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## Interventions to encourage uptake of cancer screening for people with severe mental illness (Review)

Barley EA, Borschmann RD, Walters P, Tylee A

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[Intervention Review]

# Interventions to encourage uptake of cancer screening for people with severe mental illness

Elizabeth A Barley<sup>1</sup>, Rohan D Borschmann<sup>2</sup>, Paul Walters<sup>3</sup>, Andre Tylee<sup>4</sup>

<sup>1</sup>College of Nursing, Midwifery and Healthcare, University of West London, Brentford, UK. <sup>2</sup>Centre for Adolescent Health, Murdoch Childrens Research Institute, Royal Children's Hospital, Melbourne, Australia. <sup>3</sup>Department of Mental Health, Dorset HealthCare University NHS Foundation Trust and Bournemouth University, Weymouth, UK. <sup>4</sup>Health Service and Population Research Department, Institute of Psychiatry, King's College London, London, UK

Contact address: Elizabeth A Barley, College of Nursing, Midwifery and Healthcare, University of West London, Paragon House, Boston Manor Road, Brentford, Middlesex, TW8 9GA, UK. [elizabeth.barley@uwl.ac.uk](mailto:elizabeth.barley@uwl.ac.uk).

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## ABSTRACT

### Background

Adults with severe mental illness (i.e. schizophrenia or other related psychotic disorders and bipolar disorder) can be at greater risk of cancer than those without severe mental illness (SMI). Early detection of cancer through screening is effective in improving patient outcomes including death. However, people with SMI are less likely than others to take up available cancer screening.

### Objectives

To determine the effectiveness of interventions targeted at adults with SMI, or their carers or health professionals, and aimed at increasing the uptake of cancer screening tests for which the adults with SMI are eligible.

### Search methods

We searched the Cochrane Schizophrenia Group's Trials Register (October 25, 2012; December 19, 2014; April 07, 2015; July 04, 2016).

### Selection criteria

All randomised controlled trials (RCTs) of interventions, targeted towards adults with SMI or their carers or health professionals, to encourage uptake of cancer screening tests for which the adults with SMI were eligible.

### Data collection and analysis

Two review authors independently screened titles and abstracts and assessed these against the inclusion criteria.

### Main results

We did not find any trials that met the inclusion criteria.

## Authors' conclusions

A comprehensive search showed that currently there is no RCT evidence for any method of encouraging cancer screening uptake in people with SMI. No specific approach can therefore be recommended. High-quality, large-scale RCTs are needed urgently to help address the disparity between people with SMI and others in cancer screening uptake.

## PLAIN LANGUAGE SUMMARY

### Interventions to encourage cancer screening uptake in severe mental illness

Cancer is a leading cause of death worldwide, accounting for approximately 13% of all deaths in 2007. Some studies have reported an increased incidence of cancer in people with mental health problems. The Schizophrenia Commission reports that people with schizophrenia who develop cancer are three times more likely to die than those in the general population with cancer.

Mental illness is associated with certain health problems, including: obesity; smoking; drinking alcohol; and poor diet, all of which increase risk of cancer. It has been estimated that approximately one-third of cancer deaths could be prevented with early detection, of which cancer screening is the most effective method. However, people with mental illness are less likely than others to take up available cancer screening. Reasons for non-uptake include: low income; increasing age; lack of transport; embarrassment; lack of reminders; and lack of familiar care providers.

In the general population, telephone invitations, telephone counselling, prompts following the initial invitation and opportunistic screening are good at increasing uptake of cancer screening. Reducing financial barriers (i.e. providing free screening tests, bus passes or postage) may also help. GPs have also been offered incentives under the Quality and Outcomes Framework to provide regular physical health checks to people with mental illness. People with mental illness may require more individualised care, such as more intense counselling, to encourage screening.

A comprehensive search showed that currently there is no trial evidence for any method of encouraging uptake of cancer screening for people with mental illness. No specific approach can therefore be recommended. Early detection of cancer through screening is effective in improving patient outcomes, including death. Given that people with mental illness are at greater risk of cancer but less likely than others to take up available screening, better approaches that encourage uptake of cancer screening are needed urgently. Further research is required to ensure that people with mental illness do not miss out on cancer screening.

