

# Patterns of Antidepressant Prescriptions for the Treatment of Depression: A Scoping Review

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## Research Article

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## Abstract

**Introduction:** Depression is an important global public health problem due to its relatively high lifetime prevalence and significant disability caused by it. It is associated with functional impairment and high morbidity and mortality. Antidepressant medication is considered to be the best treatment option for depression

**Method:** Literature searches (2000-2019) were performed using PubMed, HINARI and Google Scholar that analyze the pattern of prescription of antidepressants among the patients of depression. .

**Results:** Females suffered from depression more than their male counterparts. Married people, housewives, lower income people, employees and highly educated people suffered more from depression. Selective Serotonin Reuptake Inhibitors (SSRI) like Sertraline, was found out to be the most preferred antidepressant among the depressive patients.

**Conclusion:** Our Study suggested that out of five major antidepressant drugs being available for the treatment of depression, selective serotonin reuptake inhibitors are preferred over others because of their better side effect and tolerability profile.

## Introduction

Depression is a common mental disorder and a major cause of functional disability <sup>1,2</sup>. According to the World Health Organization (WHO), by 2020, it will be the second-highest known cause of worldwide disability <sup>3,4</sup>. Depression is characterized by a sad mood, pessimistic thought, lowered interest in day-to-day activities, poor concentration, insomnia or increased sleep, significant weight loss or gain, decreased energy, continuous feelings of guilt and worthlessness, decreased libido and suicidal thoughts occurring for at least two weeks <sup>5,6</sup>. Depressed patients can be of any gender, age, or background. Due to fear of stigmatization associated with mental disorders, patients lack to seek medical treatment in their early stages <sup>7-9</sup>. To maintain normal human health in patients, drugs play a crucial role. Antidepressant drugs are the most widely used and are most effective in the treatment of depression <sup>10,11</sup>. For many years, tricyclic antidepressants (TCAs) have been the drug of choice for treating depression in patients <sup>12-14</sup>. Many new antidepressants with better tolerance and broader indications have been discovered because of an increase in the prevalence of depression throughout the world <sup>15</sup>. This results in the gradual replacement of conventional drugs such as TCAs and monoamine oxidase inhibitors (MAOIs) by SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), and atypical antidepressants <sup>7,16,17</sup>. The most appropriate antidepressants should be selected according to symptoms and patient characteristics, with adequate dose and duration of therapy, to enhance the treatment success rate <sup>18,19</sup>. However, other factors, such as adverse effect profiles, cost, safety profile, history of prior medication treatment, and patient preference, are important in the initial selection of antidepressants and should be considered by

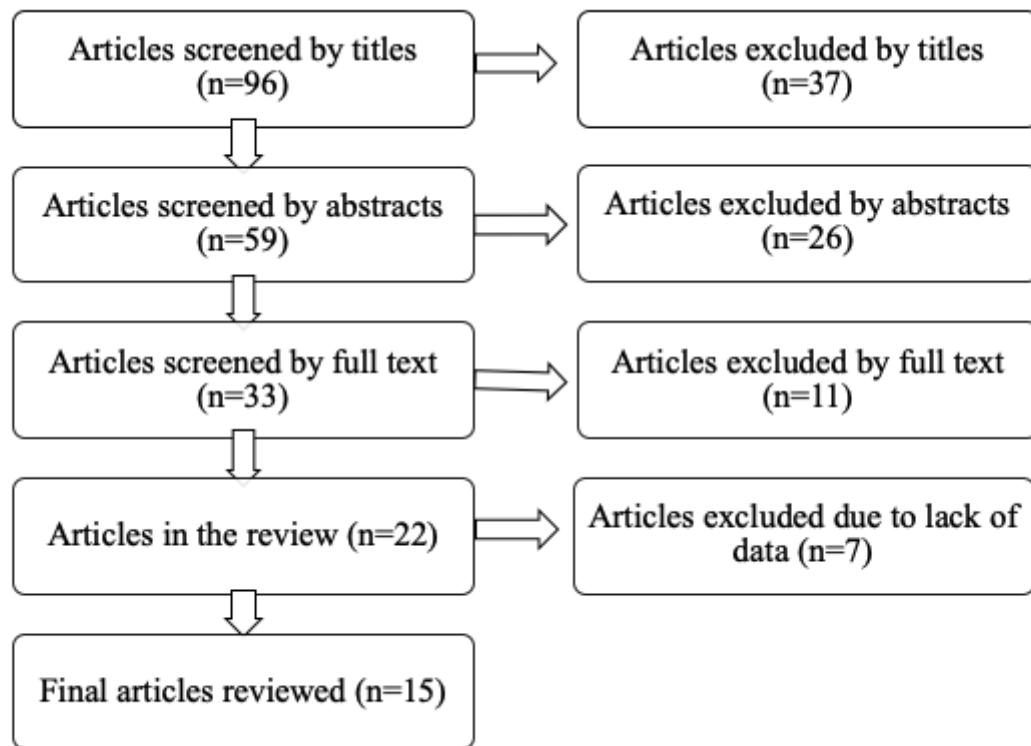
physicians<sup>20,21</sup>. The optimal use of antidepressants could reduce individual distress, along with the social burden of depression<sup>22</sup>. The aim of the analysis of prescribing patterns is to evaluate the prescription habits of medical practitioners and to suggest necessary modifications if required to make drug therapy rational and cost-effective<sup>6,16</sup>. The use of antidepressants has increased within the last two decades<sup>24</sup>. As a result of the increased prescription and use of antidepressants, the need for information regarding the actual prescribing practices has become vitally important to maintain patient safety as well as to ensure that the optimal therapeutic outcome is achieved, especially when the nature of the side effects of these drugs are considered. Hence, this review aims to investigate and summarize the studies on antidepressant prescription patterns for the treatment of depressive disorders.

