Antidepressants Among Special and Vulnerable Populations: Examining Clinical Trials for Generalizability of Findings

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OBJECTIVE
Assess the degree of generalizability of antidepressant clinical trials involving patients with Major Depressive Disorder (MDD), particularly those among vulnerable populations and with comorbidities.

BACKGROUND
- 1977: Guidelines for the Clinical Evaluation of Antidepressant Drugs
- 1977 - 2013: FDA approvals of 7 Selective Serotonin Reuptake Inhibitors (SSRIs)
- 2018: Major Depressive Disorder: Developing Drugs for Treatment (Draft Guidance)
- Current framework still draws from 1977 Guidelines

METHODOLOGY
- Literature Review
  - List of all FDA-approved SSRIs was compiled
  - Common comorbidities were identified
- Keyword Search
  - Each SSRI was searched on clinicaltrials.gov under MDD
  - Filtered for studies in the United States
  - Clinical trials with results were selected
- Categorization of Exclusion Criteria

FINDINGS
- Major Depressive Disorder
  - Bipolar spectrum disorders
  - Substance use disorders
  - Anxiety disorders
  - Eating disorders
  - Schizophrenia spectrum disorders
  - Diabetes
  - Chronic respiratory diseases
  - Extrapyramidal diseases
  - Pregnancy

- Axis I (119 studies)
- Axis II (50 studies)

CONCLUSIONS
- Exclusion criteria were assessed for similarities and trends
- Formal revisions of the FDA's current regulations, along with greater representation of the clinically depressed population in studies of antidepressants, are needed to better understand their safety and efficacy.

This assessment of 126 studies for MDD revealed that:
- Outdated FDA regulations have resulted in clinical trials that do not represent the clinically depressed population.
- Prevalent exclusion criteria include various mental disorders, pregnancy, suicide risk, and unstable medical illnesses: all groups who make up the MDD population.

Additional Comorbidities:
- Unstable Medical Illness (90 studies)
- Suicide Risk (88 studies)
- Pregnant Women (77 studies)

*Some individuals may have more than one condition.

Figure 1. Prevalence of Comorbidities in MDD

Figure 2. Most Common Exclusion Criteria of Clinical Trials of SSRIs between 1994-2021

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