitoring delivered in several ways. We are interested in these studies and will endeavour to include them in a relevant comparison.

- Differences in who undertakes the monitoring - self monitoring versus monitoring by healthcare professional.
- Differences in complexity of monitoring - simple routine check or test versus complex check or test.
- Differences in focus of checks - specific health check versus non-specific health check.
- Differences in pattern of checking - once only checks versus regular checks.
- Differences in guidance followed - one set of guidelines versus another.

#### Types of outcome measures

For the purposes of this review we divided the outcomes into four time periods: i. immediate (within one week), ii. short term (one week to six months), iii. medium term (six months to one year), and iv. long term (over one year).

#### Primary outcomes

##### 1. Physical health - immediate

- 1.1 Failure to identify a disease state and provide appropriate treatment
- 1.2 Failure to effectively manage a known disease state
- 1.3 Failure to act on known risk factors
- 1.4 Unchecked adverse effects of treatment

## 2. Quality of life

- 2.1 Loss of independence
- 2.2 Loss of Activities of Daily Living (ADL) skills
- 2.3 Chronic pain
- 2.4 Immobility
- 2.5 Loss of earnings
- 2.6 Loss of social status
- 2.7 Healthy days

## Secondary outcomes

### 1. Physical health - periods other than immediate

- 1.1 Failure to identify a disease state and provide appropriate treatment
- 1.2 Failure to improve management of a known disease state
- 1.3 Failure to act on known risk factors
- 1.4 Unchecked side-effects of treatment

### 2. Adverse events

- 2.1 Number of participants with at least one adverse effect
- 2.2 Clinically important specific adverse effects (cardiac effects, death, movement disorders, prolactin increase and associated effects, weight gain, effects on white blood cell count)
- 2.3 Average endpoint in specific adverse effects
- 2.4 Average change in specific adverse effects
- 2.5 Death - natural or suicide

### 3. Service use

- 3.1 Hospital admission
- 3.2 Emergency medical treatment
- 3.3 Use of emergency services

### 4. Financial dependency

- 4.1 Claiming unemployment benefit
- 4.2 Claiming financial assistance because of a physical disability

### 5. Social

- 5.1 Unemployment
- 5.2 Social Isolation as a result of preventable incapacity
- 5.3 Increased burden to caregivers

### 6. Quality of life or general functioning

- 6.1 No clinically important change in general quality of life
- 6.2 Average endpoint general quality of life score
- 6.3 Average change in general quality of life score
- 6.4 No clinically important change in general functioning
- 6.5 Average endpoint general functioning score
- 6.6 Average change in general functioning score

## 7. Economic

- 7.1 Increased costs of health care
- 7.2 Days off sick from work
- 7.3 Reduced contribution to society
- 7.4 Family claiming carer's allowance

## 8. Leaving the studies early (any reason, adverse events, inefficacy of treatment)

### 9. Global state

- 9.1 No clinically important change in global state (as defined by the individual studies)
- 9.2 Relapse (as defined by the individual studies)

### 10. Mental state (with particular reference to the positive and negative symptoms of schizophrenia)

- 10.1 No clinically important change in general mental state score
- 10.2 Average endpoint general mental score
- 10.3 Average change in general mental state score
- 10.4 No clinically important change in specific symptoms (positive symptoms of schizophrenia, negative symptoms of schizophrenia)
- 10.5 Average endpoint specific symptom score
- 10.6 Average change in specific symptom score

### 11. Satisfaction with treatment

- 11.1 Participant satisfaction with treatment
- 11.2 Carer satisfaction with treatment

### 12. Summary of findings table

In future updates we will use the GRADE approach to interpret findings (Schünemann 2008) and we will use the GRADEprofiler to import data from Review Manager (RevMan) 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 the 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 table.

- Physical health - immediate

Failure to identify a disease state and provide appropriate treatment  
Failure to effectively manage a known disease state

- Quality of life

Loss of ADL skills

- Adverse event

Clinically important specific adverse effects (cardiac effects, death, movement disorders, prolactin increase and associated effects, weight gain, effects on white blood cell count)

Death - natural or suicide

- Economic

Increased costs of health care

- Social

Social Isolation as a result of preventable incapacity

## Search methods for identification of studies

### Electronic searches

For the previous search please see [Appendix 1](#).

The Trials Search Co-ordinator, Samantha Roberts, searched the Cochrane Schizophrenia Group Trials Register (October 2012) using the phrase:

[(\*physical\* or \*cardio\* or \*metabolic\* or \*weight\* or \*HIV\* or \*AIDS\* or \*Tobacc\* or \*Smok\* or \*sex\* or \*medical\* or \*dental\* or \*alcohol\* or \*oral\* or \*vision\* or \*sight\* or \*hearing\* or \*nutrition\* or \*advice\* or \*monitor\* in title of REFERENCES) AND (\*education\* OR \*health promot\* OR \*preventi\* OR \*motivate\* or \*advice\* or \*monitor\* in interventions of STUDY)].

The Cochrane Schizophrenia Group Trials Register is compiled by systematic searches of major databases and handsearches of relevant journals and conference proceedings (see [Group Module](#)). Incoming trials are assigned to relevant existing or new review titles.

### Searching other resources

#### 1. Unsystematic search

We undertook unsystematic searches of a sample of the component databases (BNI, CINHALL, EMBASE, MEDLINE and PsycINFO) to determine if any material may have been overlooked. We searched the databases using specific phrases ('physical health', 'monitoring' and 'mental illness') as the searches that create the Cochrane Schizophrenia Group Trials Register are methodology specific. We did not identify any relevant trials.

#### 2. Reference searching

We inspected the references of all identified studies for other relevant studies.

#### 3. Personal contact

We planned to contact the first author of each included study for information regarding unpublished trials; however, no studies were included in this review. This will be done as and when future updates of this review identify relevant studies.

## Data collection and analysis

In this update there are a few changes to the data collection and analysis methods to reflect changes in the Cochrane Schizophrenia Group's template methodology. For comparison please see [Appendix 2](#).

### Selection of studies

For the original version, review authors GT, AC and SM screened the results of the electronic search. MB inspected a random sample of these results, comprising 10% of the total. The principal reviewer (GT) and co-reviewer (AC) inspected all abstracts of studies identified through screening and identified potentially relevant reports. Where disagreement occurred we resolved this by discussion, and where there was still doubt we acquired the full article for further inspection. We then requested the full articles of relevant reports for reassessment and carefully inspected them for a final decision on inclusion (see [Criteria for considering studies for this review](#)). In turn, GT and AC inspected all full reports and independently decided whether they met the inclusion criteria. We were not blinded to the names of the authors, institutions or journal of publication. Where difficulties or disputes arose, we asked author MB for help and if it was impossible to decide these studies were added to those awaiting assessment and the authors of the papers were contacted for clarification.