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

## BACKGROUND

### Description of the condition

People with schizophrenia (and related non-organic psychotic disorders) and bipolar disorder involving prolonged treatment and disability or dysfunction are considered to have severe mental illness (SMI) (Howard 2010; Ruggeri 2000). Schizophrenia is characterised by distortions of thinking and perception, often accompanied by delusions, hallucinations and blunting or incongruity of emotional responses. Apathy and paucity of speech may also develop, which can result in reduced social performance. Bipolar

disorder is characterised by repeated episodes during which the individual's mood and activity are substantially disturbed, alternating between elevated mood and activity and decreased energy and activity. Prevalence rates of SMI vary according to how its definition is operationalised (Ruggeri 2000), but, using a conservative definition (NIMH 1987), the total population-based annual prevalence in Europe has been found to be approximately two per thousand (Ruggeri 2000).

Cancer is a leading cause of death worldwide, accounting for approximately 13% of all deaths in 2007 (WHO 2009). Some studies have reported an increased incidence of cancer in people with SMI, although data are conflicting (Howard 2010; Leucht 2007). This may be due to lack of consideration by researchers of the

influence of missing cancer diagnoses, shortened life expectancy, historical and health service contexts, behavioural risk factors and genetic or drug effects (Howard 2010). However, SMI is associated with certain adverse health behaviours and health problems (Brown 1999), including obesity (Allison 1999), smoking (Dalack 1998; McReadie 2002), drinking (McReadie 2002) and poor diet (Osborn 2007) which predispose individuals to cancer, especially lung and breast cancer (Howard 2010). Cancer screening (the systematic application of a test in an asymptomatic population in order to identify individuals with an abnormality suggestive of a specific cancer) (WHO 2007), is associated with reduced rates of morbidity and mortality (Anttila 2004; Botha 2003; Draisma 2003; Rhodes 2000). It has been estimated that approximately one-third of cancer deaths could be prevented with early detection, of which screening is the most effective method (WHO 2007). Many countries offer screening routinely for a wide range of cancers including cervical (Anttila 2004), prostate (Draisma 2003), breast (Botha 2003) and colorectal (Rhodes 2000). However, a recent review (Howard 2010), which identified 12 studies (conducted in Iceland, USA, Canada, Australia, and the UK) of cancer screening uptake in people with mental illness, concluded that adults with SMI were less likely than other groups to receive screening for a range of cancers (i.e. cervical, breast, colorectal, and prostate cancer).

### Description of the intervention

In the general population, telephone invitations, telephone counselling prompts following the initial invitation and opportunistic screening are effective in increasing screening uptake across a range of screening programmes (Jepson 2000). Reducing financial barriers (i.e. providing free screening tests, bus passes or postage) may also be effective (Jepson 2000). Health service level interventions may also be important. A recent study (Abrams 2012), conducted in Maryland, USA, found, in contrast to other studies using similar methods, that cervical cancer screening was increased in women with SMI compared with controls without SMI; study participants were all enrolled in Maryland's Medicaid programme and the authors conclude that their novel finding may be explained by participation in this programme, which is situated in a wealthy state that has achieved relatively high grades for its public mental health system. In the UK, since 2003, GPs have been offered incentives under the Quality and Outcomes Framework (BMA 2003) to offer regular physical health reviews to people with SMI. Since 2006 (BMA 2006), a specific recommendation was made to offer preventative screening appropriate to age and gender, including mammography and cervical screening. It is not known what effect this has had on screening uptake in people with SMI in the UK.

### How the intervention might work

Screening uptake may be determined by client- or service-related factors (Bonfill Cosp 2001; Jepson 2000). Studies that examined the reasons for non-uptake of cancer screening in people with SMI identified similar reasons for individuals with and without mental illness (Martens 2009; Owen 2002; Werneke 2006). Reasons for non-uptake included low income, increasing age, lack of transport, embarrassment, lack of reminders and lack of familiar care providers. Interventions found to increase screening uptake in other populations may therefore also be effective in people with SMI. However, one study (Dickerson 2003) found that people with SMI were more likely to perceive barriers to receiving medical care than those in a matched sample from the general population, so individualised consideration of perceived barriers or more intensive counselling to address barriers may be necessary in people with SMI. Qualitative research (Miller 2007) suggests that poor communication between primary care and psychiatric services may also contribute to reduced screening uptake, so interventions that address this may also be important.

