Supplementary appendix to:

Larkin, A., & Hutton, P. (submitted). What helps or hinders treatment decision making capacity in psychosis? A systematic review and meta-analysis.

**Content of supplementary material**

1. **Review protocol**
2. **Full inclusion & exclusion criteria**
3. **Excluded studies**
4. **Study quality assessment tool**
5. **GRADE assessment criteria**
6. **Results from individual studies**
7. **PRISMA checklist**
8. **Additional references**
9. **Review Protocol**

*Title:* Treatment decision making capacity in psychosis: what are the risk factors and correlates?

*Reviewers:* Amanda Larkin, Paul Hutton

*Citation*

Amanda Larkin, Paul Hutton. Treatment decision making capacity in psychosis: what are the risk factors and correlates?. PROSPERO 2015:CRD42015025568 Available from http://www.crd.york.ac.uk/PROSPERO/display\_record.asp?ID=CRD42015025568

*Review question(s)*

What are the risk factors and correlates of impaired treatment decision making capacity in people who have experienced psychosis?

*Searches*

PsycINFO, EMBASE, MEDLINE, theses databases, grey literature. The author also plans to contact researchers in the area as well as hand searching the reference lists of key papers.

The databases will be searched using the keywords “psychosis”, “psychotic disorders”, “delusions”, “hallucinations”, “capacity”, “decision making”, “treatment decision making capacity” “MacCAT-T” “consent” “decisional capacity” “schizophrenia”.The search strategy will be amended appropriately for each database.

*Types of study to be included*

All studies that assess treatment decision making capacity in people who have experienced psychosis. Cross-sectional, correlational studies, cohort studies, case-control studies, audits and prospective studies and trials will be included where other inclusion criteria are met.

*Condition or domain being studied*

Treatment decision making capacity. Psychosis.

*Participants/ population*

People who have received a diagnosis of non-affective psychotic disorder

*Intervention(s), exposure(s)*

Not applicable

*Comparator(s)/ control*

The reviewer will consider both clinical and non-clinical comparison groups

*Context*

Studies included will assess capacity in the context of a decision about medical / psychiatric treatment. These decisions may be real or hypothetical.

*Outcome(s)*

*Primary outcomes*

Treatment decision making capacity

*Secondary outcomes*

This review will take an exploratory approach, investigating what factors have been evidenced to be associated with treatment decision making capacity in people who have experienced psychosis. These factors are expected to include insight, symptoms, and cognitive impairment.

*Data extraction, (selection and coding)*

Studies that include an assessment of treatment decision making capacity in the specified population will be included in the review. Data on the type of study design, measure of capacity used, and strength of association between factors examined and capacity will be extracted. Data relating to the quality of the study will also be extracted including reliability and validity of measures used, characteristics of sample, and power of the sample size to detect effects.

*Risk of bias (quality) assessment*

Risk of bias will be assessed using a modified tool based on the one developed by the Agency for Healthcare Research and Quality (Williams, Plassman, Burke, Holsinger & Benjamin, 2010). Each study will be given a rating based on the risk of bias in the study. Studies that receive a rating of high risk of bias will be excluded from the review. Included studies will be weighted according to the quality rating and this will be reported.

*Strategy for data synthesis*

The studies will be reviewed in aggregate. The evidence for each factor that has been examined will be taken in aggregate and reported as such. A narrative review of each of the factors will be undertaken.

*Analysis of subgroups or subsets*

None planned

*Dissemination plans*

The completed systematic review will be published in an academic journal.

*Contact details for further information*

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*Review team*

Ms Amanda Larkin,

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*Collaborators*

Dr Paul Hutton, University of Edinburgh

*Anticipated or actual start date*

01 September 2015

*Anticipated completion date*

01 May 2016

*Funding sources/sponsors*

NHS Dumfries and Galloway and University of Edinburgh.

