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Common antidepressant side effect profiles and their management: A literature review

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Abstract

Background: Antidepressant medications are widely used as a first-line treatment for depressive disorders and various other mental health conditions in both primary and hospital-based healthcare settings. Despite their proven efficacy in alleviating depressive symptoms, antidepressants are frequently associated with a range of adverse effects that may negatively impact patient adherence, treatment satisfaction, and long-term therapeutic outcomes. Understanding the safety profile of antidepressants is therefore essential for optimizing clinical management and improving treatment success.

Purpose: To review and synthesize current scientific evidence regarding the commonly encountered adverse effect profiles of antidepressant medications and the strategies used for their management in clinical practice.

Results: A literature review of studies published between 2020 and 2025 identified several frequently reported adverse effects associated with antidepressant use, including gastrointestinal disturbances, sleep disorders, sexual dysfunction, weight changes, and neurological symptoms such as headache and tremor. The adverse effect profiles varied across antidepressant classes, including selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and atypical antidepressants. Management strategies commonly reported in the literature included dose adjustment, switching antidepressant agents or drug classes, the use of adjunctive therapies to alleviate specific adverse effects, and continuous patient education and monitoring to enhance treatment tolerability and adherence.

Conclusion: Antidepressant medications exhibit diverse adverse effect profiles that may compromise treatment effectiveness if not appropriately addressed. This literature review highlights the importance of recognizing commonly encountered adverse effects and implementing individualized, evidence-based management strategies to improve drug tolerability and patient adherence. An integrated and patient-centered approach is essential to optimize antidepressant therapy in clinical practice.

Keywords: Antidepressants; Adverse Effects; Drug Safety Profile; Management; Literature Review.

INTRODUCTION

The use of antidepressant medications remains a central pillar in the management of depressive disorders and related mental health conditions, from primary healthcare settings to tertiary referral hospitals. Although effective in reducing depressive symptoms, antidepressant therapy is frequently associated with a range of adverse effects that may reduce patient adherence, prolong treatment duration, and increase the overall cost burden of healthcare

services (Cipriani, Furukawa, Salanti, Chaimani, Atkinson, Ogawa, & Geddes, 2018). These adverse effects are of particular concern, as failure to adequately manage drug tolerability is one of the leading causes of premature treatment discontinuation. Over the past five years, the literature has consistently shown that the most common adverse effects of antidepressants involve the gastrointestinal, neurological, metabolic, and sexual

systems, with variation in profiles depending on the drug class (Edinoff, Akuly, Hanna, Ochoa, Patti, Ghaffar, & Kaye, 2021). Selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) are frequently reported to cause nausea, insomnia, agitation, and sexual dysfunction, whereas tricyclic antidepressants are more commonly associated with anticholinergic and cardiovascular effects (Jolstedt, 2019).

Sexual dysfunction is one of the most consistently reported adverse effects and has a substantial impact on patients' quality of life. Observational studies and systematic reviews indicate that more than half of SSRI users experience reduced libido, anorgasmia, or erectile dysfunction, which are often not spontaneously reported by patients (Montejo, Montejó, & Navarro-Cremades, 2025). Moreover, recent reports have highlighted the phenomenon of post-SSRI sexual dysfunction (PSSD), defined as persistent sexual dysfunction that continues even after discontinuation of the medication (Healy, Le Noury, & Mangin, 2018). In addition, weight gain and metabolic disturbances have emerged as important issues in long-term antidepressant therapy. Recent evidence suggests that certain antidepressants, particularly specific SSRIs and atypical antidepressants, may induce weight gain through neuroendocrine mechanisms and alterations in appetite regulation (Gafoor, Booth, & Gulliford, 2018). These effects may increase the risk of metabolic comorbidities and further reduce patient adherence to treatment.

The management of antidepressant-related adverse effects has been widely discussed in recent literature and includes both pharmacological and non-pharmacological approaches. Commonly recommended strategies involve dose adjustment, switching to agents with more favourable tolerability profiles, the use of adjunctive therapies to target specific adverse effects, and ongoing patient education and monitoring (American Psychiatric Association, 2020). Individualized approaches based on patient characteristics and drug-specific risk profiles have been shown to improve long-term treatment outcomes. Overall, previous studies emphasize three key aspects in the management of antidepressant adverse effects: early identification

and understanding of side-effect profiles according to drug class, the implementation of adaptive and individualized management strategies, and the importance of patient communication and education to enhance treatment adherence. Nevertheless, the existing scientific evidence remains dispersed across studies with diverse designs and research focuses (Wang, Han, Bahk, Lee, Patkar, Masand, & Pae, 2018).