### Why it is important to do this review

Cancer screening may be especially important for people with SMI who may be at increased risk of some cancers and of worse cancer outcome (Howard 2010). However, there is a reduced uptake of screening in this population (Howard 2010). Systematic reviews (Bonfill Cosp 2001; Jepson 2000) have demonstrated the effectiveness of a range of interventions to increase cancer screening uptake. However, there are likely to be both client-related and service-related barriers to uptake of screening which are specific to people with SMI. This review is needed to determine whether interventions tailored to the needs of people with SMI are effective in increasing their uptake of cancer screening.

## OBJECTIVES

To determine the effectiveness of interventions targeted at adults with severe mental illness (SMI) (i.e. schizophrenia or other related psychotic disorders and bipolar disorder), or their carers or health professionals, and aimed at increasing the uptake of cancer screening tests for which the adults with SMI are eligible.

## METHODS

### Criteria for considering studies for this review

## Types of studies

All relevant randomised controlled trials (RCTs). If trials were described as 'double blind' but implied randomisation, we planned to include such trials in a sensitivity analysis (see [Sensitivity analysis](#)). If their inclusion did not result in a substantive difference, they would have remained in the analyses. If their inclusion did result 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. Quasi-randomised studies, such as those allocating by alternate days of the week, were not eligible for inclusion.

## Types of participants

Male and female participants (aged 18 years and over) with SMI (i.e. schizophrenia or other related psychotic disorders and bipolar disorder), however diagnosed, being treated in any setting and who were eligible for any cancer screening programme (e.g. for cervical, breast, prostate, colorectal cancer) as defined by the entry criteria for that programme. Those people due, overdue, returning for a repeat test or returning for follow-up subsequent to an abnormal test were eligible for inclusion. We planned to include trials where participants had only the designation of having SMI, but not include those trials where bipolar was the sole diagnosis. We would have included study participants with substance abuse disorders co-morbid with SMI. Since people with non-severe mental illness (e.g. anxiety disorder, depression) may be more likely to attend screening, possibly due to increased contact with health care ([Carney 2006](#)), we planned to include studies with populations involving people with non-severe mental disorders only if at least 80% of participants had SMI, or if data limited to those with SMI were available. Trials of study participants with SMI and concomitant physical illness were also eligible for inclusion.

## Types of interventions

### 1. Intervention target

Studies of interventions targeted at adults with SMI, or their carers or health professionals or both, and aimed at increasing the uptake of cancer screening tests for which the adults with SMI were eligible. Interventions targeted at health professionals specifically had to relate to increasing uptake of screening in people with SMI, as interventions aimed at health professionals to increase overall screening uptake are the subject of other Cochrane reviews ([Freemantle 1997](#); [Gordon 1998](#); [Gorman 1998](#); [Hulscher 2006](#); [Ivers 2012](#); [OBrien 2001](#); [Romero 2004](#)). We intended to exclude studies with interventions aimed at populations, such as mass media campaigns, as these have been covered by another Cochrane review ([Grilli 2000](#)) and the studies are unlikely to be targeted at those with SMI.

## 2. Cancer screening tests

Cancer screening tests may be universal (aimed at the entire population), selective (aimed at specific groups) or opportunistic (screening is proposed during a normal consultation) and aimed at detecting the presence or absence of cancer during the pre-symptomatic phase or before clinical detection. Screening procedures should involve a healthcare professional; examples include: mammography, cervical 'Papanicolaou' smears, colorectal cancer screening and prostatic cancer screening (prostate-specific antigen (PSA) test, digital rectal examination). This is not an exhaustive list. We excluded studies of self-examination procedures, such as breast or testicular self-examination.