## Methods

### Data Sources, Search, and Selection

A comprehensive literature review was conducted using PubMed and Google Scholar. The search was limited to English language articles published in journals between January 2000 and 2019. The search keywords used were depression, drug use evaluation, antidepressants, prescription patterns of antidepressants in depression, SSRIs, TCAs, SNRIs, and atypical antidepressants. We also included articles listed in “related articles” from PubMed and the author's reference lists. To improve the comprehensiveness of the literature, available review articles on the topic were also examined. This review provides a comprehensive review of the available literature.

### Data screening and extraction



## **Study selection**

(1) The literature on varying methodologies (observational, cross-sectional, retrospective, survey, case reports) analyzes the prescription pattern of antidepressants for the treatment of depression.

(2) Patients irrespective of age and sex with a primary diagnosis of depression and prescription of at least one antidepressant drug.

Our study outcomes were the demographic profile and prescription pattern of antidepressants among patients with depression. Studies that did not meet our criteria were excluded during the review. Studies were discarded if they were clinical trials and reviews.

## **Results**

The studies included were published between 2000 and 2019. The total sample size was 1,88,713 patients. The studies were conducted in Sweden<sup>25</sup>, India<sup>26</sup>, Bangladesh<sup>27</sup>, Malaysia<sup>28</sup>, Korea<sup>29</sup>, Nigeria<sup>30</sup>, Singapore<sup>31</sup>, China<sup>32</sup>, Italy<sup>33</sup>, Saudi Arabia<sup>34</sup>, USA<sup>35</sup>, Australia<sup>36</sup>, Germany<sup>37</sup>, Canada<sup>38</sup>, and the Netherland<sup>39</sup>. The summarized main findings of the studies are presented in Table 1.

**Table 1: Study, sample, methods, and major findings of the studies**

<b>Study</b>	<b>Objective</b>	<b>Methodological review</b>	<b>Major findings</b>
Lagerberg et al., 2019 <sup>25</sup>	To examine antidepressant prescription patterns and dispensations among children, adolescents, and young adults in Sweden between 2006 and 2013.	Population-based study n=1,74,237 age: 0-24 years (January 2006 and December 2013)	Sertraline was common in children followed by fluoxetine in younger age and citalopram in young adults.  SSRIs were the most common drug in both males and females. SNRIs and other antidepressants (Mirtazapine and bupropion) prescription were most common for young adults and TCAs were more prevalent in 0-11 years female.
Tejashwini et al., 2019 <sup>26</sup>	To assess the pattern of use of different classes of antidepressants and ADR.	Prospective observational study n=598  age: ≥18 years (April 2016 to September 2016)	More males were receiving antidepressants (57.86%).  The age group with maximum antidepressant: 41-60 years  Common antidepressant drug prescribed: fluoxetine (50.27%), followed by sertraline (40.29%), amitriptyline (25.31%), and escitalopram (3.43%).  The majority of the individuals suffering from depressive disorder were married, employees, and housewives with secondary education.
Islam et al., 2019 <sup>27</sup>	To obtain information regarding the prescribing pattern of antidepressant drugs following WHO prescribing indicators in two teaching hospitals.	Hospital-based descriptive cross-sectional study. n=300  age: 18-60 years (June 2015 to June 2016)	The majority of the patients were of age group 18-27 years (52.66%, 48%), females (53%, 58%), married females, housewives, less educated, unemployed, and the lower-income group from a rural area. Most commonly prescribed antidepressants: SSRI (sertraline followed by escitalopram, citalopram, and fluoxetine), TCA (amitriptyline followed by imipramine), SNRI (venlafaxine) and atypical group (mirtazapine).
Nahas and Sulaiman, 2018 <sup>28</sup>	To explore the pattern of prescribed antidepressants among depressive men in Malaysia.	Cross-sectional study n=107  Age: ≥18 years  (from May 2015 to ten months period)	The mean age of the patients was 49.9 years. SSRIs (72.9%) were the most commonly prescribed antidepressants, followed by TCAs (10.3%), SNRI (8.4%) and MAOIs (2.8%) were the least frequent antidepressants.
Chon et al., 2017 <sup>29</sup>	To investigate the extent and pattern of antidepressant prescription for	Population-based study n=2,190	Depressive disorder was more prevalent in the adolescent age group (age 13–18 years).  Escitalopram (24.1%) and fluoxetine (20.5%) were the two most frequently prescribed