RESEARCH METHOD

This literature review aimed to compile and analyse scientific evidence regarding the commonly encountered adverse effect profiles of antidepressant medications and their management strategies in clinical practice. The review was conducted to obtain a comprehensive overview of variations in adverse effects across different classes of antidepressants and the approaches used to improve tolerability and treatment adherence. A systematic literature search was carried out using the PubMed, Scopus, and Google Scholar databases. The search strategy employed combinations of the keywords “antidepressants,” “adverse effects,” “side effects,” and “management,” adapted to the features of each database. Articles published between 2020 and 2025 were considered to ensure the relevance and currency of the scientific evidence.

The articles included in this review comprised original research and systematic reviews published in reputable journals and written in English or Indonesian. Selected literature specifically addressed antidepressant-related adverse effects and their management strategies in human populations, using observational study designs, clinical trials, or cohort studies. Editorials, letters to the editor, case reports, and conference abstracts were excluded from the analysis. The literature selection process involved title and abstract screening, followed by full-text review to assess eligibility in relation to the study objectives. Articles that met the inclusion criteria were analysed descriptively and narratively. Extracted data included study characteristics, the types and classes of antidepressants investigated, reported adverse effect profiles, and recommended management approaches. The findings were then synthesized to illustrate the most common adverse effect patterns and their management strategies based on the most recent scientific evidence.