## 3. Intervention type

Any type of intervention was eligible for inclusion; for instance, invitations, reminders, education, counselling, use of technology such as mobile phones and email, interventions to improve access, procedural changes to increase acceptability, incentives or removal of financial barriers, office systems or audit. Interventions could be specific to a particular cancer screening test or could include invitations to other healthcare services.

We planned to exclude interventions focused on promoting 'informed uptake' unless they included screening uptake as a secondary outcome. This is because it is recognised that the concept of informed uptake is complex: screening may have associated harms as well as benefits, non-uptake can also be informed; individual choice should be respected ([Jepson 2000](#)) and provision of risk information may sometimes lead to reduced uptake ([Edwards 2006](#)).

Studies that sought only to measure the psychological impact of screening or intention to undertake screening unless screening uptake was reported as a secondary outcome were not eligible for inclusion. We also planned to exclude studies concerning compulsory screening (for example, in prisons or secure units) or hypothetical decisions to participate in screening.

## 4. Control

No intervention or usual care as defined by the study authors. We planned to record and assess details of the usual care for heterogeneity between studies.

## Types of outcome measures

### Primary outcomes

#### 1. Uptake of screening

1.1 Uptake of screening as recorded by health service records (such as screening administration system, hospital or primary care records)

1.2 Uptake of screening as collected via self-report (i.e. directly reported by the participant in a telephone interview or questionnaire)

## Secondary outcomes

### 1. Attitudes to screening as measured by the study authors

1.1 Satisfaction with screening

1.2 Decisional conflict

1.3 Clinically significant change in anxiety

1.4 Any change in anxiety

1.5 Clinically significant change in emotional wellbeing

1.6 Any change in emotional wellbeing

### 2. Knowledge of screening as measured by the study authors

2.1 Any change in knowledge of eligibility for tests

2.2 Any change in knowledge of cancer risk

2.3 Any change in accurate cancer risk perception

### 3. Reported intention to attend screening (i.e. directly reported by the participant in a telephone interview or questionnaire)

### 4. Booking of appointments as recorded in health service records

### 5. Economic outcomes

5.1 Direct costs of the intervention

5.2 Indirect costs

### 6. Intervention acceptability

6.1 Number of participants leaving the trial early - total proportion leaving the study early

6.2 Number of participants who left the study early due to adverse events during the trial - proportion leaving the study early due to adverse events

## Search methods for identification of studies

### Electronic searches

### Cochrane Schizophrenia Group's Study-Based Register of Trials

On July 4, 2016, the information specialist searched the the register using the following search strategy:

\*Cancer\* in Health Care Condition Field of STUDY

In such study-based register, searching the major concept retrieves all the relevant keywords and studies because all the studies have already been organised based on their interventions and linked to the relevant topics.

The Cochrane Schizophrenia Group's Register of Trials is compiled by systematic searches of major resources (including AMED, BIOSIS, CINAHL, EMBASE, MEDLINE, PsycINFO, PubMed, and registries of clinical trials) and their monthly updates, hand-searches, grey literature, and conference proceedings (see [Group's Module](#)). There is no language, date, document type, or publication status limitations for inclusion of records into the register.

For previous searches, please see [Appendix 1](#).

### Searching other resources

#### 1. Reference searching

We planned to search the bibliographies of all retrieved articles for additional references. We would have recorded the number of cited trials not detected by the electronic search as a measure of the sensitivity of the electronic search.

#### 2. Personal communication

We planned to contact the authors of all the included studies and authors with at least two publications amongst those studies that we excluded, but which appeared related to the review, to ask if they knew of any study which met the inclusion criteria of this review. This would have helped to identify unpublished or ongoing studies.

## Data collection and analysis

### Selection of studies

Two review authors (EB and RB) independently examined the titles and abstracts of studies identified by the above searches for relevance. The full text of studies deemed potentially relevant by either author would have been obtained if we had identified suitable studies. The same two review authors would have then independently assessed each text for eligibility based on the above inclusion criteria. We planned to calculate inter-rater agreement using Cohen's Kappa and report results. Disagreements would have been resolved by discussion until consensus was reached. We would have recorded any excluded and included studies. If it was



not possible to obtain sufficient information to judge whether a study was eligible for inclusion, we would have recorded the study as 'awaiting assessment'.

