PROSPERO International prospective register of systematic reviews

Review title and timescale

1   Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
Do antipsychotics increase the risk for sudden death and serious adverse events, and what are risk factors?

2   Original language title
For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.
Do antipsychotics increase the risk for sudden death and serious adverse events, and what are risk factors?

3   Anticipated or actual start date
Give the date when the systematic review commenced, or is expected to commence.
08/02/2016

4   Anticipated completion date
Give the date by which the review is expected to be completed.
31/03/2017

5   Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started   ✕

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.
Protocoll for funding accepted

Review team details

6   Named contact
The named contact acts as the guarantor for the accuracy of the information presented in the register record.
Johannes Schneider-Thoma

7   Named contact email
Enter the electronic mail address of the named contact.
joh.schneider@tum.de

8   Named contact address
Enter the full postal address for the named contact.
Department of Psychiatry and Psychotherapy, Klinikum rechts der Isar, Technical University of Munich, Ismaningerstrasse 22, 81675 Muenchen

9   Named contact phone number
Enter the telephone number for the named contact, including international dialing code.
0049 89 4140 6415

10   Organisational affiliation of the review

Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.
Department of Psychiatry and Psychotherapy, Technische Universität München, München

Website address:
https://www.tum.de/

11   Review team members and their organisational affiliations
Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

Title	First name	Last name	Affiliation
Dr	Johannes	Schneider-Thoma	Department of Psychiatry and Psychotherapy, Technische Universität München, München
Professor	Stefan	Leucht	Department of Psychiatry and Psychotherapy, Technische Universität München, München
Dr	Maximilian	Huhn	Department of Psychiatry and Psychotherapy, Technische Universität München, München

12   Funding sources/sponsors
Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.
German ministry of education and research (Grant) Department of Psychiatry and Psychotherapy, Klinikum rechts der Isar, Technical University of Munich

13   Conflicts of interest
List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.
Are there any actual or potential conflicts of interest?
Yes

14   Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

Title	First name	Last name	Organisation details

Review methods

15   Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.
Do antipsychotic drugs increase the risk for death and which are the associated reasons of death?

Do antipsychotics increase the risk of serious adverse events and which are the associated serious adverse events?

What are risk factors for incidence of death and serious adverse events for patients treated with antipsychotic drugs?

16   Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.
We will run electronic searches in the databases MEDLINE, EMBASE, Cochrane Central Register of Randomised Trials (CENTRAL), BIOSIS, CINAHL, Dissertation Abstracts, LILACS, PSYNDEX, PsycINFO). We will contact the Cochrane Review Groups in psychiatry to run additional searches in their registers. So that we can bridge the delay with which these groups forward their material to CENTRAL We will search the databases of the Food and Drug Administration (FDA) and of the European Medical Association (EMA). We will search the websites of pharmaceutical companies and we will contact them directly by e-mail and telephone. We will contact the first-authors of all individual included trials for our outcomes of interest, we will search other systematic reviews such as those of the Cochrane Schizophrenia Group and our own ones [4] for relevant trials and data, and we will inspect the references of all

identified studies for more trials.

17 URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available
Yes

18 Condition or domain being studied
Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.
All indications and off-label uses of antipsychotic drugs. This covers mainly schizophrenia, bipolar disease, major depressive disorder, agitation in dementia, insomnia, PTSD, personality disorders, etc.

19 Participants/population
Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.
partizipants of clinical antipsychotic drug trials irrespective of disease, age, gender or ethnicity.

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed
Experimental intervention: Antipsychotic drugs. The review focuses on second generation antipsychotic drugs. First generation antipsychotics are only included when they were used as an active comparator in a placebo-controlled trial. All forms of application are eligible.

21 Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).
Control intervention: Placebo

22 Types of study to be included initially
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.
Randomized placebo-controlled trials of second generation antipsychotic drugs. No further restrictions.

23 Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

24 Primary outcome(s)
Give the most important outcomes.
Number of death in drug and placebo arms Number of serious adverse events in drug and placebo arms

Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
Reasons of death in drug and placebo arms Names of occuring serious adverse event in drug and placebo arms

Give information on timing and effect measures, as appropriate.

26 Data extraction, (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.
All data will be extracted independently by two reviewers. Doubts will be resolved in a discussion with a third reviewer or by written request to the authors. Data entry will be checked by double data entry in Covidence software.

27 Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and

whether and how this will influence the planned synthesis.
Study quality in terms of sequence generation, allocation concealment, blinding, the completeness of outcome data, selective reporting, and other biases will be assessed with the Cochrane Collaboration risk of bias tool.

28   Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.
Pairwise meta-analyses within a Bayesian framework will be used to estimate the summary comparative effect sizes. All outcomes will be dichotomous and be primarily analysed as odds ratios, supplemented by NNT/NNH. Special statistical attention in terms of data synthesis and heterogeneity assessment will be paid to the fact that events will be rare.

29   Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. 'None planned' is a valid response if no subgroup analyses are planned.
Predefined subgroups analyses will address: diagnostic subgroup, age, gender, antipsychotic drug used, antipsychotic combinations, dose. Publication bias will be examined with funnel-plot methods, recommendations will be made with GRADE.

Review general information

30   Type of review
Select the type of review from the drop down list.
Intervention

31   Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English

Will a summary/abstract be made available in English?
Yes

32   Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
Germany

33   Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34   Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35   Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
review for funding ministry publication in scientific journal implementation in guidelines

Do you intend to publish the review on completion?
Yes

36   Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)
Second generation antipsychotic drug

Placebo

mortality

serious adverse events

37   Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38   Current review status
Review status should be updated when the review is completed and when it is published.
Ongoing

39   Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40   Details of final report/publication(s)
This field should be left empty until details of the completed review are available.
Give the full citation for the final report or publication of the systematic review.
Give the URL where available.