	Korean children and adolescents.	age: 6-18years (Subjects who had received any antidepressant medication in the year 2013)	drugs followed by imipramine (13.2%), sertraline (10.3%), amitriptyline (9.1%), and tianeptine (5.6%).
Kehinde et al., 2017 <sup>30</sup>	To evaluate the drug utilization patterns of antidepressants in the tertiary care hospital in Lagos.	Retrospective study n=683 age: ≥18 years (January 2013 to December 2014)	Most prevalent age group:31-45 67.2% were females. Married (57%) and self-employed (49.7%) patients have more incidents of depression. Among the antidepressants prescribed, 61.3% were TCAs while 38.7% were accounted for by SSRIs. Amitriptyline (TCA) and sertraline (SSRI) were the most frequently prescribed antidepressants (60.6% and 20.2% respectively).
Soh et al., 2015 <sup>31</sup>	To investigate the prescribing patterns of antidepressants for depressive disorder in a psychiatric department of a general hospital in Singapore.	Retrospective study n=206 age: ≥18 years (January 2013 to December 2013)	Mean age: 50 years Females: 63.6% The majority of the patients were: married (70.9%), highly educated (46.1% had tertiary education) and full-time employees (60.2%). Prescribed antidepressants: SSRIs (75.5%), followed by atypical antidepressants (13.5%) and TCAs (8.5%).
Chen et al., 2015 <sup>32</sup>	To investigate the prevalence and prescription of antidepressants in depression in Asia.	Cross-sectional study n=956 age: ≥18 years	Mean age: 45.2 years The majority of the female were prescribed antidepressants. The most commonly used antidepressants were sertraline (19.6%), escitalopram (18.6%), and mirtazapine (16.1%). SSRIs were the most commonly prescribed type (67.4%), followed by SNRIs (17.1%) and atypical type (16.1%).
Trifiro et al., 2013 <sup>33</sup>	To evaluate the prescribing pattern of AD use in Italian primary care in recent years.	A prospective, observational cohort study n=1,377 age: ≥18 years (1 January 2007 to 1 June 2008)	Mean age: 52 years Most of the antidepressant users were of age group: 45-64 years More were females (71.5%), homemakers (31.1 %), married or cohabiting (60.4 %), with a high level of education (44.2 %), current or former smokers and alcohol consumers and obese (53.5 %) and lack of physical activity. Most frequently prescribed drug: SSRIs (paroxetine 25.9% and escitalopram 18.4%),