### Data extraction and management

Two review authors (EB and RB) would have independently extracted data using data extraction forms. We would have piloted the data extraction forms and extracted the following data from each trial: number of participants in each condition; age and gender of participants; type of mental disorder; study location and setting; type of cancer screening test; testing stage (i.e. due, overdue, returning for a repeat test or returning for follow-up subsequent to an abnormal test); type of control condition; length of follow-up; type, duration, intensity and theoretical basis (if applicable) of intervention undertaken; data for assessment of risk of bias; primary and secondary outcome measures. We would have published these data in an appendix. In the case of missing data, we would have made up to two attempts to contact the trial authors. We would have resolved disagreements by discussion between authors (EB and RB) and by referral to a third author (PW).

### Assessment of risk of bias in included studies

Again, EB and RB working independently, would have assessed 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, we would have made the final rating 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 would have contacted authors of the studies in order to obtain further information. We would have reported non-concurrence in quality assessment, but if disputes arose as to which category a trial was to be allocated, again, we would have achieved resolution by discussion.

We planned to note the level of risk of bias in both the text of the review and in the 'Summary of findings' table.

### Measures of treatment effect

#### 1. Dichotomous data

For each study described as 'randomised', we would have calculated risk ratio (RR) with 95% confidence intervals (CI). Within a meta-analysis (see below), we would have combined comparable dichotomous measures by calculating an overall RR and 95% CI. We chose RR over the odds ratio because the latter tends to overstate effect size when event rates are high (Higgins 2011).

### 2. Continuous data

2.1 For each study, we planned to calculate mean differences (MD) with 95% CIs for comparisons of continuous outcome measures. Within a meta-analysis (see below), we planned to calculate MD scores and 95% CIs for comparisons of continuous data from the same or similar scales, and standardised mean differences (SMD) where an outcome has been measured differently across studies. If we had calculated SMD, we would have transformed the effect back to the units of one or more of the specific instruments. This would have aided the interpretation of the clinical relevance and impact of the intervention effect.

2.2 Data synthesis: if standard errors (SEs) instead of standard deviations (SDs) were presented, we planned to convert the former to SDs. If SDs were not reported and we could calculate them from available data, we planned to ask study authors to supply the data. In the absence of data from authors, we would have used the mean SD from other studies (Furukawa 2006).

2.3 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) 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 the calculation described above would have been modified to take the scale starting point into account. In these cases skew is present if  $2 \text{ SD} > (S - S_{\text{min}})$ , 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 would have entered skewed data from studies of fewer 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 would have been entered into syntheses.

### Unit of analysis issues

#### 1. Cluster trials

Studies increasingly employ 'cluster randomisation' (such as randomisation by ward or GP surgery), but analysis and pooling of clustered data poses 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).

If clustering had not been accounted for in primary studies, we planned to present data in a table, with a (\*) symbol to indicate



the presence of a probable unit of analysis error. In subsequent versions of this review, if we find such cluster studies, we will seek to contact first authors of these studies to obtain intra-class correlation coefficients (ICCs) for their clustered data and to adjust for this by using accepted methods (Gulliford 1999).

If clustering had been incorporated into the analysis of primary studies, we planned to 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 ICC [Design effect =  $1+(m-1)*ICC$ ] (Donner 2002). If the ICC was not reported, we would assume it to be 0.1 (Ukoumunne 1999). If cluster studies have been appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies may be possible using the generic inverse variance technique.

## 2. Cross-over trials

Cross-over trials for these types of intervention are unlikely, but we would have considered them as follows. 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

Where a study involved two or more intervention groups compared against a control, if relevant, we planned to present the additional intervention groups in additional comparisons. If data were continuous, we would have combined data following the formula in section 7.7.3.8 (Combining groups) of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). If the additional treatment arms were not relevant, we would not have reproduced these data. For dichotomous data, we planned to collapse active treatment groups into a single arm for comparison against the control group, or split the control group equally into two.

