***Types of reviews to be included**

Give details of the type of evidence synthesis (systematic review, pairwise meta-analysis, and/or network meta-analysis) eligible for inclusion in the U-REACH project.

Study Designs for Inclusion

- Systematic reviews with meta-analysis of randomized controlled trials (RCTs), including:
  - Pairwise meta-analyses (PWMA)
  - Network meta-analyses (NMA)
  - Individual participant data meta-analyses (IPD-MA)
- No restrictions on language or publication date

Methodological Requirements

- Systematic Reviews characterized by:
  - Search in at least two databases
  - Clear reporting of inclusion/exclusion criteria

Special Considerations

- PWMA/NMA combining RCTs with non-RCTs are eligible if the results from RCTs can be reliably extracted separately
- IPD-MA and NMA are eligible if the raw data is available for analysis replication, or if they present the results of a PWMA in a way allowing for their replication (such as forest plots)
- Conference proceedings: Authors will be contacted for additional information if no other PWMA is available for the same PICO
- Pre-publication manuscripts are eligible if they meet inclusion criteria

Exclusion Criteria

- Umbrella reviews (but their references will be checked)
- Non-systematic reviews
- Systematic reviews without meta-analysis
- Dose-response meta-analyses without pooled effect sizes
- Meta-regressions without pooled effect sizes
- Imaging studies
- Genetic studies
- PhD theses
- Books

***Selection and data extraction**

Describe the process that will be used for selecting the studies and for extracting the data from the reports (e.g., two independent authors for the screening, assessment of eligibility and selection of studies, and data extraction).

Study Selection

- Independent pairs of blind reviewers will conduct:
  - Initial screening of titles and abstracts
  - Full-text assessment of potentially eligible PWMA/NMA/ IPD-MA
  - Final selection of included PWMA/NMA/IPD-MA

Data Extraction

- Independent pairs of blind reviewers will extract data from included PWMA/NMA/ IPD-MA (see the data extraction sheet attached).

- All extracted data will be cross-checked for accuracy and completeness by the lead authors

Quality Assessment

- Independent pairs of blind reviewers will conduct AMSTAR-2 scoring for each included PWMA/NMA/IPD-MA

***Participants/population**

Give summary criteria for the participants or populations being studied by the U-REACH project. The preferred format includes details of both inclusion and exclusion criteria.

Inclusion Criteria

The synthesis will include meta-analyses focused on individuals diagnosed with attention-deficit/hyperactivity disorder (ADHD). Eligible diagnoses must be established using established diagnostic criteria from:

- Diagnostic and Statistical Manual of Mental Disorders (DSM) (Version III through 5-TR)
- International Classification of Diseases (ICD) (Version 9-11)
- Studies including participants with ADHD and comorbid conditions will be included, provided all participants have a confirmed ADHD diagnosis.
- All age groups will be considered (preschoolers [<6 yo]; Children and adolescents [6-17 yo]; Adults [≥18 yo])

Exclusion Criteria

PWMA/NMA/ IPD-MA will be excluded if they include participants with unconfirmed or unclear ADHD diagnoses, such as those based on:

- Screening scale cut-off scores alone
- Self-reported diagnoses
- Informal diagnostic statements (e.g., "doctor said")

Additionally, meta-analyses will be excluded if they combine data from participants with confirmed and unconfirmed diagnoses in a way that prevents reliable separation of information from individual RCTs based on diagnostic status.

***Intervention(s), exposure(s)**

Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed. If no specific restriction is anticipated, please try to expose the general categorization of interventions you plan to make.

Overview

This synthesis will examine all pharmacological and non-pharmacological interventions for ADHD identified in systematic reviews, provided they are clearly defined and distinguishable from other intervention categories.

Here are examples of interventions we expect to include:

Pharmacological

- Amphetamines
- Methylphenidate
- Atomoxetine
- Alpha-2 agonists (guanfacine, clonidine)
- Viloxazine
- Antidepressants (e.g, bupropion, venlafaxine, desipramine)

- Antipsychotics (e.g, aripiprazole, risperidone, thioridazine)
- Other medications (e.g., modafinil, reboxetine, carbamazepine)

Psychosocial interventions

- Cognitive Behavioral Therapy (CBT)
- Dialectical Behavioral Therapy (DBT)
- Parent-mediated behavioral interventions
- Teacher-mediated behavioral training
- Child-focused behavioral therapy
- Social skill training
- Organizational skills interventions
- Psychoeducation
- Mindfulness
- Relaxation therapy
- Hypnotherapy

Complementary and Alternative Medicine

- Physical training/exercise
- Dietary interventions
- Neurofeedback
- Transcranial magnetic stimulation (rTMS)
- Transcranial direct current stimulation (tDCS)
- Nutritional supplements:
    - Polyunsaturated fatty acids
    - Vitamin D
    - Zinc
    - Iron
    - Carnitine
- Herbal supplements:
    - Asian herbal medicine
    - Ginkgo biloba
    - Ginseng
    - Hypericum
    - Pine bark extract
- Acupuncture

Intervention Classification Criteria

- Each intervention must be clearly defined and distinguishable from other categories.
- Broad, overlapping categories will be excluded, such as:
    - Generic "psychosocial interventions" that combine multiple distinct approaches
    - General "medication" categories that merge different pharmacological classes
- Classification Validation:
    - Corrected Coverage Area (CCA) analysis will be conducted using the Metaumbrella R package
    - Expected overlap thresholds:
        - Pharmacological interventions: <5% overlap
        - Non-pharmacological interventions: <10% overlap
    - If higher overlap is found:

- Intervention definitions will be revised to broader constructs where meaningful
- Or specific intervention subtypes will be removed from analysis

Note: This list is not exhaustive and may be expanded to include additional interventions identified in eligible meta-analyses, provided they meet the classification criteria.

***Comparator(s)/control**

Where relevant, give details of the alternatives against which the interventions/exposures selected in your U-REACH project will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Primary Analysis: Intervention versus inactive Control Groups

Acceptable Control Conditions

1. Standard Inactive Controls
   - Placebo pill
   - « Psychological » placebo
   - Waiting-list
   - Treatment as usual/standard care
   - Non-therapeutic activities (e.g., cooking classes)
   - Control groups referred to as "inactive" by the original meta-analysis authors (however, these must not include interventions typically associated with substantial therapeutic effects, e.g.: manualized, structured psychoeducation sessions delivered by study investigators
2. Augmentation Studies Control groups, considered eligible when:
   - Both experimental and control groups receive the same active intervention
   - The experimental group receives an additional intervention under investigation (e.g., : in studies where both groups receive methylphenidate, but the experimental group also receives cognitive training, the control group (methylphenidate only) will be considered valid

Secondary Analysis: Head-to-head comparisons

The secondary analysis will focus exclusively on network meta-analyses that include direct and indirect head-to-head comparisons between interventions included in the primary analysis.