For the 2012 update, two review authors (MW and JX) screened the results of the electronic search. GT and AC were consulted on all potentially relevant reports and a consensus was reached between all authors in deciding to include or exclude a particular study.

## Data extraction and management

### 1. Extraction

For the original version of this review, no studies were included. If studies had been available, authors GT and AC would have independently extracted data from the included studies. GT and AC would have discussed any disagreement, documented decisions and, if necessary, contacted the authors of studies for clarification. With remaining problems MB would have helped clarify issues and we would have documented our final decisions. Data presented only in graphs or figures would have been extracted whenever possible, but only included if two review authors independently had the same result. Attempts would have been made to contact authors through an open-ended request in order to obtain any missing information or for clarification whenever necessary. Where possible, the review authors would have extracted data relevant to each component centre of multi-centre studies separately. Again, for the 2012 update no studies were included and no data extracted, so the above methods were not applied.

## 2. Management

### 2.1 Forms

For the original version, GT and AC would have extracted data onto standard, simple forms. No data were extracted for the 2012 update.

### 2.2 Scale-derived data

We planned to include continuous data from rating scales only if:

- the psychometric properties of the measuring instrument had been described in a peer-reviewed journal (Marshall 2000); and
- 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; for future updates of this review we will note whether or not this is the case in the description of studies.

### 2.3 Endpoint versus change data

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

### 2.4 Skewed data

Continuous data on clinical and social outcomes are often not normally distributed. To avoid the pitfall of applying parametric tests to non-parametric data, we aimed to apply the following standards to all data before inclusion: a) standard deviations and means are reported in the paper or obtainable from the authors; b) when a scale starts from the finite number zero, the standard deviation, 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 PANSS, which can have values from 30 to 210), we would have modified the calculation described above to take the scale starting point into account. In these cases skew is present if  $2SD > (S - S_{min})$ , where  $S$  is the mean score and  $S_{min}$  is the minimum score. Endpoint scores on scales often have a finite start and endpoint and these rules can be applied. Had we included any studies we would have entered skewed endpoint data from studies of fewer than 200 participants as 'other data' within the [Data and](#)

[analyses](#) rather than into a statistical analysis. Skewed endpoint data pose less of a problem when looking at the mean if the sample size is large; we would have entered such data into syntheses, and will do so in future updates if relevant studies are identified.

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 the data are skewed or not and skewed change data will be entered into analyses in future updates.

### 2.5 Common measure

To facilitate comparison between trials, we intended to convert 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 (for example mean days per month).

### 2.6 Conversion of continuous to binary outcomes

In future updates of this review we will, where possible, make an effort 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 Positive and Negative Syndrome Scale (PANSS, Kay 1986), this could be considered as a clinically significant response (Leucht 2005; Leucht 2005a). If data based on these thresholds are not available, we will use the primary cut-off presented by the original authors in future updates.

### 2.7 Direction of graphs

In future updates we will enter data in such a way that the area to the left of the line of no effect indicates a favourable outcome for physical health monitoring. Where keeping to this makes it impossible to avoid outcome titles with clumsy double-negatives (for example 'Not unimproved') we plan to report data where the left of the line indicates an unfavourable outcome. This will be noted in the relevant graphs in future updates.

### Assessment of risk of bias in included studies

For this update, review authors JS and MW were to work independently by using criteria described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) to assess trial quality. This new set of criteria is based on evidence of associations between overestimate of effect and high risk of bias of the trial report, such as sequence generation, allocation concealment, blinding, incomplete outcome data and selective reporting. If inadequate details of randomisation and other characteristics of trials were provided, we would have attempted to contact the authors of the studies in order to obtain additional information. Had we identified studies relevant to this review we would have noted the level of risk of bias in both the text of the review and

in a [Summary of findings for the main comparison](#). This will be done in future updates if relevant studies are identified.

## Measures of treatment effect

### 1. Binary data

We had planned to calculate a standard estimation of the risk ratio (RR) and its 95% confidence interval (CI) for binary outcomes. It has been shown that RR is more intuitive ([Boissel 1999](#)) than odds ratios and that odds ratios tend to be interpreted as RRs by clinicians ([Deeks 2000](#)). The Number Needed to Treat or Harm (NNT/H) statistic with its CI is intuitively attractive to clinicians but is problematic both in its accurate calculation in meta-analyses and the interpretation ([Hutton 2009](#)). For future updates if relevant studies are identified, for binary data presented in the 'Summary of findings' table(s), where possible, we will calculate illustrative comparative risks.

### 2. Continuous data

It was planned that we would estimate mean difference (MD) between groups for continuous outcomes. In future updates we prefer not to calculate effect size measures (standardised mean difference (SMD)). However, if scales of very considerable similarity are used, we will presume there is a small difference in measurement and we will calculate effect size and transform 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 pose problems. 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, CIs unduly narrow and statistical significance overestimated. This causes type I errors ([Bland 1997](#); [Gulliford 1999](#)).

In future updates, where clustering is not accounted for in primary studies, we will present the data in a table with a (\*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review we will seek to contact the first authors of studies to obtain intra-class correlation coefficients for their clustered data and to adjust for this by using accepted methods ([Gulliford 1999](#)). Where clustering has been incorporated into the analysis of primary studies, we will present these data as if from a non-cluster randomised study but adjust 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 intra-class correlation coefficient (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 have been appropriately analysed taking into account intra-class correlation coefficients and the relevant data documented in the report, synthesis with other studies would be possible using the generic inverse variance technique, which will be used in future updates.

### 2. Cross-over trials

A major concern of cross-over trials is the carry-over effect. It occurs if an effect (for example 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, in future updates we will only use the data from the first phase of cross-over studies.

### 3. Studies with multiple treatment groups

For future updates, it is planned that where a study involves more than two treatment arms, if relevant, we will present the additional treatment arms in comparisons. If the data are binary we will add these and combine them within the two-by-two table. If the data are continuous we will combine the data following the formula in section 7.7.3.8 (Combining groups) of the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). Where the additional treatment arms are not relevant, we will not reproduce these data.

## Dealing with missing data

### 1. Overall loss of credibility

At some degree of loss of follow-up, data must lose credibility ([Xia 2009](#)). For future updates of this review, for any particular outcome, should more than 50% of data be unaccounted for we will not reproduce these data or use them within analyses. If, however, more than 50% of those in one arm of a study are lost but the total loss is less than 50%, we will address this within the 'Summary of findings' table(s) by down-rating their quality. Finally, we will also downgrade quality within the 'Summary of findings table(s)' should the loss be 25% to 50% in total.

## 2. Binary

In the case where attrition for a binary outcome is between 0% and 50%, and where these data are not clearly described, for future updates we will present the 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. For these outcomes the rate of those who stay in the study, in that particular arm of the trial, will be used for those who did not. We will undertake a sensitivity analysis testing how prone the primary outcomes are to change when data only from people who completed the study to that point are compared to the intention-to-treat analysis using the above assumptions.