## Dealing with missing data

### 1. Overall loss of credibility

At some degree of loss of follow-up, data must lose credibility (Xia 2009). We chose that, for any particular outcome, should more than 50% of data be unaccounted for, we would not reproduce

these data or use them within analyses, except for the outcome of 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 planned to present data on a 'once-randomised-always-analyse' basis (an intention-to-treat analysis). We would have assumed those leaving the study early to have the same rates of negative outcome as those who completed. We planned to undertake a sensitivity analysis to test how prone the primary outcomes were to change when 'completer' data only were compared to the intention-to-treat analysis using the above assumptions.

## 3. Continuous

### 3.1 Attrition

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

### 3.2 Standard deviations (SDs)

If SDs were not reported, we planned first try to obtain the missing values from the authors. If not available, where there were missing measures of variance for continuous data, but an exact SE and CIs available for group means, and either P value or T value available for differences in mean, we could have calculated them according to the rules described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). When only the SE are reported, SDs are calculated by the formula  $SD = SE \times \sqrt{n}$ . Chapters 7.7.3 and 16.1.3 of the *Cochrane Handbook* (Higgins 2011) present detailed formulae for estimating SDs from P values, T or F values, CIs, ranges or other statistics. If these formulae did not apply, we would have calculated 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 planned to examine the validity of the imputations in a sensitivity analysis excluding 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 would reproduce these data and indicate 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. If such situations or participant groups arose, we would have discussed these fully.

### 2. Methodological heterogeneity

We planned 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. If such methodological outliers arose, we would have discussed these fully.

### 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

We planned to investigate heterogeneity between studies by considering the  $I^2$  method alongside the  $\text{Chi}^2$  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  $\text{Chi}^2$  test, or a confidence interval for  $I^2$ ). We would have interpreted an  $I^2$  estimate greater than or equal to around 50% accompanied by a statistically significant  $\text{Chi}^2$  statistic as evidence of substantial levels of heterogeneity (Section 9.5.2 - Higgins 2011). If we had found substantial levels of heterogeneity in the primary outcome, we would have explored reasons for 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 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. In future updates of this review, we will not use funnel plots for outcomes where there are 10 or fewer studies, or where all studies are of similar sizes. In other cases, where funnel plots are possible, we will seek statistical advice in their interpretation.

## Data synthesis

Where there were sufficient data, we planned to perform meta-analyses. The random-effects method incorporates an assumption that the different studies are estimating different, yet related, intervention effects and takes into account differences between studies even if there is no statistically significant heterogeneity. A disadvantage of the random-effects model is that 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 planned to use the random-effects model for all analyses, but would have tested in a sensitivity analysis of the primary outcome what happens if we had used a fixed-effect model.

## Subgroup analysis and investigation of heterogeneity

### 1. Subgroup analyses - only primary outcomes

#### 1.1 Intervention target

We proposed to undertake this review and provide an overview of the effects of any intervention to increase cancer screening uptake in people with severe mental illness. In addition, however, we planned to examine the effects of differential targeting of the interventions to people with SMI, carers, health professionals or a combination of the above.

#### 1.2 Intervention

If there were sufficient data, we planned also investigate the effects of: type of cancer screening test - for example breast, cervical, prostate, bowel; intervention type; setting - for example primary care, care home, hospital.

## 2. Investigation of heterogeneity

First, we planned to investigate whether data had been entered correctly. Second, if data were correct, we would have visually inspected the graph and successively removed outlying studies to see if homogeneity was restored. We would have reported this. 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, we would present data. If not, we would not pool data and would discuss issues. 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.

When unanticipated clinical or methodological heterogeneity was 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

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

### 2. Assumptions for lost binary data

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

Where assumptions have to be made regarding missing SDs data (see [Dealing with missing data](#)), we planned to compare the findings on primary outcomes when we used our assumption compared with complete data only. We planned to undertake a sensitivity analysis to test how prone results were to change when 'completer' data only were compared to the imputed data using the above assumption. If there had been a substantial difference, we would have reported results and discussed them but continued to employ our assumption.

### 3. Risk of bias

We planned to analyse the effects of excluding trials 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 we would have included data from these trials in the analyses.

### 4. Imputed values

We planned 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 we had noted substantial differences 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 would have presented them separately.

