Systematic reviews and meta-analyses of controlled homeopathic studies: 1.) Clinical effects of ultra low-dose and highly diluted dynamised drugs compared to placebo in nine pathology-based subgroups; 2.) Clinical effects of ultra low-dose and highly diluted dynamised drugs compared to conventional treatment in nine pathology-based subgroups and 3.) Clinical effects of ultra low-dose and highly diluted dynamised drugs in preventive use

Citation

Katharina Gaertner, Michael Frass, Michael Kundi, Loredana Torchetti. Systematic reviews and meta-analyses of controlled homeopathic studies: 1.) Clinical effects of ultra low-dose and highly diluted dynamised drugs compared to placebo in nine pathology-based subgroups; 2.) Clinical effects of ultra low-dose and highly diluted dynamised drugs compared to conventional treatment in nine pathology-based subgroups and 3.) Clinical effects of ultra low-dose and highly diluted dynamised drugs in preventive use. PROSPERO 2015 CRD42015025399 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42015025399

Review question

The aim of the planned analyses is to systematically review the literature on homeopathic clinical studies and to evaluate by meta-analytical means whether the clinical effects of ULD and HD drugs are different from control. Additionally, we aim to identify publication status and quality of trials with special regard to congruence with homeopathic criteria (‘model validity’) and to investigate whether the effect of using ULD and HD differs with the type of pathology.In contrast to former meta-analyses, and in order to consider both internal and external validity, not only RCTs but also controlled observational studies will be taken into account and a separate analysis for the preventive use of homeopathy is planned. Thus, three systematic reviews and meta-analytical reports will be presented (prior to the analysis, we will pilot the feasibility of the proposed classification):

1. Evaluation of the clinical effects of ULD and HD drugs in comparison to placebo in nine pathology-based subgroups: 1.) acute inflammatory diseases; 2.) diseases of traumatic origin; 3.) chronic inflammatory diseases; 4.) chronic degenerative diseases; 5.) polygenetic diseases and cancer; 6.) functional and multifactorial diseases; 7.) psychiatric diseases; 8.) pediatric diseases; 9.) side-effects from chemotherapy and chronic poisoning.

2. Evaluation of the clinical effects of ULD and HD drugs in comparison to conventional treatment alone or as an add-on. Pathology-based subgroup analyses will be performed as long as > 1 study per subgroup can be included.

3. Evaluation of the clinical effects of ULD and HD drugs for preventive purposes in comparison to control.

4. Evaluation of the impact on the clinical effects of the various homeopathic methods and study-designs used as well as to the differences throughout the various investigated pathologies

Searches

Information sources:

The databases MEDLINE (PubMed interface), EMBASE (EMBASEinterface), Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley interface), CORE-Hom and CAM-Quest® (both Carl and Veronica Carstens-Stiftung) Scopus (Scopus interface), Science Citation Index (Thompson-Reuters interface), AMED and CINAHL (both EBSCO interface) and LILACS (Biblioteca virtual em salud interface) will be used for the literature search.

The internet-based search engine Google Scholar will be used to complement the search with unpublished studies.

The print-library of the Carstens-Stiftung, Essen, Germany and of the faculty of Homeopathy, Glasgow, UK, will supplement the electronic databases.

source: https://doi.org/10.57694/912 | downloaded: 23.5.2024

Types of study to be included

Study designs: RCTs and controlled observational studies will be included.All other study designs will be excluded.

Condition or domain being studied

Any disease or health care intervention, using potentized, e.g. 'homeopathic' drugs are of interest for the systematic review and meta-analysis respectively.

Participants/population

Only studies on human organisms will be included. Participants must have exhibited a clinically relevant disease or been healthy and enrolled in a study on disease prevention.

Intervention(s), exposure(s)

We will include studies employing one or more substances, which were homeopathically processed by trituration and ‘succussion’. Any Q-potency will be included. Studies analyzing mother tinctures only will not be included.

Comparator(s)/control

The clinical effects of potentized drugs will be compared 1) to placebo, and 2) to conventional treatments that have shown effectiveness for the respective condition, and waiting-list controls, as long as they received standard care. Studies with other types of control (e.g. waiting-list without standard care, other complementary medicine methods) will not be included.

Studies with other types of control (e.g., waiting list, other complementary medicine methods) will not be included.