## 3. Continuous

### 3.1 Attrition

In the case where attrition for a continuous outcome is between 0% and 50%, and data only from people who completed the study to that point are reported, we will in future updates reproduce these in updated versions of this review if relevant studies with useable data are identified.

### 3.2 Standard deviations

In future updates of this review, if standard deviations are not reported we will first try to obtain the missing values from the authors. If not available, where there are missing measures of variance for continuous data but an exact standard error and confidence interval are available for group means, and either the P value or t value is available for differences in the mean, we can calculate them according to the rules described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011): when only the standard error (SE) is reported, standard deviations (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, CIs, ranges or other statistics. If these formulae do not apply, we will calculate the SDs according to a validated imputation method which is based on the SDs of the other included studies (Furukawa 2006). Although some of these imputation strategies can introduce error, the alternative would be to exclude a given study's outcome and thus to lose information. We nevertheless will examine the validity of the imputations in a sensitivity analysis excluding the imputed values.

### 3.3 Last observation carried forward

We anticipate that in some studies the method of last observation carried forward (LOCF) will be employed within the study report. As with all methods of imputation to deal with missing data,

LOCF introduces uncertainty about the reliability of the results (Leucht 2007). Therefore, where LOCF data have been used in the trial, if less than 50% of the data have been assumed we will present and use these data and indicate that they are the product of LOCF assumptions.

## Assessment of heterogeneity

### 1. Clinical heterogeneity

In future updates, we will consider all included studies initially, without seeing comparison data, to judge clinical heterogeneity. We will simply inspect all studies for clearly outlying people or situations which we had not predicted would arise. When such situations or participant groups arise in future updates we will fully discuss them.

### 2. Methodological heterogeneity

In future updates we will consider all included studies initially, without seeing comparison data, to judge methodological heterogeneity. We will simply inspect all studies for clearly outlying methods which we had not predicted would arise. When such methodological outliers arise in updates, we will fully discuss them.

### 3. Statistical heterogeneity

#### 3.1 Visual inspection

We plan to visually inspect graphs of included studies in future updates to investigate the possibility of statistical heterogeneity.

#### 3.2 Employing the $I^2$ statistic

We had planned to investigate heterogeneity between studies by considering the  $I^2$  statistic alongside the  $\text{Chi}^2$  test P value. The  $I^2$  statistic 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 the effects, and ii. strength of evidence for heterogeneity (for example P value from  $\text{Chi}^2$  test, or a CI for the  $I^2$  statistic). An  $I^2$  estimate greater than or equal to around 50%, accompanied by a statistically significant  $\text{Chi}^2$  statistic, is interpreted as evidence of substantial levels of heterogeneity (Higgins 2011). If relevant studies are identified in updated versions of this review where substantial levels of heterogeneity are found in the primary outcome, we plan to explore the reasons for the heterogeneity (Subgroup analysis and investigation of heterogeneity).

## Assessment of reporting biases

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of the results (Egger 1997). 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 do not plan to use funnel plots for outcomes where there are 10 or fewer studies, or where all studies were of a similar size, in updates of this review. In other cases 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 of fixed-effect or random-effects models. The random-effects model 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 as 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 will choose the fixed-effect model for all analyses in future updates of this review. The reader will be, however, able to choose to inspect the data using the random-effects model.

## Subgroup analysis and investigation of heterogeneity

### 1. Subgroup analyses, only primary outcomes

#### 1.1 Clinical state, stage or problem

We proposed to undertake this review and provide an overview of the effects of physical health monitoring for people with schizophrenia in general. We anticipated no subgroup analyses.

#### 2. Investigation of heterogeneity

For future updates, if inconsistency was high we will report this. First, we will investigate whether the data have been entered correctly. Second, if the data are correct, we will visually inspect the graph and successively remove studies outside the company of the rest to see if homogeneity is restored. For this review we have decided that should this occur with data contributing no more than around 10% of the total weighting to the summary finding, we would present the data. If not, then we will not pool the data and will discuss the issues. We know of no supporting research for this 10% cut-off, but we use prediction intervals as an alternative to this unsatisfactory state.

When unanticipated clinical or methodological heterogeneity is obvious, we will simply state hypotheses regarding these for future reviews or versions of this review. We do not anticipate undertaking analyses relating to them.

## Sensitivity analysis

We will, in future, apply all sensitivity analyses to the primary outcomes of this review.

### 1. Implication of randomisation

We aimed to include trials in a sensitivity analysis if they were described in some way as to imply randomisation. For future updates of this review, for the primary outcomes we will include these studies and if there was no substantive difference when the implied randomised studies were added to those with better descriptions of randomisation then we would enter all data from these studies.

### 2. Assumptions for lost binary data

Where assumptions have to be made regarding people lost to follow-up and missing SDs (see [Dealing with missing data](#)), we will compare the findings for the primary outcomes when we use our assumptions compared with the complete data only. We plan to undertake a sensitivity analysis testing how prone the results are to change when 'completer' data only are compared to the imputed data using the above assumption. If future updates find there is a substantial difference, we will report the results and discuss them but will continue to employ our assumption.

### 3. Risk of bias

We plan to analyse the effects of excluding trials that are 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 does not substantially alter the direction of effect or the precision of the effect estimates, then we will include the data from these trials in the analysis.

### 4. Imputed values

We will also 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 data of this kind are included in future updates of this review, we will note substantial differences in the direction or precision of effect estimates in any of the sensitivity analyses listed above. We will not pool data from the trials with imputed values with the other trials contributing to the outcome but present them separately.

### 5. Fixed-effect and random-effects models

We plan to synthesise data in future updates of this review using a fixed-effect model.