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

We planned to synthesise data using a random-effects model; however, we would also have synthesised data for the primary outcomes using a fixed-effect model. This would have determined whether the greater weights assigned to larger trials with greater event rates altered the significance of the results compared to the more evenly distributed weights in the random-effects model.

## RESULTS

### Description of studies

#### Results of the search

We identified 158 citations. It was clear from the titles and abstracts that none were relevant, therefore, we did not obtain the full texts.

#### Included studies

No studies met the inclusion criteria for this review.

#### Excluded studies

It was clear from titles and abstracts that no identified study even potentially met the eligibility criteria for this review.

### **Studies awaiting assessment**

No studies are currently awaiting assessment.

### **Ongoing**

We are not aware of any relevant ongoing studies.

### **Risk of bias in included studies**

No studies met the inclusion criteria for this review.

### **Allocation**

No studies met the inclusion criteria for this review.

### **Blinding**

No studies met the inclusion criteria for this review.

### **Incomplete outcome data**

No studies met the inclusion criteria for this review.

### **Selective reporting**

No studies met the inclusion criteria for this review.

### **Other potential sources of bias**

No studies met the inclusion criteria for this review.

### **Effects of interventions**

No studies met the inclusion criteria for this review.

## **DISCUSSION**

### **Summary of main results**

We did not find any randomised controlled trials (RCTs) of any intervention to encourage uptake of any form of cancer screening compared with no intervention or usual care in adults with severe mental illness (SMI). There is currently no adequate evidence base to support any intervention to encourage cancer screening uptake for people with SMI.

### **Overall completeness and applicability of evidence**

The Cochrane Schizophrenia Group's register is the most comprehensive trials register of its kind, a detailed search was devised yet none of the identified trials even potentially met the inclusion criteria. The reason for the identification of the 158 citations tended to be that they referred to cancer either as a possible side-effect of a treatment being tested in people with SMI or as an exclusion criterion for participation in the reported trial. One of the review authors (EB) has contributed previously to a detailed review of the literature concerning cancer in people with SMI published in *Lancet Oncology* (Howard 2010); no trials of interventions to increase cancer screening uptake in people with SMI were identified through that work either.

### **Quality of the evidence**

Despite lack of uptake of cancer screening by people with SMI compared with others, there is no evidence to support how this disparity can be reduced. Interventions to encourage cancer screening uptake in people with SMI are needed and should be tested in large, multi-centre RCTs.

### **Potential biases in the review process**

No potential biases could be determined apart from the fact that our search was mainly based on the register of the Cochrane Schizophrenia Group. While extensive methodological searches are continuously run for this register, it is still largely based on published trials, but there may be unpublished studies that we are not aware of.

### **Agreements and disagreements with other studies or reviews**

To our knowledge, no similar review has been conducted.

## **AUTHORS' CONCLUSIONS**

### **Implications for practice**

#### **1. For people with severe mental illness**

There is currently no high quality research evidence to suggest that any particular intervention would encourage a person with severe mental illness to take up cancer screening.

## 2. For clinicians

Early detection of cancer through screening is effective in improving patient outcomes including death. Given that people with SMI are at greater risk of cancer but less likely than others to take up available screening, implementation of appropriate and effective interventions to encourage cancer screening uptake is needed urgently. Potentially, this could be addressed by a range of professionals in a variety of healthcare settings including mental health, primary and social care. Since there is currently no evidence available from randomised controlled trials to allow assessment of the efficacy of any specific intervention to encourage uptake of cancer screening for people with severe mental illness, clinicians will have to rely on their personal experience and clinical judgement when discussing with individuals the importance of taking up cancer screening opportunities.

## 3. For policy and decision makers

Currently, policy makers have no trial-based evidence upon which to base guidelines for promoting cancer screening uptake in people with severe mental illness. Funding bodies may wish to make this a priority for future research in order to reduce the health disparity between people with and without severe mental illness which will result from lower uptake by the former of cancer screening.

