

Feb 12, 2025

A Systematic Review on Adverse Effects of Antidepressants for Pharmacological Treatment of Depression Over a Decade

DOI

<https://dx.doi.org/10.17504/protocols.io.dm6gp9q21vzp/v1>

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Protocol Citation: Razia Abdul Rasheed, Dr.Sridevi, krishna kishore, Dr.Vijayalakshmi s, Dr.T.A.R Raja, Dr.Senthil G, Dr.Renuga Devi P, Dr.Ramanarayana Reddy, P sanjay Rathinam 2025. A Systematic Review on Adverse Effects of Antidepressants for Pharmacological Treatment of Depression Over a Decade. **protocols.io**

<https://dx.doi.org/10.17504/protocols.io.dm6gp9q21vzp/v1>

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Protocol status: Working

We use this protocol and it's working

Created: February 05, 2025

Last Modified: February 12, 2025

Protocol Integer ID: 119585

Keywords: adverse effects of antidepressant, antidepressants for pharmacological treatment, pharmacological treatment of depression, antidepressant, name of antidepressant, dropout rates on antidepressant, depression treatment modality, pharmacological treatment, systematic review on adverse effect, prevention of side effect, pharmacotherapy, adverse effect, side effect, ssri, depression, decade depression, drug reaction, dosing regimen, side effects of each agent, dosage, cochrane, treatment

Abstract

Depression is a severe heterogeneous disease that affects a person's mood, physical health and behavior. Depression was ranked the fourth leading cause of disability and premature death. Depression treatment modalities involve pharmacotherapy, psychotherapy or both. However, some studies have reported that, dropout rates on antidepressants are 50% in first 2-4 months. Adverse drug reactions are an important factor in non-adherence to antidepressant treatment. Therefore, prevention of side effects should be the vital part of treatment. **Objectives:** To assess the Adverse Effects of Antidepressants for Pharmacological Treatment of Depression Over a Decade. **Materials and method: Databases:** PUBMED/MEDLINE and COCHRANE. **Search strategies :** Antidepressants, SSRIs, SNRIs, Side effects, TCAs, ADRs with year limit 2011-2020. **Data extraction:** Authors will review the electronic abstracts and selected full-text articles for inclusion. The following information will be extracted from each included study: Mean age, sample size, study population, study design, category and name of antidepressants used, dosage, dosing regimen, side effects of each agent. Data extraction will be performed according to PRISMA guidelines.

INTRODUCTION

1 Depression is a severe heterogeneous disease that affects a person's mood, physical health and behavior. Depression was ranked the fourth leading cause of disability and premature death.¹ Globally, An estimated 3.8% of the population suffers from depression, including 5% of adults (4% of men, 6% of women) and 5.7% over the age of 60.¹ A report by WHO in 2015 found that 4.5% of the Indian population, suffer from depressive disorders.²⁻⁴

Major depressive disorder is characterized by a depressed mood or loss of pleasure/interest for at least 2 weeks. It is also accompanied by at least three (for a total of at least five) of the following symptoms present most days: weight loss or change in appetite, insomnia or hypersomnia, psychomotor retardation or agitation, fatigue or loss of energy, excessive/inappropriate guilt or feelings of worthlessness, indecisiveness or diminished ability to concentrate or think, and recurrent thoughts of death or suicidal ideation or suicide plan or attempt.⁵⁻⁷

Depression treatment modalities involve pharmacotherapy, psychotherapy or both. Without treatment, 10 to 15% of people suffering from severe depressive disorder commit suicide.⁸ The American Psychiatric Association (APA) in 2012 and the American College of Physicians (ACP) in 2016, published guidelines for major depressive disorder (MDD), where antidepressants were recommended as the first treatment option.^{9, 10} It also guided that, drug selection should be based on side effect profile, patient preference, dosing schedule, cost, and drug interactions. Overall, the guidelines suggested that selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), bupropion, or mirtazapine are the optimal initial treatment for the majority of patients.¹¹

Tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) are recognized pharmacological classes for treating depression, but due to safety concerns and drug properties, these classes are not considered first-line therapy.¹²

Although antidepressants have excellent therapeutic effects, they all have potential side effects. TCAs are more sedative (eg drowsiness), (anti)cholinergic (eg dry mouth) and cause cardiovascular side effects (eg heart palpitations). In contrast, SSRIs have been shown to have more activating (such as insomnia) and gastrointestinal (such as nausea) adverse events.^{13, 14}

Taking antidepressant medication for at least 6 to 9 months will prevent relapse after the remission of a depressive episode.¹⁵ However, some studies have reported that, dropout rates on antidepressants are 50% in first 2-4 months.¹⁶ Adverse drug reactions are an important factor in non-adherence to antidepressant treatment.¹⁷ Therefore, prevention of side effects should be the vital part of treatment.

AIM AND OBJECTIVE

2 To assess the Adverse Effects of Antidepressants for Pharmacological Treatment of Depression Over a Decade.

3 **Materials and method:**

3.1 **Databases** : PUBMED/MEDLINE and COCHRANE.

4 **Search strategies** : Antidepressants, SSRIs, SNRIs, Side effects, TCAs, ADRs with year limit 2011-2020.

5 **Selection criteria** :

Inclusion criteria :

1. RCTs that diagnosed major depressive disorder (MDD) based on; Diagnostic and Statistical Manual of Mental Disorders (DSM-5), International classification of diseases (ICD-10), Montgomery-Asberg depression rating scale (MADRS), Hamilton depression rating scale (HDRS).
2. RCTs with primary or secondary outcome documenting adverse effects
3. RCTs that documented antidepressants adverse effect with Generic Assessment of Side Effects Scale antidepressants (GASE-AD), Toronto Side Effects Scale

5.1 **Exclusion criteria:**

1. Duplicated studies
2. Language other than English
3. Phytochemical based RCT

Data extraction:

6 Authors will review the electronic abstracts and selected full-text articles for inclusion. The following information will be extracted from each included study: Mean age, sample size, study population, study design, category and name of antidepressants used, dosage, dosing regimen, side effects of each agent. Data extraction will be performed according to PRISMA guidelines.

Data collection procedure:

7 1. Antidepressant side effects will be assessed according to the Generalized Side Effects Assessment Scale GASE-AD (Antidepressant Specific Side Effects) - 36 points

and the Toronto Side Effects Scale (TSES) - 32 points. These scales are used directly by treating physicians to identify adverse events.

2. Central nervous system (CNS) side effects - Nervousness, Agitation, Tremor, Myoclonus, Fatigue, Dizziness, Postural hypotension, Somnolence, Increased sleep, Decreased sleep Sweating, Flushing, Edema, Headache and Blurred vision
3. Gastrointestinal (GI) side effects - Abdominal pain, Dyspepsia, Nausea, Diarrhea, Constipation, Decrease appetite, Increase appetite, Dry mouth, Weight gain and Weight loss. Sexual functioning (SF) side effect – Anorgasmia, Increased libido, Decreased libido, premature ejaculation, Delayed ejaculation and Erectile dysfunction.

Analysis plan:

- 8 Data will be entered and analyzed using SPSS version 23.0 software. Descriptive statistics will be used to analyze the data.

Implications of the study

- 9 The study highlights the need for careful consideration of adverse effects when prescribing antidepressants for depression. By systematically reviewing side effects over the past decade, it emphasizes improving patient adherence through personalized treatment plans, monitoring, and minimizing adverse reactions, ultimately optimizing pharmacological management of depression

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source of funding

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