## RESULTS

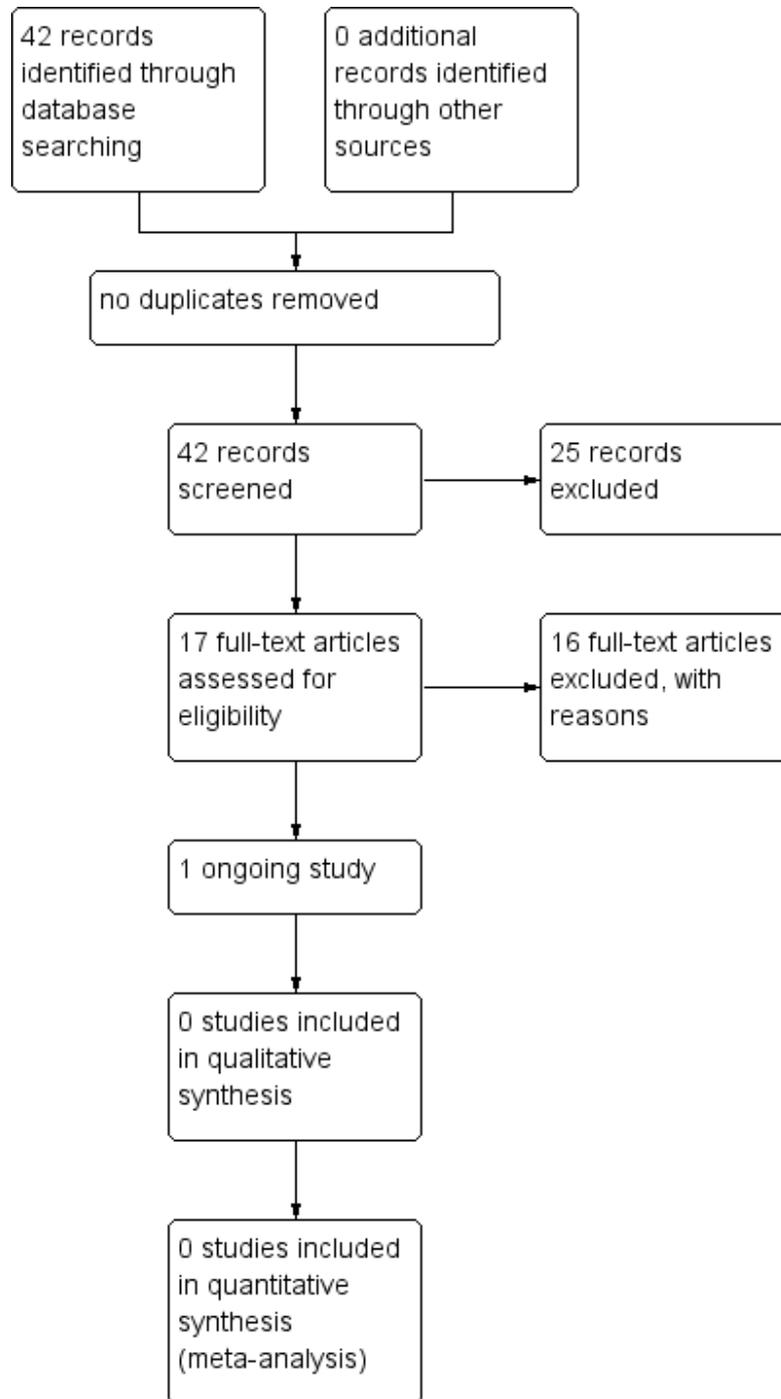
### Description of studies

#### Results of the search

The initial search of the Cochrane Schizophrenia Group Trials Register in 2009 was a combined search designed to identify studies which would be relevant to this review and to another sister

review on physical health advice for people with serious mental illness (Tosh 2013). The search identified 2382 references (from 1558 studies). After examining the reports, only three were suitable for further examination and all were excluded. Forty-two additional studies were identified in the 2012 update, 17 underwent detailed evaluation and all were excluded apart from one which is ongoing (Figure 1). Despite the fact that the Cochrane Schizophrenia Group Trials Register is compiled from large comprehensive and systematic searches for trials, we undertook unsystematic searches of a sample of the component databases (BNI, CINHALL, EMBASE, MEDLINE and PsycINFO) to determine if any material may have been overlooked. We searched using specific phrases ('physical health', 'monitoring' and 'mental illness') as the searches that create the Cochrane Schizophrenia Group Trials Register are methodology specific. We did not identify any further relevant trials.

**Figure 1. Study flow diagram for 2012 update..**



## Included studies

There are no still no studies that have met the criteria for this review.

## Excluded studies

One trial was excluded on the basis that it is an ongoing trial, in the recruitment stage, which is focusing on the monitoring of mental health parameters and not physical health (Jürgens 2008). Another trial had to be excluded as it monitored the effects of a pharmacological intervention on a physical health parameter (Lan 2007). The third exclusion was on the basis that the trial compared the effects of different ways of monitoring a specific anxiety symptom and did not look at a physical health (Rostow 1980). Of the 11 studies that were excluded in the 2012 search, eight did not focus on general physical health as a primary outcome (Becker 2005; Bushe 2010; Carmeli 2012; Kluge 2012; Krakowski 2011; Peuskens 2011; Tanasiewicz 2011; Lin 2010). Two studies had no standard care comparisons (Ozguven 2011; Peuskens 2011) and one provided data on the prevalence of morbidities in the absence of an intervention (Saddichha 2011). For more details please see [Characteristics of excluded studies](#).

### 1. Awaiting assessment

There are no studies awaiting assessment.

### 2. Ongoing studies

We identified one ongoing study (ISRCTN63382258). This trial, for which a protocol is available, is monitoring the oral and dental health of people with serious mental illness, is a cluster randomised trial from the UK and should report in 2015.

## Risk of bias in included studies

There were no studies that fulfilled the criteria for inclusion. We did not exclude any studies on the grounds of poor methodology.

### Allocation

No studies met the criteria for this review.

### Blinding

No studies met the criteria for this review.

## Incomplete outcome data

No studies met the criteria for this review.

## Selective reporting

No studies met the criteria for this review.

## Other potential sources of bias

There were no studies that fulfilled the criteria for inclusion. We did not exclude any studies on the grounds of poor methodology.

## Effects of interventions

See: [Summary of findings for the main comparison Physical health monitoring compared to no monitoring for people with serious mental illness](#)

Currently we know of no fully reported randomised studies describing the effects of monitoring the physical health care of people with serious mental illnesses.

## DISCUSSION

Note: no studies are included in this review, one study is ongoing.

## Summary of main results

Please also see [Summary of findings for the main comparison](#).

### 1. No trial-based evidence

Current medical practice in the UK is led by guidance from bodies such as the National Institute of Clinical Excellence (NICE 2006) and The Maudsley Prescribing Guidelines (Taylor 2009), who predominantly base their guidance on little more than anecdotal evidence, consensus of opinion (Marder 2004) and good intentions. The association between schizophrenia and poor physical health is well established (Robson 2007) and, taken at face value, current guidance seems to make sense. Unfortunately history is littered with treatments and policies which 'seemed like a good idea at the time' but which, with the benefit of hindsight, were at best ineffective and at worst resulted in harm. Extreme examples of well intentioned treatments could be trepanation for epilepsy (Adams 1856), ice-pick lobotomies for unruly children (El-Hai 2008), or radium water for high blood pressure (JAMA 1925). More contemporary and subtle is the wide use of oil of evening

primrose oil for many ailments when evidence for efficacy is poor (Bayles 2009). This could mean that hopes are raised inappropriately and, perhaps, other more effective treatments are avoided. When it comes to mental health policy, the early legislation for the Care Programme Approach in the UK was well intentioned but ultimately it imported a largely wasteful and ineffective package of care from the US (Marshall 1996; Marshall 1998) at a time when even those in the US had found it necessary to substantially evolve the approach into a more effective package (Assertive Outreach). In more recent times the evidence to support the view that specialist mental health services such as Dual Diagnosis Teams, Early Intervention or Assertive Outreach Teams are more beneficial than appropriately supported Community Mental Health Teams is not as strong as would have been originally thought (Ley 2000). Care, and the time of people with serious mental illness, are too costly to waste on ideas that are not of proven benefit. Vulnerable people with serious mental illness should surely expect that all aspects of their care have been subject to some degree of evaluation.