## Implications for research

### 1. General

This review has highlighted the absence of RCTs investigating the efficacy of interventions to encourage cancer screening uptake by people with SMI. Given the increased morbidity and mortality

of people with SMI, for instance, the Schizophrenia Commission (Schizophrenia Commission 2012) reports that people with schizophrenia who develop cancer are three times more likely to die than those in the general population with cancer, it is surprising that there has been so little research in this area. The reasons for this are unclear. In order to develop effective, evidence-based interventions, there is an urgent need for high-quality RCTs.

### 2. Specific

Future interventions should address known barriers to screening uptake, including low income, increasing age, lack of transport, embarrassment, lack of reminders, and lack of familiar care providers (Howard 2010). Research is also needed to identify whether there are barriers specific to people with SMI which may inhibit cancer screening uptake and which could be addressed in a future intervention (Howard 2010). In order to facilitate future meta-analyses, reports of trials of interventions to encourage cancer screening uptake in people with SMI should comply fully with the latest CONSORT guidance (Moher 2010).

## ACKNOWLEDGEMENTS

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.

The CSG register search was conducted by the Trial Search Co-Ordinator of the Cochrane Schizophrenia group, Samantha Roberts.

We would like to thank Chris Jones for peer reviewing this review, his comments were very helpful.

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- \* Indicates the major publication for the study



## DATA AND ANALYSES

This review has no analyses.

## APPENDICES

### Appendix I. Previous searches

#### Search in 2012, 2014, and 2015

##### Electronic searches

##### Cochrane Schizophrenia Group's Trials Register

The Trials Search Coordinator (TSC) searched the Cochrane Schizophrenia Group's Registry of Trials (October 25, 2012; December 19, 2014; April 07, 2015) using the following search strategy:

(\*cancer\* OR \*neoplasms\* OR \*mass screening\* OR \*maligna\* OR \*tumour\*) in Title, Abstract and Index Terms Fields of REFERENCE

The Cochrane Schizophrenia Group's Registry of Trials is compiled by systematic searches of major resources (including AMED, BIOSIS, CINAHL, EMBASE, MEDLINE, PsycINFO, PubMed, and registries of clinical trials) and their monthly updates, hand-searches, grey literature, and conference proceedings (see [Group's Module](#)). There is no language, date, document type, or publication status limitations for inclusion of records into the register.

##### Searching other resources

##### 1. Reference searching

We planned to search the bibliographies of all retrieved articles for additional references. We would have recorded the number of cited trials not detected by the electronic search as a measure of the sensitivity of the electronic search.

##### 2. Personal communication

We planned to contact the authors of all the included studies and authors with at least two publications amongst those studies that we excluded, but which appeared related to the review, to ask if they knew of any study which met the inclusion criteria of this review. This would have helped to identify unpublished or ongoing studies.

## WHAT'S NEW

Last assessed as up-to-date: 4 July 2016.

Date	Event	Description
7 September 2016	New citation required but conclusions have not changed	Update search completed. Conclusions unchanged.
4 July 2016	New search has been performed	Update search conducted. No new studies found.
7 April 2015	Amended	Update search conducted. No new studies found.

## HISTORY

Protocol first published: Issue 2, 2012

Review first published: Issue 7, 2013

Date	Event	Description
19 December 2014	Amended	Update search conducted. No new studies found. Assessed as Up-to-date amended

## CONTRIBUTIONS OF AUTHORS

Elizabeth Barley - proposed the review, helped write the protocol, contributed to formulating searches, screened studies and wrote the review.

Rohan Borschmann - helped write the protocol, screened studies and contributed to writing the review.

Paul Walters - commented on drafts of the protocol, helped arbitrate disagreements and commented on drafts of the review.

Andree Tylee - commented on drafts of the protocol and of the review.

## DECLARATIONS OF INTEREST

None known.

## **SOURCES OF SUPPORT**

### **Internal sources**

- King's College London, UK.
- EB, RB and AT are employed by King's College London
- Dorset Healthcare University Foundation Trust, UK.
- PW is employed by Dorset Healthcare University Foundation Trust

### **External sources**

- None provided, Other.

## **INDEX TERMS**

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

\*Bipolar Disorder; \*Early Diagnosis; \*Psychotic Disorders; \*Schizophrenia; Early Detection of Cancer [\*utilization]; Risk

### **MeSH check words**

Adult; Humans