*Conflicts of interest*

None known

*Language*

English

*Country*

Scotland

*Subject index terms status*

Subject indexing assigned by CRD

*Subject index terms*

Decision Making; Humans; Psychotic Disorders; Risk Factors

*Stage of review*

Ongoing

*Date of registration in PROSPERO*

25 August 2015

*Date of publication of this revision*

11 November 2015

*DOI*

10.15124/CRD42015025568

|  |  |  |
| --- | --- | --- |
| *Stage of review at time of this submission*  | *Started*  | *Completed* |
| Preliminary searches  | Yes  | No |
| Piloting of the study selection process  | Yes  | No |
| Formal screening of search results against eligibility criteria  | No  | No |
| Data extraction  | No  | No |
| Risk of bias (quality) assessment  | No  | No |
| Data analysis  | No  | No  |

1. **Full inclusion & exclusion criteria**

| **Category** | **Criteria** |
| --- | --- |
|  |  |
| Study population | Population consisted of people who had been diagnosed with a non-affective psychotic disorder (ICD-10 F20 – F29 diagnoses). Studies that used a mixed population were included if >50% of the population was people diagnosed with non-affective psychotic disorders.  |
| Study geography | Studies from all countries were accepted if they had used a definition of capacity that included at least one of the four accepted factors in capacity as defined above.  |
| Factors / Interventions  | Any factors that were measured using a valid measure and had been assessed as contributing to treatment decision-making capacity were included. Baseline and change data from studies of interventions designed to enhance treatment decision-making capacity, or studies which had assessed treatment decision-making capacity pre- and post-intervention were included.  |
| Time period | Studies published between 1947 and October 2015 were included in the review.  |
| Publication language | Studies published in the English language only were included in the review.  |
| Admissible evidence (study design and other criteria)  | Case studies and descriptions were excluded from the review.  |
|  |  |

1. **Excluded studies**

The following table details studies or reports excluded after inspection of the full-text report, or via correspondence with authors. Studies or reports excluded on basis of title or abstract alone are not detailed as these are too numerous and the vast majority were of different conditions or were otherwise unrelated to the review question.

| **Study ref** | **Reason for exclusion** |
| --- | --- |
|  |  |
| 1. Ackerman et al. (2015)
 | Case description  |
| 1. Ang et al. (2009)
 | Case description |
| 1. Baklar (1998)
 | Editorial  |
| 1. Bingham (2012)
 | Case description |
| 1. Bitter et al. (2015)
 | No measure of capacity or did not examine correlates |
| 1. Bowen & Barnes (1994)
 | No measure of capacity or did not examine correlates |
| 1. Bunn et al. (1997)
 | No measure of capacity or did not examine correlates |
| 1. Bursztajn et al. (1991)
 | Case description |
| 1. Burton & Twamley (2015)
 | No measure of capacity or did not examine correlates |
| 1. Dudzinski & Sullivan (2004)
 | Case description |
| 1. Falzer & Garman (2012)
 | No measure of capacity or did not examine correlates |
| 1. Gray & O’Reilly (2009)
 | Case description |
| 1. Grimes et al. (2000)
 | No measure of capacity or did not examine correlates |
| 1. Grisso & Appelbaum (1995)
 | No measure of capacity or did not examine correlates |
| 1. Grisso & Appelbaum (1995) (2)
 | Brief report – no usable data |
| 1. Hamann et al. (2011)
 | No measure of capacity or did not examine correlates |
| 1. Irwin, Knight, & Pirl (2014)
 | No measure of capacity or did not examine correlates |
| 1. Jacob et al. (2005)
 | Sample <50% psychosis or schizophrenia |
| 1. Jeste, Depp, & Palmer (2006)
 | Review paper |
| 1. Karel et al. (2010)
 | Sample <50% psychosis or schizophrenia |
| 1. Krogsgaard Bording, Munk-Jorgensen, & Puschner (2012)
 | No measure of capacity or did not examine correlates |
| 1. Lee et al. (2010)
 | No measure of capacity or did not examine correlates |
| 1. Linden & Chaskel (1991)
 | No measure of capacity or did not examine correlates |
| 1. Mahone (2004)
 | No measure of capacity or did not examine correlates |
| 1. Mandarelli et al. (2014)
 | No measure of capacity or did not examine correlates |
| 1. Maxmin et al. (2009)
 | Sample <50% psychosis or schizophrenia  |
| 1. McSherry & Bruckard (2009)
 | Editorial |
| 1. Meszaros et al. (2011)
 | No measure of capacity or did not examine correlates |
| 1. Moye et al. (2008)
 | No measure of capacity or did not examine correlates |
| 1. Parsons & Kennedy (2007)
 | No measure of capacity or did not examine correlates |
| 1. Paul & Oyebode (1999)
 | No measure of capacity or did not examine correlates |
| 1. Roth et al. (1982)
 | Sample <50% psychosis or schizophrenia |
| 1. Schlecter (2008)
 | Case description |
| 1. Seeman (2014)
 | Case description |
| 1. Shek, Lyons, & Taylor (2010)
 | No measure of capacity or did not examine correlates |
| 1. Vollman et al. (2003)
 | No measure of capacity or did not examine correlates |
| 1. Weinstock, Copelan, & Bagheri (1984)
 | No measure of capacity or did not examine correlates |
| 1. Wirshing et al. (1998)
 | Research decision making capacity |
| 1. Wirshing, Sergei, & Mintz (2005)
 | Research decision making capacity |
| 1. Zalpuri et al. (2015)
 | Case description |
|  |  |
|  |  |