			SNRIs (venlafaxine 11.6% and duloxetine 5.6%) (80.2%) and TCA 2%.
Alhulwah et al., 2011 <sup>34</sup>	To ascertain the long-time presenting patients on antidepressants at Riyadh Military Hospital.	Cross-sectional study n= 120  age: ≥18 years  (July 2009 to September 2010)	Female: 57.5%  Mean age: 42 years (46% of the patients were between 35-50 years old)  SSRI was started in 61.7% patients, an atypical antidepressant (Mirtazapine) on 14.2%, and 11.7% on TCA on 11.7%.
Shiroma et al., 2011 <sup>35</sup>	To determine the antidepressant prescription pattern in the hospice program.	Retrospective cohort study n=17  age: ≥18 years  (June 2007, and December 2008)	Most users were female. SSRIs were the most commonly prescribed antidepressants (n=9) in depression than TCAs (n=1).
Prukkanone et al., 2010 <sup>36</sup>	To measure adherence and to determine the pattern of antidepressant prescriptions for the treatment of major depression.	Retrospective study, n=1,058  age: ≥18 years  (patient treated between August 2005 and September 2008)	Female: 64%  Average age: 46 years (age range of 15-86 years)  Commonly prescribed drug: fluoxetine (in two-thirds of patients) and TCAs being the next followed by other drugs and other SSRIs.
Bauer et al., 2008 <sup>37</sup>	To determine the current prescribing patterns of Antidepressants in European countries.	Prospective, observational study  n=3,468  age: ≥ 8 years  (May 2004 to September 2005)	Mean age of the patient: 46.8 year  More females (68.2%) involved.  Married, less educated, unemployed, and those in paid work and smokers were more likely to be prescribed with antidepressants.  SSRIs (63.3%) were the most commonly prescribed antidepressant followed by TCAs (26.5%) and SNRIs (13.6%).
Beck et al., 2005 <sup>38</sup>	To characterize antidepressant utilization in Canada, including	Cross-sectional survey n=2,145	The majority of antidepressant users were: age group (25-64) years female, married, lowest income group, and people with higher education.

	the relationships of antidepressant use with sociodemographic variables.	age: $\geq 15$ years (May-December 2002)	
Meijer et al., 2001 <sup>39</sup>	To observe prescribing patterns in patients using new antidepressants.	<p>Observational cohort study</p> <p>n=1,251</p> <p>age: <math>\geq 18</math> years (1995-1997)</p>	<p>49 (35.9%) were male and 802 (64.1%) female.</p> <p>Sertraline was used by 659 patients (52.7%), 390 patients (31.2%) used paroxetine, 115 patients (9.2%) used fluoxetine and 87 patients (7.0%) used clomipramine. The gender distribution was similar in all treatment groups. The majority (59.0%) of patients were under 45 years of age.</p> <p>The median age was 41 years (s.d. 18 years)</p> <p>49 (35.9%) were male and 802 (64.1%) female.</p> <p>Sertraline was used by 659 patients (52.7%), 390 patients (31.2%) used paroxetine, 115 patients (9.2%) used fluoxetine and 87 patients (7.0%) used clomipramine. The gender distribution was similar in all treatment groups. The majority (59.0%) of patients were under 45 years of age.</p> <p>The median age was 41 years (s.d. 18 years)</p> <p>49 (35.9%) were male and 802 (64.1%) female.</p> <p>Sertraline was used by 659 patients (52.7%), 390 patients (31.2%) used paroxetine, 115 patients (9.2%) used fluoxetine and 87 patients (7.0%) used clomipramine. The gender distribution was similar in all treatment groups. The majority (59.0%) of patients were under 45 years of age.</p> <p>The median age was 41 years (s.d. 18 years)</p> <p>49 (35.9%) were male and 802 (64.1%) female.</p>

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## Discussion

We identified fifteen studies through this review, and the majority of the patients were in the economically productive age group of 40-50 years<sup>25-32, 34-39</sup>, whereas in the result of a study on antidepressant use in Italy, the mean age of the patients who received antidepressant prescriptions was more than 50 years<sup>33</sup>. Our review showed that the majority of the patients receiving antidepressants for the treatment of their depression were females<sup>27, 30-43</sup>. This could be due to hormones that are associated with the regulation of the menstruation cycle and pregnancy affecting mood in females. These alterations in hormonal regulation cause dysregulation of the stress response, which makes them more sensitive to developing depression and often shows magnified neuroendocrine responses to even low levels of stress<sup>30, 40, 41, 44</sup>. Women play multiple roles in family and society, such as homemakers, spouses, mothers, professionals, and caregivers. These multiple responsibilities may be the source of increased stress that might have led to depression in them<sup>45, 46</sup>. In many societies, until today women are not given equal respect, they are thoughtless powerful with low status, they cannot make a choice, and they are sexually abused, which all results in the development of depression in them<sup>5, 44</sup>. In contrast to our findings, one study reported more depressive males than females, which could be due to more stress at work, a monotonous lifestyle, and lack of entertainment, low income, and economic burden of family<sup>26</sup>. Our review suggests that