### Overall completeness and applicability of evidence

No studies met the criteria for this review.

### Quality of the evidence

The three studies we obtained for closer inspection were not excluded because of issues of quality. We were unable to find any studies that were vaguely relevant, regardless of whether they were high or poor quality.

### Potential biases in the review process

The search strategies both for the Cochrane Schizophrenia Group Trials Register (October 2009 and October 2012) and in our un-systematic search (see: [Searching other resources](#)) should have been robust enough to detect relevant studies. It is possible that we have failed to identify small studies but we think it unlikely that we would have missed large trials. Studies published in languages other than English, and those with equivocal results, are often difficult to find (Egger 1997). Our search was biased by the use of English phrases. However, given that the Cochrane Schizophrenia Group Trials Register covers many languages but is indexed in English we feel that we would not have missed many studies within the register. For example, the search uncovered 101 studies for which the title was only available in Chinese characters. These were checked for relevance by a Chinese speaking colleague (Jun Xia) and none were identified as possibly relevant to this review.

### Agreements and disagreements with other studies or reviews

The only other similar systematic review that we are aware of is Bradshaw 2005, which investigated the efficacy of healthy living interventions for people with schizophrenia. They too identified no trials of monitoring and we agree that rigorous studies are needed.

## AUTHORS' CONCLUSIONS

### Implications for practice

#### 1. For people with schizophrenia

Due to the lack of evidence for the current guidance around physical health monitoring it is important that people with schizophrenia expect clinicians to explain their intentions clearly. It would seem reasonable that people with schizophrenia are given the choice of whether they want to be monitored in this way, or whether they would want to add to the body of evidence by being part of a well designed trial from which outcomes relevant to their care would be derived.

#### 2. For clinicians

Clinicians should be aware that current guidance on monitoring the physical health for people with serious mental illness is not supported by any evidence from randomised controlled trials. It would seem reasonable that this is explained to people with serious mental illness. It is possible clinicians are expending much effort, time and financial expenditure on monitoring the physical health of people with serious mental illnesses which is unnecessary, intrusive and costly. It is possible that the monitoring may differ depending on who is undertaking the procedure. For example, psychiatrists may not be as good at it as general practitioners. Clinicians should, therefore, take a much more critical view of current guidance and attempt to initiate or get involved with any studies which could provide an evidence base for this practice.

#### 3. For policy makers or managers

Current policies and guidelines are born out of good intentions and “the evidence for such interventions remains uncertain” (NICE 2006). This puts policy makers in a difficult position of galvanising consensus rather than evidence. There remains an enduring concern that “L'enfer est plein de bonnes volontés ou désirs” (Hell is full of good intentions or wishes) (St. Bernard of Clairvaux 1150 quoted in Ammer 2003). Policy makers or managers should be better at recommending an active research interest in this area.

These conclusions have not been altered after completing the assessment of the 42 studies identified in the most recent 2012 search.

## Implications for research

### 1. General

We could not identify any randomised trials that assessed the effectiveness of physical health monitoring in people with serious mental illness and which contradicted the view that current guidance and practice are based on good intentions and expert opinion. Basing care solely on evidence from trials is not realistic (Cooper 2003; Tanenbaum 2005), however many treatments or approaches that are not well evaluated are given to people when it is actually entirely possible to evaluate these approaches. Healthcare professionals may be doing far more good than they realise, or far more harm. As part of a duty of care, we argue that 'what could be known, should be known'.

### 2. Specific

#### 2.1 Reviews

This review should be the focus of regular updates. One new trial will completely change the overview. The excluded studies do suggest other reviews that may be of interest (Table 2).

### 2.2 Trials

We realise that much thought and care goes into the design of randomised studies. We have, however, also given this issue some consideration and suggest what we think to be a feasible design; please see Table 3.

## ACKNOWLEDGEMENTS

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The 2012 version of this review was peer reviewed by Tareq Al Saadi, Mohammed Sawan, Abdul Mounaem Majzoub, Saria Al-nahas, Tarek Nayfeh and MHD Homam Alabaji.

The Cochrane Schizophrenia Group Editorial Base in Nottingham produces and maintains standard text for use in the Methods sections 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 excluded studies *[ordered by study ID]*

| Study          | Reason for exclusion  |
|----------------|---|
| Becker 2005    | Allocation: cluster randomisation.<br>Participants: majority with affective disorder, 1/3 with schizophrenia, remainder with another IDC-Chapter V diagnosis<br>Intervention: education in outcome management - not physical health monitoring                                      |
| Bushe 2010     | Allocation: randomised.<br>Participants: people diagnosed with schizophrenia.<br>Intervention: effects of olanzapine or quetiapine on glucose, lipids and weight - not physical health monitoring   |
| Carmeli 2012   | Allocation: randomised.<br>Participants: people diagnosed with schizophrenia.<br>Intervention: looked at whether increase glutathione levels modulate EEG synchronization - not physical health monitoring  |
| Jürgens 2008   | Allocation: randomised.<br>Participants: people diagnosed with schizophrenia.<br>Intervention: genotype monitoring versus intense clinical monitoring - not physical health monitoring  |
| Kluge 2012     | Allocation: randomised, double-blind.<br>Participants: people diagnosed with schizophrenia.<br>Intervention: effects of clozapine and olanzapine on sleep propensity - not physical health monitoring   |
| Krakowski 2011 | Allocation: randomised, double-blind.<br>Participants: people diagnosed with schizophrenia.<br>Intervention: effects of clozapine, olanzapine and haloperidol on cholesterol levels and cognition - not physical health monitoring  |
| Lan 2007       | Allocation: randomised.<br>Participants: people diagnosed with schizophrenia, schizoaffective disorder, schizophreniform disorder.<br>Intervention: monitoring of the effect of aripiprazole and aripiprazole plus haloperidol on prolactin levels - not physical health monitoring |
| Lin 2010       | Allocation: randomised.<br>Participants: people with schizophrenia.<br>Intervention: effect of health intervention on constipation - not physical health monitoring   |
| Nielsen 2012   | Allocation: randomised.<br>Participants: people with schizophrenia.<br>Intervention: evaluating capillary blood sampling device versus venous sampling in patients taking clozapine - not physical health monitoring  |