1. **Study quality assessment tool**

We adapted a tool for assessing the methodological quality of observational studies that has been successfully employed in prior research undertaken by the Agency for Healthcare Research and Quality (AHRQ). The main methodological quality criteria were retained but the underlying factors related to each study quality criterion were adapted in some instances for this specific context. Each study is assessed on a number of methodological quality criteria (for example, unbiased selection of groups, sample-size calculations, and so on) that are rated as being met, not met, partially met, or being unclear.

General instructions: Grade each criterion as ‘Yes’, ‘No’, ‘Partially’, or ‘Can’t tell’. Factors to consider when making an assessment are listed under each criterion. Where appropriate (particularly when assigning a ‘No’, ‘Partially’, or ‘Can’t tell’ score), please provide a brief rationale for your decision (in parentheses) in the evidence table.

**1. Unbiased selection of the cohort?**

Factors that help reduce selection bias:

○ Inclusion/exclusion criteria:

○ Recruitment strategy

▪ Clearly described.

▪ Relatively free from bias (selection bias might be introduced, for example, by recruitment via advertisement).

**2. Selection minimizes baseline differences in prognostic factors**?

Factors to consider:

○ Was selection of the comparison group appropriate?

○ Is the comparison group matched with the clinical group on key demographics (that is age and gender)?

**3. Sample size calculated?**

Factors to consider:

○ Did the authors report conducting a power analysis or describe some other basis for determining the adequacy of study group sizes for the primary outcome(s) of interest to us?

○ Where a power calculation is presented, do the final numbers obtained match up to this (for example, within 10% of required numbers)?

**4. Adequate description of the cohort?**

Consider whether the cohort is well-characterized in terms of baseline:

○ Age

○ Sex

○ Ethnicity

○ Diagnosis/clinical status

**5. Validated measure of treatment decision making capacity or of domains of treatment decision making capacity?**

Factors to consider:

○ Was the method used to assess treatment decision making capacity clearly described (details should be sufficient to permit replication in new studies)?

○ Was a valid and reliable measure used to assess treatment decision making capacity (subjective measures based on self-report tend to have lower reliability and validity than objective measures such as clinical interview)?

**6. Validated measures for assessing associated factors of interest?**

Factors to consider:

○ Where possible studies should use validated measures to assess factors, for example a validated measure of depression rather than a subjective rating of mood.

○ Were these measures implemented consistently across all study participants?

**7. Outcome assessment blind to exposure? (Note: subsequently excluded from overall assessment of study quality)**

Factors to consider:

○ Were the study investigators who assessed outcomes blind to whether participants had impaired treatment decision making capacity and vice versa?

**8. Analysis controls for confounding?**

Factors to consider for controlled studies:

○ If groups were not matched as baseline, did the analysis control for any baseline differences between groups?