Context

Publication status: substantive research articles (either peer-reviewed or not) as well as conference proceedings, minor articles (under 500 words) and masters and doctoral theses will be eligible for further screening.

Book chapters and abstracts will be excluded.

Main outcome(s)

Outcomes will be considered as reported, and a primary outcome will be selected according to the prioritization criteria outlined in 'Outcomes and prioritization'. Outcomes in all data formats (e.g., dichotomous, continuous) will be considered.

Additional outcome(s)

One outcome per study will be identified. As we expect a considerable variety in outcomes, we plan to apply the following approach in order to reduce heterogeneity: within each pathology-based subgroup, the most often used outcome will be given priority. For the studies without such outcome, ‘alternative’ outcomes will be chosen with regard to clinical relevance following an hierarchical ranking regarding clinical relevance, consistent with the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization. This approach will be followed regardless of the main outcomes chosen in the primary study.

Data extraction (selection and coding)

Data extraction will be performed utilizing standardized and piloted Excel-files. Two reviewers will extract the data and will double-check the information independently. The following data will be extracted from the included studies:

- Publication type (substantive research article peer-reviewed; substantive research article non peer-reviewed; minor research article peer-reviewed; thesis; minor research article non peer-reviewed; master thesis; doctoral thesis; conference proceedings);

- Study aim and target population; inclusion and exclusion criteria;

- Study design (RCT, controlled cohort study, case -controlled study;

- Intervention details (LD, ULD or HD remedy; potency; type of homeopathy (classical (open; restricted; selective); clinical; complex; isopathic; preventive); placebo or conventional treatment as control; homeopathy as add-on (i.e. homeopathy provided as an addition to conventional medicine as basic therapy) or not; conventional intervention);

- All endpoints and corresponding outcomes (see 'Outcomes and prioritization');

- Number of patients that have participated, and that have been evaluated in each group; attrition rate; intention-to-treat or per-protocol analysis;

- Statistical values: measures of central tendency and dispersion for continuous data, number

of favorable events for dichotomous data; 95% confidence intervals;

- Allocation to the pathology-based subgroups;

- Risk of bias indicators (see 'Risk of bias of individuals studies');

- External validity indicators (see 'Risk of bias of individuals studies');

- Homeopathic model validity indicators (see 'Risk of bias of individuals studies');

- Funding and declared conflicts of interest.

Data synthesis

Subgroup analyses:

- Type of homeopathy (classical (open; selective; restricted); clinical; complex; isopathy);

- Whether or not homeopathy was provided as an add-on to standard care;

- Within the comparison to conventional treatment: comparison of effects of potentized drugs

vs. active control and potentized drugs vs. waiting-list receiving standard care;

- Potency (D1-C3, C4-C12; >C12);

- Whether or not sponsor had vested interesStudy design (RCT, controlled cohort study, case-controlled study; number of study arms, special design characteristics).

Cross-over studies will be included and the adequacy of the wash-out-period will be assessed as an additional risk of bias evaluation. Sensitivity analyses will be carried out.

If in a study with more than two study arms one group could be used for more than one comparison, a penalization will be applied to correct for multiple comparisons. In this case, the variance of the respective group will be enlarged by doubling the group size, so that the SD will be enlarged by the factor v2.

Nominal outcomes with more than two categories will be dichotomized as appropriate.

Whenever possible, results of an intention-to-treat analysis will be used. Disagreements on data extraction will be resolved by discussion. If information should be missing, the study authors will be contacted by e-mail (maximum of three e-mail attempts).

Risk of bias (quality) assessment

The included individual studies were assessed in the following way:

- The internal validity of the RCTs will be evaluated by the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials for the seven following domains: (I) random sequence generation; (II) allocation concealment; (III) blinding of participants and personnel; (IV) blinding of outcome assessment; (V) incomplete outcome data; (VI) selective reporting; (VII) anything else.

- The internal validity of the observational studies will be assessed by the Cochrane risk of bias assessment tool for non-randomized studies of interventions (ACROBAT-NRSI) for the seven following bias domains: (I) confounding; (II) selection of participants into the study; (III) measurement of interventions; (IV) departures from intended interventions; (V) missing data; (VI) measurement of outcomes; (VII) selection of reported results.