depression is associated with various psychological factors, such as loneliness, lack of family care and affection, poor family support, insufficient time with children, high use of emotional coping, low level of spirituality, stressful incidents, poor health, and dependency<sup>26, 40</sup>. Sedentary lifestyle, lack of physical exercise, lack of hobby, irregular dietary habits, smoking, and taking alcoholic beverages or substance use are also interconnected with depression<sup>26, 32, 37</sup>. Continuous arguments, stressful daily routines, unsupportive spouses, continuous discouragement, lack of family time or husbands or wives going to other countries for employment, and ignorance from family members may be the reason for more married, housewives, and lower-income people being vulnerable to depression<sup>26, 27, 30, 31, 33, 37, 38, 47</sup>. One study<sup>48</sup> showed that a spouse's weekly working hours are greatly associated with the partner's risk of developing depression and suicidal thoughts. This means that long working hours not only affect individuals' own mental health but also affect their spouses<sup>48</sup>. Unsatisfactory job, lower income, level of physical activity, lack of encouragement, job demands, time pressure, promotion, and job security, all of which make an individual lose their confidence; hence, could be the reason for taking antidepressants by a high number of employees involved in paid work<sup>26, 31, 37</sup>. Similarly, being concerned about more profit or suffering a continuous loss in their business may also lead to depression in people involved in self-employed business<sup>30</sup>. Our review showed that education is another source of depression in many people. Highly educated people become depressed because of not getting their level of work, no place to implement their knowledge and skills in their jobs, more workload but low paid jobs, challenges with high competition in jobs, and lack of growth in the particular job<sup>26, 31, 33, 38</sup>. However, other studies have displayed less educated people as victims of depression<sup>27, 37</sup>. These people work as machine operators, laborers, farmers, and unskilled manual workers, where there is more physical and psychological related stress along with less respect from other employees. The prescribing pattern of antidepressants for patients with depression varies across different countries. This could be due to differences in availability and antidepressant prices as well as variations in recommendations in each country's national guidelines<sup>30, 38</sup>. Medical treatment of depression not only improves the mental health of patients but also increases their physical and social performance, making them optimistic and encouraged towards life<sup>34</sup>. Our review revealed that SSRIs are the dominant antidepressants prescribed over TCAs, SNRIs, and other atypical antidepressants for the treatment of depression<sup>25-29, 31-39</sup>. The frequent use of SSRIs could be because of the advantages they offer. Antidepressants other than SSRIs nonselectively inhibit the reuptake of norepinephrine, dopamine, and serotonin into presynaptic vesicles and affect adrenergic, cholinergic, postsynaptic serotonin, and histaminic receptors in the brain, which are unrelated to depression, leading to intolerable adverse effects<sup>49</sup>. SSRIs do not cause life-threatening adverse effects, such as overdose-related cardiotoxicity and CNS toxicity, as they do not have receptor antagonism<sup>50</sup>. Additionally, they can be administered once daily, require less dose titration than TCAs, are safer, and show fewer side effects compared to other antidepressants<sup>28, 33, 35-37, 51</sup>. Hence, it could be safer for many patients. In contrast, a study<sup>30</sup> showed that TCAs are most commonly prescribed despite SSRIs being more advantageous, which could be due to the affordability and easy availability of TCAs over SSRIs. In developing countries, the affordability of drugs plays an important role, where not all people can buy expensive medicines. Many have to rely on government insurance policies to obtain drugs for their

treatment. Many people buy antidepressants from the hospital since they are available at cheaper prices than in retail pharmacies. Such regional differences in the use of antidepressants may also contribute to differences in culture, promotional activity, and national income<sup>52, 53</sup>. Our review showed that sertraline was the most frequently used SSRI, followed by others such as escitalopram, fluoxetine, paroxetine, and fluvoxamine. Amitriptyline is commonly used among TCAs, venlafaxine, and duloxetine among SNRIs and mirtazapine, and bupropion among atypical antidepressants.

## Conclusion

Our study revealed that the majority of antidepressant users were aged 40-50 years, mostly females, married, housewives, lower-income, and highly educated. SSRIs were found to be highly prescribed antidepressants over TCAs, SNRIs, MAOIs, and atypical antidepressants. Among the prescribed SSRIs, sertraline was the dominant SSRI. Physicians who treat patients with depression should have sufficient knowledge of the safety and effectiveness of available medications and should be updated with newer treatment strategies.

## Declarations

### ACKNOWLEDGMENTS

We acknowledge all the authors of the retrieved original articles and surveys.

### Conflicts of interest

The authors declare that they have no competing interests.

### Ethical approval and consent to participate

Not applicable.

### Availability of data and materials

Not applicable.

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