○ Does the study identify and control for important confounding variables and effect modifiers (for example, IQ)?

**9. Analytic methods appropriate?**

Factors to consider:

○ Was the kind of analysis done appropriate for the kind of outcome data (categorical, continuous, and so on)?

○ Was the number of variables used in the analysis appropriate for the sample size (the statistical techniques used must be appropriate to the data and take into account issues such as controlling for small sample size, clustering, rare outcomes, multiple comparison, and number of covariates for a given sample size)?

For intervention studies (non-randomised controlled trials only) the following additional criteria were rated:

**10. Adherence to intervention?**

Factors to consider:

* Was the intervention manualised?
* Did all participants receive the same number of sessions / intensity of intervention?

**11. Adequate follow-up period?**

Treatment decision making capacity is time and decision specific. As such it is expected to change over time. To ensure that the change in capacity can be attributable to the intervention studied, a short follow up period is more valid than a longer follow up period.

Factors to consider:

* How long was the follow up period? Maximum follow up period – 2 weeks

**12. Completeness of follow up?**

Factors to consider:

* Did attrition from any group exceed 30%? (Attrition is measured in relation to the time between baseline/allocation and outcome measurement. Where different numbers of patients are followed up for different outcomes, use the number followed up for the primary outcome for this calculation.)
* Did attrition differ between groups by more than 10% percent?
1. **GRADE assessment criteria**

Outcomes where more than one study contributed evidence were assessed for overall quality using the GRADE approach. The rating of quality was conducted by the first author, and discussed with second author PH. The following criteria for downgrading were applied to each outcome.

*Study limitations*

Individual studies were rated for risk of bias using a tool adapted from Williams et al. (2010) ([1](#_ENREF_1)). We downgraded by 1 point if three of the parameters in our risk of bias assessment had ≥50% studies with at least one ‘no’ or ‘unclear’ rating, and 2 points if four or more parameters had ≥50% studies with ratings of ‘no or unclear’.

*Imprecision*

Imprecision was judged by examining the 95% CI of the effect sizes for the outcome of interest across studies. We downgraded 1 point for imprecision when optimal sample size had not been reached.

*Inconsistency*

For outcomes included in meta-analysis where the I2 statistic was calculated we downgraded by 1 point for inconsistency if the I2 statistic was ≥40% in the context of an unclear direction of effect or ≥75% in the context of a clear direction of effect. We downgraded by 2 points if the I2 statistic was ≥75% in the context of an unclear direction of effect. For outcomes included in the narrative review, we downgraded by 1 point for inconsistency in cases where 95% CI did not overlap, and heterogeneity could not be explained.

*Indirectness*

The review was exploratory in nature, therefore outcomes had not been pre-specified. However, for outcomes that had used significantly different measures of the same construct, we downgraded by 1 point for indirectness.

*Rating up the quality of evidence*

In the context of a large effect size, we upgraded by 1 point where the effect size calculated was consistently large. Using Cohen’s criteria ([2](#_ENREF_2)), an effect size of r ≥ .50 or d ≥ .80 was considered large.

1. **Narrative synthesis of results from individual studies**

*Executive functioning*

In a very small study, Koren et al (2005) ([3](#_ENREF_3)) found that executive functioning had non-significant moderate correlations with the three MacCAT-T subdomains of understanding (r = -0.35, 95% CI -0.68, 0.10; trials to first category), appreciation (0.41, 95% CI -0.03, 0.72; N categories), and reasoning (r = 0.31, 95% CI -0.14, 0.65; N categories) whereas Mandarelli et al (2012) ([4](#_ENREF_4)) found that poor executive functioning was significantly associated with large reductions in understanding (d = 1.13, 95% CI 0.49, 1.77) and appreciation (d = 0.86, 95% CI 0.24, 1.49), but not reasoning, where the reduction was small and non-significant (d = 0.32, 95% CI -0.28, 0.92). The inconsistent and very imprecise findings meant the overall quality of evidence was rated as very low in quality.