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RESEARCH RESULTS

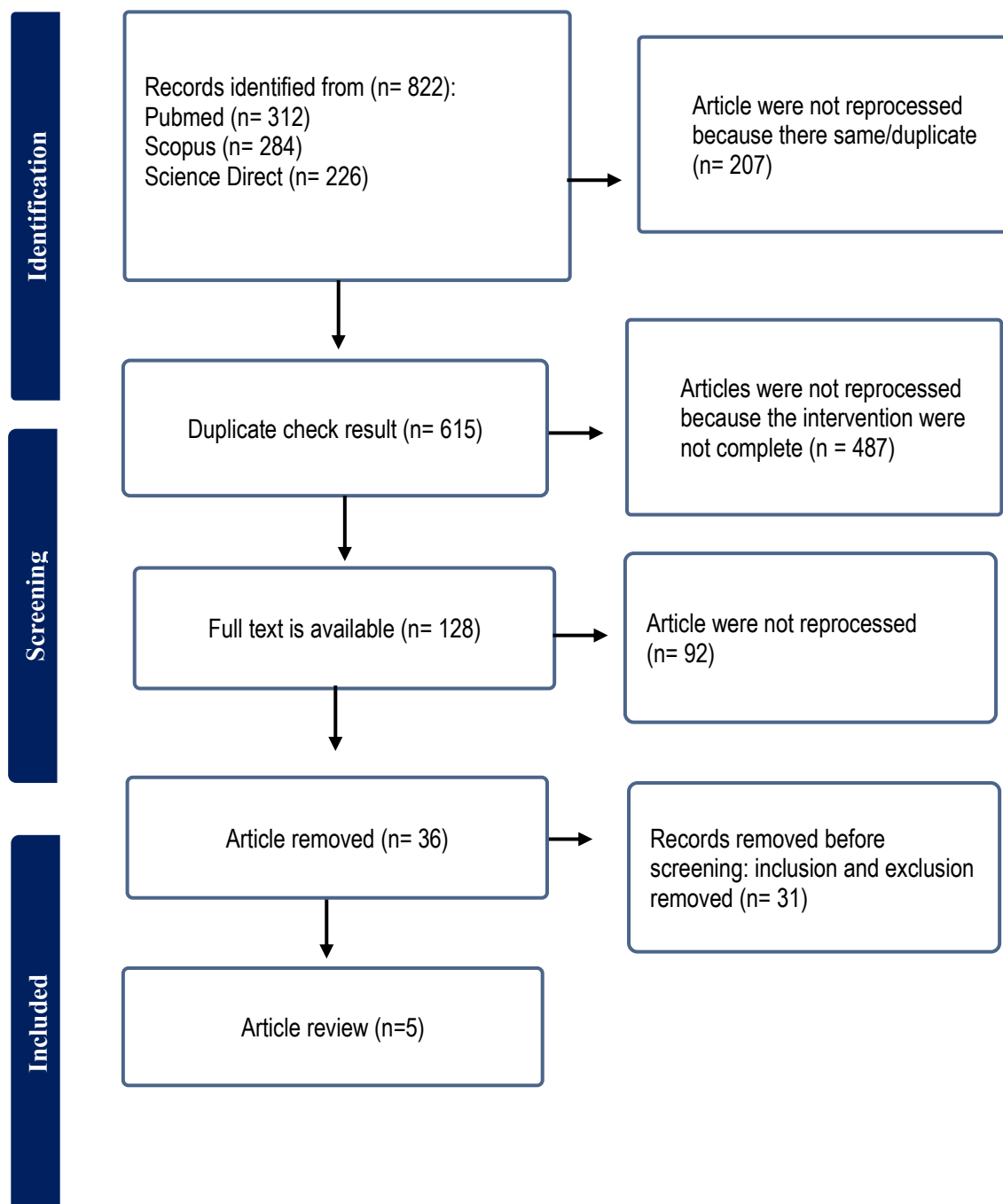


Figure. Diagram Prisma Flow

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Table. Article Review

(Author,Year) (Country)	Purpose	Method	Results
(Asqiya et al., 2023) (Indonesia)	To determine the effect of drugs consumption in depression patients on subjective success.	Non-experimental descriptive	Subjective therapeutic success is in the form of a reduction in side effect symptoms, such as dizziness, hallucinations, mood swings, and anxiety.
(Braund et al., 2021) (Australia)	To assess the severity of side effects and the impact of the type of treatment and anxiety symptoms during treatment, and whether side effects are related to treatment outcomes.	Randomized Clinical Trial (RCT)	Side effects (frequency, intensity, and load on the FIBER scale) and therapy success.
(Davis et al., 2021) (Columbia)	To investigate the effect of psilocybin therapy in patients with MDD.	(RCT)	Antidepressant efficacy and temporary side effects include headaches and intense emotional experiences.
(Hadawiyah et al., 2025) (Indonesia)	To identify the occurrence and number of DRP events in the drug interaction categories of overdose, underdose, drug presence without indication, indication without drug, unexpected drug reactions in depressed patients.	Retrospective descriptive	<i>Drug Related Problems (DRP): 100% of drug interactions occurred in 15 patients; no cases of overdose, underdose, unsolicited indications, or adverse drug reactions.</i>

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(Zolghadriha et al., 2024) (Iran)	To investigating the clinical effects of intravenous ketamine on symptoms of MDD and suicidal ideation.	(RCT)	Changes in depressive symptoms (MADRS) and suicidal ideation with side effects such as increased heart rate, headache, dizziness, and dissociative symptoms.
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DISCUSSION

Based on the review of studies included in this analysis, the pattern of antidepressant adverse effects appears relatively consistent, although it varies according to drug class and therapeutic regimen. In aggregate, the most frequently reported adverse effects consist of mild to moderate physical symptoms, such as headache, dizziness, nausea, and somnolence, as well as transient psychiatric manifestations, including agitation, intense emotional experiences, and dissociation. These findings are reflected across various types of interventions, including conventional oral antidepressants (SSRIs or SNRIs), combinations of antidepressants and antipsychotics in clinical practice, and newer antidepressant interventions such as ketamine and psilocybin. Each of these modalities exhibits a distinct adverse effect profile; however, the effects are generally acute and reversible (Asqiya, Ningrum, Muthoharoh, & Permadi, 2023). The timing of adverse effect onset and patients' perceptions of side-effect burden have been shown to be crucial. The frequency and intensity of adverse effects tend to peak during the second week of therapy, while side-effect burden is the strongest predictor of clinical outcomes, with effects observable as early as the fourth day of treatment and associated with a lower probability of remission at the end of the observation period. These findings underscore the importance of early evaluation and subjective measurement of side-effect burden as clinical indicators for further intervention (Braund, Tillman, Palmer, Gordon, Rush, & Harris, 2021).