(Continued)

|                  |   |
|------------------|---|
| Ozguven 2011     | Allocation: randomised.<br>Participants: women with unclear diagnosis (within spectrum of atypical antipsychotic monotherapy)<br>Intervention: measured effects of olanzapine and quetiapine on weight gain, BMI, lipid profile - no standard care comparison |
| Peuskens 2011    | Allocation: randomised.<br>Participants: people with schizophrenia.<br>Intervention: evaluated the effect of sertindole or risperidone on metabolic profile - no standard care comparison   |
| Rostow 1980      | Allocation: randomised.<br>Participants: people with “compulsive or persistent pacing”, not necessarily having a diagnosis of serious mental illness  |
| Saddichha 2011   | Allocation: not randomised, cross-sectional survey.<br>Participants: patients diagnosed with schizophrenia or schizoaffective disorder<br>Intervention: reported prevalence of diabetes hypertension and obesity on patients on antipsychotic medications     |
| Strom 2011       | Allocation: randomised.<br>Participants: patients with schizophrenia.<br>Intervention: death associated with olanzapine and ziprasidone use   |
| Tanasiewicz 2011 | Allocation: randomised.<br>Participants: people with schizophrenia on atypical and classical neuroleptics<br>Intervention: oral hygienic training - not physical health monitoring  |

### Characteristics of ongoing studies [ordered by study ID]

#### ISRCTN63382258

|                     |   |
|---------------------|---|
| Trial name or title | Three Shires Early Intervention Dental Trial (ISRCTN63382258).  |
| Methods             | Allocation: cluster randomised.<br>Blindness: none.<br>Duration: 12 months.   |
| Participants        | Diagnosis: serious mental illness.<br>N = 1074.<br>Age: >18 years.<br>Sex: not reported.<br>History: not reported.<br>Exclusion: any Early Intervention in Psychosis team that does not wish to take part, any individual care co-ordinator or service user within a team that does not wish to take part, any service user aged less than 18 years old at randomisation<br>Setting: multi-centre, community; Early Intervention in Psychosis teams, UK |
| Interventions       | 1. dental awareness training for care co-ordinators + an oral health checklist for service users + standard care<br>2. standard care.   |

ISRCTN63382258 (Continued)

|                     |   |
|---------------------|---|
| Outcomes            | Visit to dentist within one year of exposure to checklist.<br>Registration with a dentist.<br>Frequency of tooth brushing.<br>Reason for dental visit (routine versus for problem).<br>Quality of life (Oral Impacts on Daily Performance, OIDP).<br>Economic data.<br>Leaving the study. |
| Starting date       | February 2012.  |
| Contact information | Miss Hannah Jones, CLAHRC-NDL, Institute of Mental Health, University of Nottingham, Triumph Road, Nottingham, NG7 2TU, UK. Email: Hannah.Jones@nottingham.ac.uk  |
| Notes               | Study protocol available. Contacted author to request data, data will be available September 2013   |

## DATA AND ANALYSES

This review has no analyses.

## ADDITIONAL TABLES

**Table 1. Series of related reviews**

| Title                                | Reference                    |
|--------------------------------------|------------------------------|
| Physical health care monitoring      | This review                  |
| General physical health advice       | <a href="#">Tosh 2011</a>    |
| Advice regarding smoking cessation   | <a href="#">Khanna 2012</a>  |
| Advice regarding oral health care    | <a href="#">Khokhar 2011</a> |
| Advice regarding HIV/AIDs prevention | <a href="#">Wright 2012</a>  |
| Advice regarding substance use       | Underway                     |

**Table 2. Reviews suggested by excluded studies**

| Broad issue                                    | Specific issue  | Excluded study                 | Existing review   |
|--|---|--------------------------------|---|
| <b>Antipsychotic adverse effects</b>           | clozapine and olanzapine on sleep propensity                              | <a href="#">Kluge 2012</a>     | <a href="#">Komossa 2010</a>                              |
| <b>Antipsychotic metabolic adverse effects</b> | aripiprazole and aripiprazole plus haloperidol on prolactin levels        | <a href="#">Lan 2007</a>       |   |
|  | clozapine, olanzapine and haloperidol on cholesterol levels and cognition | <a href="#">Krakowski 2011</a> | <a href="#">Asenjo 2010</a> ; <a href="#">Essali 2009</a> |
|  | olanzapine and quetiapine on weight gain, BMI, lipid profile              | <a href="#">Ozguven 2011</a>   | <a href="#">Komossa 2010</a>                              |
|  | olanzapine or quetiapine on glucose, lipids and weight                    | <a href="#">Bushe 2010</a>     |   |
|  | sertindole or risperidone on metabolic profile                            | <a href="#">Peuskens 2011</a>  | <a href="#">Komossa 2009</a>                              |
| <b>Education</b>                               | education in outcome management   | <a href="#">Becker 2005</a>    |   |

**Table 2. Reviews suggested by excluded studies** (Continued)

|                                       |  |                  |              |
|---------------------------------------|--|------------------|--------------|
| <b>Physiological monitoring</b>       | evaluating capillary blood sampling device vs venous sampling in patients taking clozapine | Nielsen 2012     |              |
|                                       | genotype monitoring versus intense clinical monitoring                                     | Jürgens 2008     |              |
|                                       | glutathione levels modulate EEG-synchronization  | Carmeli 2012     |              |
| <b>Specific physical health issue</b> | health intervention on constipation  | Lin 2010         |              |
|                                       | oral hygienic training   | Tanasiewicz 2011 | Khokhar 2011 |

**Table 3. Suggested design of study**

|                      |   |
|----------------------|---|
| <b>Methods</b>       | Allocation: randomised, clearly described.<br>Blinding: single - particular to specific outcomes (see below).<br>Duration: 6 months.  |
| <b>Participants</b>  | Diagnosis: schizophrenia, or any serious mental illness.<br>N=450.*<br>Age: any.<br>Sex: both.<br>History: any.   |
| <b>Interventions</b> | 1. General physical health care checklist (e.g. Physical Health Improvement Profile see White 2009): administered by Care Co-ordinator. N=150.<br>2. Specific aspect of physical health care checklist (e.g. BSDH 2000): administered by Care Co-ordinator. N=150.<br>3. Standard care: administered by Care Co-ordinator. N=150. |
| <b>Outcomes</b>      | Death.<br>Morbidity: serious or minor, categorised by type, rates of events - general or specific.<br>Healthy days.<br>Service use: visit to health care practitioner.<br>Acceptability of checklist.<br>Compliance: with physical health care advice, including treatments.<br>Adverse effects: any.                             |
| <b>Notes</b>         | * For 20% difference between groups for a binary outcome to be highlighted with reasonable degree of confidence 150 people are needed per group   |

## APPENDICES

### Appendix 1. Previous search

#### 1. Cochrane Schizophrenia Group Trials Register (October 2009)

The register was searched using the phrase: [(*\*physical\** or *\*cardio\** or *\*metabolic\** or *\*weight\** or *\*HIV\** or *\*AIDS\** or *\*Tobacc\** or *\*Smok\** or *\*sex\** or *\*medical\** or *\*dental\** or *\*alcohol\** or *\*oral\** or *\*vision\** or *\*sight\** or *\*hearing\** or *\*nutrition\** or *\*advice\** or *\*monitor\** in title of REFERENCES) AND (*\*education\** OR *\*health promot\** OR *\*preventi\** OR *\*motivate\** or *\*advice\** or *\*monitor\** in interventions of STUDY)]

The Cochrane Schizophrenia Group's Trials Register is compiled by systematic searches of major databases, handsearches of relevant journals and conference proceedings (see [Group Module](#)). Incoming trials are assigned to relevant existing or new review titles.