*Insight*

Five studies examined the relationship between insight and treatment decision making capacity. Each assessed different aspects of insight, so were not conceptually similar enough to combine in meta-analysis. In a study of 112 inpatients, Cairns et al (2005) ([5](#_ENREF_5)) found incapacity was associated with a large reduction in insight, as measured by the Expanded Schedule for the Assessment of Insight (χ2 162.50, p < 0.001). Capdevielle et al (2009) ([6](#_ENREF_6)) found that understanding and the ability to express a choice, as measured by the MacCAT-T, had moderate correlations with each of the Scale to Assess Unawareness of Mental Disorder (SUMD) subscales (higher scores equal poorer insight, hence correlations are negative), with correlations ranging from -0.32 (95% CI -0.53, -0.07) for the association between understanding and ‘awareness’ of symptoms to -0.44 (95% CI -0.62, -0.21) for the association between being able to express a choice about treament and being aware of the social consequences of their disorder. Both the reasoning and appreciation domains had large correlations with all SUMD subscales, ranging from -0.61 (95% CI -0.75, -0.42) for the correlation between reasoning and awareness of symptoms, to -0.80 (95% CI -0.88, -0.69) for the correlation between appreciation and awareness of effects of medication. Owen et al (2009) ([7](#_ENREF_7)) used the Expanded Schedule for the Assessment of Insight (SAI-E) and found a very large difference in insight between those who were judged to have and not have intact capacity (Hedge’s g =**-**2.19 95% CI -1.83, -2.55). Finally, Elbogen et al (2007) ([8](#_ENREF_8)) used the Insight and Treatment Attitudes Questionnaire (ITAQ) and again found that insight was positively associated with reasoning *(*β = 0.36, p <0.05).

Raffard et al (2013) ([9](#_ENREF_9)) examined the relationship between MacCAT-T ratings and scores on the Beck Cognitive Insight Scale (BCIS), a measure which assesses self-certainty and self-reflectiveness. For degree of self-certainty, they reported small positive (r = 0.12, 95% CI -0.14, 0.36; understanding) to small negative (r = -0.21, 95% CI -0.44, 0.05; reasoning) correlations with the MacCAT-T subscales, none of which were statistically significant in this sample of 60 participants. For degree of self-reflectiveness, they reported correlations that ranged from small and non-significant (r = 0.18, 95% CI -0.08, 0.42; ability to express a choice) to moderate and significant (r = 0.43, 95% CI 0.20, 0.62; reasoning, r = 0.33, 95% 0.08, 0.54; appreciation).

Overall we judged the evidence on insight to be of moderate quality, and consistent with the view that insight is associated with improved capacity, in particular reasoning ability.

*Duration of illness*

Two studies provided low quality data on the relationship between duration of illness (years since diagnosis) and capacity ([10](#_ENREF_10), [11](#_ENREF_11)) Raffard et al (2013) ([12](#_ENREF_12)) did not find significant correlations, with estimates ranging from -0.09 (95% CI -0.34, 0.17; appreciation) to -0.19 (95% CI -0.42, 0.06), whereas Wong et al., (2005)([13](#_ENREF_13)) reported a small yet significant relationship with understanding (r = -0.24, 95% CI -0.02, -0.44).

*Metacognitive ability*

In one small study, Koren et al (2005) ([14](#_ENREF_14)) found that metacognitive ability was significantly associated with the ability of participants to understand information relating to treatment (r = 0.60, 95% CI 0.23, 0.82 for control sensitivity). Although not significant, correlations of similar magnitude were observed for appreciation (r = 0.40, 95% CI -0.04, 0.71 for monetary gains) and reasoning (r = 0.43, 95% CI -0.00, 0.73).

*Perceived coercion*

Moderate quality evidence from Cairns et al., (2005) ([15](#_ENREF_15)) suggested that participants judged to have impaired capacity were more likely to report higher levels of perceived coercion (Mann-Whitney U = 422.5, p < 0.001).