Differences in adverse effect profiles across drug classes should also be contextualized according to their pharmacological mechanisms (Pannu & Goyal, 2025). The use of SSRIs or SNRIs commonly produces effects related to serotonin and norepinephrine modulation, including nausea, sleep disturbances, and sexual dysfunction, which tend to develop during medium- to long-term use (Bahrick & Harris, 2019). The combination of antidepressants with antipsychotics, as observed in community-based clinical practice, increases the risk of sedation, dizziness, and anticholinergic effects, particularly in the presence of polypharmacy involving shared metabolic enzymes (Zhou, Sun, Wang, Cong, Zeng,

Zhou, & Fan, 2023). In contrast, newer agents such as ketamine and psilocybin are associated with more acute and characteristic adverse effects. Ketamine use is frequently accompanied by dissociative symptoms and transient hemodynamic elevation, whereas psilocybin may induce intense emotional experiences that require structured therapeutic support. These differences are relevant when selecting therapeutic regimens based on patients' clinical conditions and the capacity of healthcare facilities to provide appropriate monitoring (Davis, Barrett, May, Cosimano, Sepeda, Johnson, & Griffiths, 2021).

The finding that side-effect burden influences therapeutic outcomes has direct practical implications. A high side-effect burden may reduce adherence, precipitate premature treatment discontinuation, or prompt suboptimal regimen changes, thereby diminishing the likelihood of remission. Therefore, the assessment of side-effect burden, measured using instruments such as the Frequency, Intensity, and Burden of Side Effects Rating (FIBSER) during the early phase of therapy, should be incorporated into clinical protocols as a screening tool for early intervention, whether in the form of symptomatic management or dose or medication adjustment. This strategy is supported by evidence indicating that rapid intervention for distressing side effects can improve treatment continuity and final clinical outcomes (Zhou, Sun, Wang, Cong, Zeng, Zhou, & Fan, 2025).

Polypharmacy and drug-related problems (DRPs) have emerged as systemic risk factors that increase both the frequency and severity of adverse effects. Analyses of medical records indicate that drug–drug interactions represent the most frequently identified category of DRPs in mental health practice. The combination of antidepressants with antipsychotics or other medications affecting cytochrome P450 pathways may result in clinically significant pharmacokinetic and pharmacodynamic interactions. Consequently, the implementation of medication reconciliation and structured medication review by clinical pharmacists should be an integral component of the care of patients with depression, particularly in populations receiving more than one psychiatric agent. This approach is effective in identifying high-

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risk combinations, planning dose adjustments, and determining the need for laboratory and vital sign monitoring (Zolghadriha, Anjomshoaa, Jamshidi, & Taherkhani, 2024).

In the context of management, several practical approaches can be applied to reduce side-effect burden and DRPs (Oliva, Lippi, Paci, Del Fabro, Delvecchio, Brambilla, & Serretti, 2021). First, clear pre-treatment education regarding potential adverse effects and follow-up plans enhances patient awareness and encourages early reporting. Second, structured monitoring, including the use of side-effect burden scales on day 4 and at week 2, allows for the identification of high-risk patients who require timely intervention. Third, symptomatic interventions—such as antiemetics for nausea, dose-timing strategies to reduce sedation, and, when necessary, dose adjustment or switching of therapeutic agents—should be considered based on an individualized benefit–risk evaluation. For ketamine and psilocybin therapies, hemodynamic monitoring protocols and structured psychotherapeutic support are prerequisites for safety and effectiveness (Hamon & Bourgoin, 2016). Overall, this review of the literature confirms that antidepressant adverse effects are not merely isolated pharmacological phenomena but are key determinants of the overall course of depression treatment. A proactive clinical approach that integrates early detection, symptomatic management, reduction of polypharmacy, and interprofessional collaboration represents the most promising strategy to minimize side-effect burden and maximize therapeutic outcomes (Hadawiyah, Lolok, & Hanafi, 2025).

CONCLUSION

Antidepressant medications have diverse adverse effect profiles that almost invariably accompany the course of treatment, with characteristics that differ across drug classes. Adverse effects most frequently occur during the early phase of therapy, particularly with the use of conventional antidepressants such as SSRIs and SNRIs, and constitute a major factor influencing patient adherence and the success of long-term treatment.

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