### Appendix 2. Previous data collection and analysis methods

#### 1. Extraction

Authors GT and AC independently extracted data from included studies. Again, we discussed any disagreement, documented our decisions and, if necessary, we contacted the authors of studies for clarification. With remaining problems MB helped clarify issues and we documented our final decisions. We extracted data presented only in graphs and figures whenever possible, we only included it if two reviewers independently had the same result. We made attempts to contact authors through an open-ended request in order to obtain any missing information or for clarification whenever necessary. Where possible, we extracted data relevant to each component centre of multi-centre studies separately.

#### 2. Management

##### 2.1 Forms

GT and AC extracted data onto standard, simple forms.

##### 2.2 Data from multi-centre trials

Where possible the authors verified independently calculated centre data against original trial reports.

#### 3. Scale-derived data

We included continuous data from rating scales only if:

- the psychometric properties of the measuring instrument had been described in a peer-reviewed journal ([Marshall 2000](#)); and
- the measuring instrument was not written or modified by one of the trialists for that particular trial; and
- the measuring instrument is either i. a self-report or ii. completed by an independent rater or relative (not the therapist).

#### 4. Endpoint versus change data

We preferred to use scale endpoint data, which typically cannot have negative values and is easier to interpret from a clinical point of view. Change data are often not ordinal and are very problematic to interpret. If endpoint data were unavailable, we used change data.

#### 5. 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 aim to apply the following standards to all data before inclusion: (a) standard deviations and means are reported in the paper or obtainable from the authors; (b) when a scale starts from the finite number zero, the standard deviation, when multiplied by two, is less than the mean (as otherwise the mean is unlikely to be an appropriate measure of the centre of the distribution, ([Altman 1996](#)); (c) if a scale starts from a positive value (such as PANSS which can have values from 30 to 210) the calculation described above will be modified to take the scale starting point into account. In these cases skew is present if  $2SD > (S - S_{min})$ , 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 which includes a possibility of negative values (such as change data), it is difficult to tell whether data are skewed or not. We entered skewed data from studies of less than 200 participants in additional tables rather than into an analysis. Skewed data pose less of a problem when looking at means if the sample size is large, and we entered skewed data from large sample sizes into syntheses.

#### 6. Common measure

To facilitate comparison between trials, we intended to convert 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).

#### 7. Conversion of continuous to binary

Where possible, efforts were made to convert outcome measures to dichotomous data. This could be done by identifying cut-off points on rating scales and dividing participants accordingly into 'clinically improved' or 'not clinically improved'. It was generally assumed that if there had been a 50% reduction in a scale-derived score such as the Brief Psychiatric Rating Scale (BPRS, [Overall 1962](#)) or the

Positive and Negative Syndrome Scale (Kay 1986, Kay 1987), 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.

#### 8. 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 physical health monitoring.

#### 9. Summary of findings table

We anticipate including the following outcomes in a summary of finding table.

##### 1. Physical health - immediate

1.1 Failure to identify a disease state and provide appropriate treatment

1.2 Failure to effectively manage a known disease state

##### 2. Quality of life

2.1 Loss of Activities of Daily Living (ADL) skills

##### 3. Adverse event

3.1 Clinically important specific adverse effects (cardiac effects, death, movement disorders, prolactin increase and associated effects, weight gain, effects on white blood cell count)

3.2 Death - natural or suicide

##### 4. Economic

4.1 Increased costs of health care

##### 5. Social

5.1 Social Isolation as a result of preventable incapacity

### Assessment of risk of bias in included studies

Again working independently, GT,AC and MB assessed risk of bias using the tool described in the Cochrane Collaboration Handbook (Higgins 2008). This tool encourages consideration of how the sequence was generated, how allocation was concealed, the integrity of blinding at outcome, the completeness of outcome data, selective reporting and other biases. We would have excluded studies where allocation was clearly not concealed.

We did not include trials with high risk of bias (defined as at least 3 out of 5 domains were categorised as 'No') in the meta-analysis. 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 are provided, we contacted the authors of the studies in order to obtain further information. Non-concurrence in quality assessment was reported.

### Measures of treatment effect

#### 1. Binary data

For binary outcomes we calculated a standard estimation of the random-effect 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). Within the Summary of Findings table we assumed for calculation of the low risk groups that the lowest control risk applied to all data. We did the same for the assumption of the highest risk groups. We used the Summary of Findings table to calculate absolute risk reduction for primary outcomes.

#### 2. Continuous data

##### 2.1 Summary statistic

For continuous outcomes we estimated a fixed-effect mean difference between groups. We preferred not to calculate effect size measures (standardised mean difference SMD). However, in the case of where scales were of such similarity to allow presuming there was a small difference in measurement, we calculated it and, whenever possible, we 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).

Where clustering is not accounted for in primary studies, we 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 co-efficient of their clustered data and to adjust for this by using accepted methods (Gulliford 1999). Where clustering had been incorporated into the analysis of primary studies, we present 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 intra class correlation co-efficient (ICC) [Design effect =  $1+(m-1)*ICC$ ] (Donner 2002). If the ICC was not reported it was assumed to be 0.1 (Ukoumunne 1999).

If cluster studies has been appropriately analysed taking into account intra class correlation co-efficient 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 carryover 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 only used data of the first phase of cross-over studies.

## 3. Studies with multiple treatment groups

Where a study involved more than two treatment arms, if relevant, we presented the additional treatment arms in comparisons. Where the additional treatment arms were not relevant, we did not reproduce these data.

## Dealing with missing data

### 1. Overall loss of credibility

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

### 2. Binary

In the case where attrition for a binary outcome is between 0 and 50% and where these data were not clearly described, we presented data on a 'once-randomised-always-analyse' basis (an intention to treat analysis). Those lost to follow up were all assumed to have the same rates of negative outcome as those who completed, with the exception of the outcome of death. A sensitivity analysis was undertaken testing how prone the primary outcomes were to change when 'completed' data only were compared to the intention to treat analysis using the above assumption.