*Anxiety*

Moderate quality evidence from two studies suggests state and trait anxiety may be positively associated with aspects of capacity – i.e., greater anxiety was linked to greater treatment decisional capacity ([16](#_ENREF_16), [17](#_ENREF_17)).State anxiety was significantly and moderately correlated with appreciation in both studies (r = 0.27, 95% CI 0.02, 0.49;([18](#_ENREF_18)) r = 0.36, 95% CI 0.12, 0.56([19](#_ENREF_19))), whereas trait anxiety was only significantly associated with appreciation in one (r = 0.33, 95% CI 0.08, 0.54;([20](#_ENREF_20)) r = 0.22, 95% CI -0.04, 0.45([21](#_ENREF_21))). A similar pattern of findings was observed for the relation between state anxiety and reasoning (r = 0.32, 95% CI 0.07, 0.53;([22](#_ENREF_22)) r = 0.27, 95% CI 0.02, 0.49([23](#_ENREF_23))) and trait anxiety and reasoning (r = 0.38, 95% CI 0.14, 0.58;([24](#_ENREF_24)) r = 0.15, 95% CI -0.11, 0.39([19](#_ENREF_19))). In both studies, non-significant small correlations were reported for state and trait anxiety and understanding and expressing a choice.

1. **PRISMA checklist**

| **Section/topic**  | **#** | **Checklist item**  | **Reported on page #**  |
| --- | --- | --- | --- |
| **TITLE**  |  |
| Title  | 1 | Identify the report as a systematic review, meta-analysis, or both.  | p1 |
| **ABSTRACT**  |  |
| Structured summary  | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.  | p2 |
| **INTRODUCTION**  |  |
| Rationale  | 3 | Describe the rationale for the review in the context of what is already known.  | pp3-4 |
| Objectives  | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).  | p4 |
| **METHODS**  |  |
| Protocol and registration  | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.  | p2, p4 |
| Eligibility criteria  | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.  | p4 |
| Information sources  | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.  | p5 |
| Search  | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.  | p5 |
| Study selection  | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).  | p5 |
| Data collection process  | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.  | p5 |
| Data items  | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.  | pp4-5 |
| Risk of bias in individual studies  | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.  | p5 |
| Summary measures  | 13 | State the principal summary measures (e.g., risk ratio, difference in means).  | p6 |
| Synthesis of results  | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.  | p6 |

| **Section/topic**  | **#** | **Checklist item**  | **Reported on page #**  |
| --- | --- | --- | --- |
| Risk of bias across studies  | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).  | p6 |
| Additional analyses  | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.  | pp6-10 |
| **RESULTS**  |  |
| Study selection  | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.  | p6, Fig 1, Supplement p7 |
| Study characteristics  | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.  | Main paper, Table 1 |
| Risk of bias within studies  | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).  | Main paper, Tables 2-4 |
| Results of individual studies  | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.  | Main paper, Table 5, Figs 2-5 |
| Synthesis of results  | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency.  | Main paper, Table 5 |
| Risk of bias across studies  | 22 | Present results of any assessment of risk of bias across studies (see Item 15).  | Main paper, Table 5 |
| Additional analysis  | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).  | pp6-10 |
| **DISCUSSION**  |  |
| Summary of evidence  | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).  | pp10-12 |
| Limitations  | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).  | pp10-12 |
| Conclusions  | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research.  | pp10-12 |
| **FUNDING**  |  |
| Funding  | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.  | p1 |

1. **Additional references**

1. Williams JW, Plassman BL, Burke J, Holsinger T, Benjamin S. Preventing alzheimer’s disease and cognitive decline. Evidence report/technology assessment No. 193. (Prepared by the duke evidence-based practice center under contract No. HHSA 290-2007-10066-I). Rockville, MD.: Agency for Healthcare Research and Quality; 2010.

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7. Adults with Incapacity (Scotland) Act 2000, (2000).

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13. National Collaborating Centre for Mental Health. Psychosis and Schizophrenia in Adults: The NICE Guideline on Treatment and Management (Updated Edition) (Clinical Guideline CG178): National Institute for Health and Care Excellence; 2014.

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