Patterns of Exclusion in Antidepressant Clinical Trials

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Objective

To assess the generalizability of clinical trials of antidepressants, for the clinically depressed population
FDA Guidance Documents

September 1977
Antidepressant Drugs—Clinical Evaluation (Final)

June 2018
Major Depressive Disorder: Developing Drugs for Treatment (Draft Guidance)

August 2021
No updates made to 2018 draft Guidance, nor has it been finalized
Background

Prevalence of Comorbid Conditions in Major Depressive Disorder (MDD)

- 60-65% of individuals with MDD have a comorbid mental disorder(s)
- Patients with chronic medical diseases are three times more likely to suffer from depression

Routine Exclusion of Patients with Comorbid Disorders

- To increase homogeneity of study populations
- Maximize drug-placebo differences
Methodology

01 Literature Review
FDA Guidance Documents for Antidepressants

02 Keyword Search
Searched seven SSRIs* on clinicaltrials.gov

03 Exclusion Criteria
Assessed studies for similarities and trends

04 Assessment Scales
Examined studies utilizing FDA-accepted assessment scales

*Selective Serotonin Reuptake Inhibitors
Exclusion Criteria

- **SSRIs** (126 studies)
- **Axis I (119 studies)**
  - Bipolar Disorder (71 studies)
  - Substance Use Disorder (70 studies)
  - Schizophrenia (54 studies)
- **Axis II (50 studies)**
  - Mental Retardation (19 studies)
  - Schizoaffective Disorder (10 studies)
  - Mania (12 studies)

- **Additional Comorbidities**
  - Unstable Medical Illness (90 studies)
  - Suicide Risk (88 studies)
  - Pregnant Women (77 studies)
FDA-Accepted Clinician-Rated Measures for Assessing Treatment Efficacy

Hamilton Depression Rating Scale (HAMD-17, HDRS)

*Purpose*: To assess severity of, and change in, depressive symptoms

*Population*: Adults

Montgomery Asberg Depression Rating Scale (MADRS)

*Purpose*: To evaluate core symptoms of depression (based on patient report and rater’s observation)

*Population*: Adults

Children’s Depression Rating Scale (CDRS-R)

*Purpose*: To diagnose depression

*Population*: Children ages 6-12
Assessment Scales

- HAM-D: 63
- MADRS: 27
- Both HAM-D and MADRS: 6
- CDRS-R: 7
- None: 11
Conclusions

❖ Regardless of the use of FDA-accepted screening instruments to assess treatment efficacy in the majority of antidepressant trials, variation remains in the assessment and version employed to determine primary and/or secondary outcomes.

❖ Specific screening instruments used in studies are often not reported or inaccurately referenced, making it difficult to compare, evaluate, and draw conclusions about findings.

A more accurate representation of the clinically depressed population, as well as standardization of study designs are necessary steps towards a better understanding of the safety and efficacy of antidepressants currently being used by the general public.
Thanks