### 3. Continuous

#### 3.1 Attrition

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

#### 3.2 Standard deviations

Where there are missing measures of variance for continuous data but exact standard error and confidence interval are available for group means, either 'p' value or 't' value are available for differences in mean, we calculated standard deviation value according to method described in Section 7.7.3 of the Cochrane Handbook (Higgins 2008). If standard deviations were not reported and could not be calculated from available data, we asked authors to supply the data. In the absence of data from authors, the mean standard deviation from other studies was used.

#### 3.3 Last observation carried forward

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

## Assessment of heterogeneity

### 1. Clinical heterogeneity

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

## 2. Methodological heterogeneity

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

## 3. Statistical

### 3.1 Visual inspection

We visually inspected graphs to investigate the possibility of statistical heterogeneity.

### 3.2 Employing the I-squared statistic

Heterogeneity between studies was investigated by considering the I-squared method alongside the Chi<sup>2</sup> 'p' value. The I<sup>2</sup> provides an estimate of the percentage of inconsistency thought to be due to chance (Higgins 2003). The importance of the observed value of I<sup>2</sup> depends on i. magnitude and direction of effects and ii. strength of evidence for heterogeneity (e.g. 'p' value from Chi<sup>2</sup> test, or a confidence interval for I<sup>2</sup>).

I<sup>2</sup> estimate greater than or equal to 50% accompanied by a statistically significant Chi<sup>2</sup> statistic, was interpreted as evidence of substantial levels of heterogeneity (Section 9.5.2 - Higgins 2008) and reasons for heterogeneity were explored. If the inconsistency was high and the clear reasons were found, we presented data separately.

## Assessment of reporting biases

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). These are described in Section 10 of the Cochrane Handbook (Higgins 2008). 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 where there were ten or fewer studies, or where all studies were of similar sizes. In other cases, where funnel plots were possible, we sought statistical advice in their interpretation.

## Data synthesis

Where possible we employed a random-effect model for analyses. We understand that there is no closed argument for preference for use of fixed or random-effect models. The random-effect method incorporates an assumption that different studies are estimating different, yet related, intervention effects. According to our hypothesis of an existing variation across studies, to be explored further in the meta-regression analysis despite being cautious that that random-effects methods does put added weight onto the smaller of the studies - we favoured using random-effect model.

## Subgroup analysis and investigation of heterogeneity

### 1. Subgroup analyses

We anticipate no sub-group analyses.

### 2. Investigation of heterogeneity

#### 2.1 Unanticipated heterogeneity

Should unanticipated clinical or methodological heterogeneity be obvious we will simply state hypotheses regarding these for future reviews or versions of this review. We do not anticipate undertaking analyses relating to these.

#### 2.2 Anticipated heterogeneity

We are concerned that focused physical health care monitoring may have different effects than a more general approach. We therefore anticipate some heterogeneity for the primary outcomes and propose to summate all data but also present them separately.

## Sensitivity analysis

### 1. Implication of randomisation

We aimed to include trials in a sensitivity analysis if they are described in some way as to imply randomisation. For the primary outcomes we included these studies and if there was no substantive difference when we added the implied randomised studies to those with better description of randomisation, we then employed all data 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 where we used our assumption and compared with completer data only. If there was a substantial difference, we reported results and discussed them but continue to employ our assumption.

## WHAT'S NEW

Last assessed as up-to-date: 1 December 2012.

| Date             | Event  | Description   |
|------------------|--|---|
| 18 November 2013 | New citation required but conclusions have not changed | Update completed, no change to conclusions.   |
| 27 June 2013     | New search has been performed                          | An update search was conducted in October 2012, which resulted in 42 studies being added to awaiting classification. Upon close inspection of these studies, none of them were included in this update. Thus, the conclusion of this review remains unchanged |

## HISTORY

Protocol first published: Issue 1, 2010

Review first published: Issue 3, 2010

| Date            | Event   | Description  |
|-----------------|---------|--|
| 17 October 2012 | Amended | <i>Update search of Cochrane Schizophrenia Group's Trial Register (see <a href="#">Search methods for identification of studies</a>), 42 studies added to awaiting classification.</i> |
| 17 March 2010   | Amended | Previously combined studies split into separated studies and included in Excluded Studies section  |
| 17 March 2010   | Amended | Amendment of outcomes to be included in summary of findings table  |

## CONTRIBUTIONS OF AUTHORS

Graeme Tosh - project initiation, protocol writing, primary reviewer, results and discussion writing.

Andrew Clifton - co-reviewer and liaison on discussion and results writing.

Jun Xia - co-reviewer, screened results of 2012 update, contributed to results writing.

Margueritte White - co-reviewer, screened results of 2012 update, contributed to results writing.

## DECLARATIONS OF INTEREST

Graeme Tosh and Andrew Clifton are involved in the trial identified as ongoing in this review.

All other authors have no conflict of interest.

## SOURCES OF SUPPORT

### Internal sources

- University of Nottingham, UK.

### External sources

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

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Subsequent to the publication of the protocol we identified that our search strategy may have excluded some relevant studies, so we added the words 'advice' and 'monitor' in the title of references section and added \*advice\* and \*monitor\* to the interventions of study field.

The original search phrase: [(*\*physical\** or *\*cardio\** or *\*metabolic\** or *\*weight\** or *\*HIV\** or *\*AIDS\** or *\*Tobacc\** or *\*Smok\** or *\*sex\** or *\*medical\** or *\*dental\** or *\*alcohol\** or *\*oral\** or *\*vision\** or *\*sight\** or *\*hearing\** or *\*nutrition\** in title of REFERENCES) AND (*\*education\** OR *\*health promot\** OR *\*preventi\** OR *\*motivate\** in interventions of STUDY)] yielded 2326 references whilst the new search phrase: [(*\*physical\** or *\*cardio\** or *\*metabolic\** or *\*weight\** or *\*HIV\** or *\*AIDS\** or *\*Tobacc\** or *\*Smok\** or *\*sex\** or *\*medical\** or *\*dental\** or *\*alcohol\** or *\*oral\** or *\*vision\** or *\*sight\** or *\*hearing\** or *\*nutrition\** or *\*advice\** or *\*monitor\** in title of REFERENCES) AND (*\*education\** OR *\*health promot\** OR *\*preventi\** OR *\*motivate\** or *\*advice\** or *\*monitor\** in interventions of STUDY)] yielded 2383 references.

We have altered the text of the objectives to reflect the title of the review and outcomes of interest more accurately.

We have also corrected a typo in the outcomes where Quality of Life/Satisfaction should have read Quality of life or general functioning. We also created a new outcome - Satisfaction with care.

## **INDEX TERMS**

### **Medical Subject Headings (MeSH)**

\*Health Status; \*Quality of Life; Disease Progression; Mental Disorders [\*complications]

### **MeSH check words**

Humans