Due to the diversity of the medical conditions in the studies to review, no prespecified confounders and co-interventions (differing between treatment and control group and potentially impacting the outcome) as required by ACROBAT-NRSI can be determined. Instead, before extracting data of the included studies, confounders and potentially biasing co-interventions will be defined for each single study and then compared to the actual ones. General confounding variables for the propensity of use of homeopathy have been shown to be a female sex and a higher education. These variables will be considered if applicable.

- The external validity will be assessed by the corresponding scale of the Downs and Black checklist with three items: (I) whether the subjects asked to participate were representative of the entire population from which they were recruited; (II) whether the subjects prepared to participate were representative of the entire population from which they were recruited; (III) whether staff, places, and facilities where the patients were treated were representative of the treatment the majority of the patients receive.

- The homeopathic model validity will be evaluated by the six judgmental domains proposed by Mathie and colleagues: (I) rationale for the choice of the particular homeopathic intervention; (II) homeopathic principles reflected in the intervention; (III) extent of homeopathic practitioner input; (IV) nature of the main outcome measure; (V) capability of the main outcome measure to detect change; (VI) length of the follow-up to the endpoint of the study.

Risk of bias and the homeopathic will be rated independently by two reviewers. External validity will be rated by all reviewers. Disagreements will be solved by discussion. Inter-rater agreement as well as the proportion of unclear judgment will be noted.

Strategy for data synthesis

The three systematic reviews of potentized drugs 1) in comparison with placebo, 2) in comparison with active treatment, and 3) in prevention, will each be complemented by a quantitative meta-analysis.

The meta-analytical comparison of potentized drugs with placebo respectively with active treatment will be evaluated once as an overall treatment effect, and once within the nine pathology-oriented subgroups (for each group with >1 study), in order to determine the reduction of heterogeneity due to the new classification.

Different summary tables will be presented:

- Descriptive information of the included studies;

- Extracted raw data;

- Risk of bias assessment.

In the distinct meta-analyses, treatment effects will be considered as follows: difference between 1) the LD, ULD and HD group and the placebo group, 2) the LD, ULD and HD group and the active treatment group, 3) the LD, ULD and HD group and the control group in the prevention studies.

For dichotomous outcomes, the OR and the 95% CI will be determined.

Analysis of subgroups or subsets

Sensitivity analyses:

- Risk of bias: internal validity (overall score and differentiated according to source of bias)

- Risk of bias: external validity

- Risk of bias: model validity

- Substantive peer-review research articles vs. “grey”/other type of literature

- Double-blinded vs. no/single-blinding

- ITT versus per protocol

- Dichotomous vs. continuous outcomes

- Inclusion of imputed SMD

- RCTs versus NRSs

- Cross-over design

- Appropriateness of conventional treatment

Subgroup analyses:

- Type of homeopathy (classical; clinical; complex; isopathy)

- Comparison with conventional treatment: whether or not the homeopathic treatment was provided as an add-on or alone

- Potency

- Whether or not sponsor had vested interest

Contact details for further information

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Type and method of review

Intervention, Prevention, Systematic review

Anticipated or actual start date

01 January 2015

Anticipated completion date

31 August 2018

Funding sources/sponsors

The Tiedemann Foundation for Classical Homeopathy and the Homoeopathies-Foundation of the DZVhÄ (deutscher Zentralverein homöopathischer Ärzte) supported Katharina Gaertner financially, but did not have any role in the design of the protocol nor will it be involved in any other aspect of the project, such as collection of the primary studies, analyses of the data or interpretation of results.

Michael Frass is the sponsor of the meta-analyses.

Conflicts of interest

None known

Language

English

Country

Austria, Switzerland

Published protocol

https://www.crd.york.ac.uk/PROSPEROFILES/25399_PROTOCOL_20181201.pdf

Stage of review

Review Completed published (Due to lack of funding, the data-extraction and risk-of-bias assessments could not be completed. We therefore adapted the concept and are working on condition-specific reviews and meta-analyses on homeopathic interventions in specific diseases (e.g. arnica in surgery, individualised homeopathy in attention deficit and hyperactivity disorder))

Details of final report/publication(s) or preprints if available

The review was discontinued. And a new strategy was defined.

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

Homeopathy; Humans; Research Design

Date of registration in PROSPERO

16 August 2015

Date of first submission

06 February 2022

Stage of review at time of this submission

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

Revision note

This review has been discontinued.

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

16 August 2015

26 September 2016

06 February 2022