

# **Protocol: Is the total score of the Hamilton Rating Scale for Depression associated with suicidality? A systematic review of observational studies**

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## **Background**

During 40 years the 17-item Hamilton Rating Scale for Depression (HDRS) [1] has been the gold standard to quantify depressive symptoms in clinical trials [2], and systematic reviews have shown that the vast majority of trials assessing the effects of intervention for depression primarily use a total score on the HDRS as an outcome measure [3-6].

A scale sensitive to measure the severity of depressive symptoms should be able to differentiate between depressive patients with and without suicidal tendencies. However, we identified no relevant systematic review with meta-analysis examining if a total score on the HDRS associate to suicidality.

## **Methods**

We plan to conduct a systematic review of observational studies involving meta-analysis, to answer the question: is the total score on the HDRS associated with suicide attempts and suicides in the past or in the future?

Our systematic review with meta-analysis will be conducted both according to MOOSE guidelines for reporting of meta-analysis of observational studies [7] adopting methodology from The Cochrane Handbook for Systematic Reviews of Interventions [8]. We will include all observational studies examining the association between a total HDRS score and suicide attempts or suicides. We want to compare homogeneous patient groups and therefore we will therefore not include studies with a control group recruited from a different setting than the experimental group - no matter how well the groups are matched.

E.g., we will not include studies comparing outpatients with inpatients even if the groups are matched regarding age, sex, etc. We will not include studies examining the association between suicide impulses and HDRS, because suicide inclination is often assessed via item three on the HDRS or other continuous outcome scales [1,9,10]. We want to avoid assessing the validity of the HDRS via an item from the HDRS itself (item 3), or via another continuous outcome scale with a questionable validity. The studies will be included irrespective of language, publication status, publication year, and publication type — based on searches in The Cochrane Library's CENTRAL, MEDLINE, EMBASE, PsycInfo, and Science Citation Index Expanded. We will also search other relevant publications for references to relevant studies. The timeframe for the search will be all studies published before October 2011.

### **Types of studies**

We will include cohort studies, case-control studies, and cross-sectional studies — both prospective and retrospective. We will classify the studies in the three following categories in prioritized order, the last category below having the highest weight according to 'levels of evidence' [11]:

#### *Prospective studies*

- Studies examining and reporting prospectively if a mean score on the HDRS differed between depressive patients who, during a follow-up period, had a suicide attempt or committed suicide.

#### *Retrospective studies*

1. Studies examining and reporting retrospectively if a mean score on the HDRS differed between depressive patients with and without a lifetime history of a suicide attempt.
2. Studies examining and reporting retrospectively if a mean score on the HDRS differed between depressive patients with and without a suicide attempt during the on-going depressive episode.

A high number of assessment tools exist to assess the risk of bias in observational studies [12]. All studies will be assessed, including the risk of bias, according to 'levels of evidence' [11] and the STROBE guidelines for reporting observational studies [12,13].

## **Selection of trials**

JCJ will select relevant trials based on criteria described in the above. If it is doubtful if a study should be included JCJ and CG will decide through discussion. Excluded studies are entered on a list, stating the reason for exclusion.

## **Data extraction**

The following data will be extracted from the included studies:

1. Date published.
2. Time frame of the study period.
3. Inclusion- and exclusion criteria.
4. Number of patients.
5. Distribution of age and sex.
6. Choice of outcome measure.

7. Outcome measures.

8. The choice of method and an evaluation of the quality of this choice of method.

### **Outcomes and statistical methods**

Our only outcome measure will be the mean value of the HDRS [1] for patients with and without a suicide attempt regardless of the attempt being successful or not. The meta-analysis will be conducted according to the recommendations stated in The Cochrane Handbook for Systematic Reviews of Interventions [8]. We will use the mean difference (MD) with a 95% confidence interval, and use RevMan version 5.0 for statistical calculations [14].

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