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# IMPACT ON SEXUAL FUNCTION IN PATIENTS WITH DEPRESSIVE DISORDERS TREATED WITH ANTIDEPRESSANTS

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**Abstract:** The relationship between depression, its treatment and sexual dysfunction is complex. Sexual dysfunction has a high comorbidity with depression. Some aspects of sexual function, especially libido, may improve with successful treatment. However, some psychotropic drugs used to treat psychological problems such as depression and anxiety can induce sexual dysfunction, especially delayed ejaculation. However, this review aims to highlight this process, as it subsidizes the development of more effective actions and treatments aimed at communities. In this context, the aim of this study was to compile the literature on the impact of sexual function in men with depression who use antidepressants, in order to elucidate risk factors and possible interventions. The survey of articles was carried out in the following databases: Medline/BVS and Medline/ Pubmed. The following descriptors and their combinations in Portuguese and English were used to search for articles: "Antidepressants AND Sexual function AND Men AND Depression // Antidepressants AND Sexual function AND Men AND Depression". This finding validates the study and confirms that a duration of 5 weeks is sufficient to observe differences in antidepressant-related changes in sexual function. References 1-3 demonstrate the association of antidepressant use with interfering with sexual function in men with depression or another psychiatric disorder. Only in article 4, it shows that there is no impact on sexual function between men who received the treatment with those who did not. This review corroborates that there is an impact on the sexual function of patients who use antidepressants to treat depressive disorder and generalized anxiety disorder. However, the drugs that had a direct influence on sexual dysfunction were paroxetine, fluoxetine and sertraline, although Trazodone and Mirtazapine were shown to be protective

factors during the 6-month follow-up.
**Keywords:** Sexual function; Antidepressant; Depression.

## INTRODUCTION

Major depressive disorder (MDD) causes severe distress and dysfunction. It is a disorder characterized by depressed mood and/or loss of interest or pleasure, along with other symptoms such as psychomotor changes, appetite, sleep, and fatigue, as well as recurrent stories about excessive guilt, worthlessness, death, and cognitive difficulties associated with thinking and taking attention. of decision. Given the almost daily occurrence of these symptoms, the consequences are serious suffering that affect all circumstances of an individual's life. (OTTE et al., 2016)

The relationship between depression, its treatment and sexual dysfunction is complex. Sexual dysfunction has a high comorbidity with depression. Some aspects of sexual function, especially libido, may improve with successful treatment. However, some psychotropic drugs used to treat psychological problems such as depression and anxiety can induce sexual dysfunction, especially delayed ejaculation. (SEGRAVES; BALON, 2014)

In the foreground, one of the causes of erectile dysfunction is related to psychosocial factors, psychiatric disorders, among others, in addition to the use of some psychotropic medications to treat depression. (MAKHLOUF; KPARKER; NIEDERBERGER, 2007). According to the WHO (World Health Organization), about 5.8% of the Brazilian population suffers from depression, 11.5 million cases in all. The rate is highest in Latin America and the second highest in the Americas, after the United States, which recorded 5.9% of the affected population and 17.4 million cases. In addition to Brazil and the United States, countries such as Ukraine, Australia and Estonia also have high rates of depression in their populations – 6.3%, 5.9% and 5.9%, respectively, the survey showed. The countries with the lowest prevalence were Solomon Islands (2.9%) and Guatemala (3.7%). According to the World Health Organization, the prevalence of the world population is 4.4%. (BRASIL, 2022).

Recently, research on the mental health of the general population is at the heart. However, this review aims to highlight this process, as it subsidizes the development of more effective actions and treatments aimed at communities. In this context, the aim of this study was to compile the literature on the impact of sexual function in men with depression who use antidepressants, in order to elucidate risk factors and possible interventions.

## METHODOLOGY

This is an integrative review study that was designed based on the criteria established in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guide, considering the flow diagram and the PRISMA checklist. Thus, based on the guiding question: "Which antidepressants interfere with sexual function in men with depression?" the articles were searched.

Keywords were defined according to the PICOS model as follows:

1. Population: men with major depressive disorder;
2. Intervention: treatment with antidepressants;
3. Comparative: control (absence or placebo);
4. Results (variables): impact of sexual function related to the use of antidepressants for the treatment of MDD;
5. Study design: clinical trial and observational studies.

### LITERATURE SEARCH

The survey of articles was carried out in

the following databases: Medline/BVS and Medline/Pubmed. The following descriptors and their combinations in Portuguese and English were used to search for articles: "Antidepressants AND Sexual function AND Men AND Depression // Antidepressants AND Sexual function AND Men AND Depression".

### INCLUSION AND EXCLUSION CRITERIA

The selection of articles was guided by inclusion and exclusion criteria. The inclusion criteria defined for the selection of articles were: articles published in Portuguese, English; original articles in full that portray the theme related to the review and articles published and indexed in the aforementioned databases in the last 10 years.

The exclusion criteria defined for the selection of articles were non-original articles, dissertations and theses, articles that addressed the subject, but from a different point of view.

After applying the inclusion and exclusion criteria, the articles were identified. The screening of studies was carried out by reading and analyzing the titles and abstracts of all articles identified in each database, guided by the adopted inclusion and exclusion criteria. In the eligibility phase, after defining the articles to be included in each database, duplicate articles were excluded.

## RESULTS

### SELECTION OF STUDIES

A total of 153 studies were identified according to our search strategy. Among them, no duplicate article was presented. After applying the adopted inclusion and exclusion criteria, a total of 140 studies in Medline/Pubmed were excluded. Then the titles, abstracts and the full text were read, 9 of the 13 references were excluded based on the eligibility criteria. Thus, 4 references were selected for full text evaluation. Finally, four articles were eligible for qualitative evaluation. The selection process for identifying eligible studies is included in the review, shown in Figure 1.

### CHARACTERISTICS OF INCLUDED STUDIES AND ANALYSIS OF SEXUAL FUNCTION RELATED TO ANTIDEPRESSANT USE

The main characteristics of the included studies are presented in Chart 1. In the article by Habibolah Khazaie from 2015, the sample of N = 195 patients, the mean gender and age group respectively: 93 women (48%) and 102 men (52%), with a mean age of 38 and a standard deviation of ± 12. Tange, when comparing interventions with two classes of antidepressants (SSRIs and SARIs), our results suggest that SSRIs are associated with more sexual side effects. Thus, the two SSRIS drugs, fluoxetine and sertraline, were associated with more impaired sexual dysfunction items in undertreated patients, while trazodone was associated with improvement.

In the 2018 study by Sinha Preeti, the sample of N = 209 patients, the mean gender and age group respectively: 123 women (59%) and 86 men (41%), with a mean age ± standard deviation (SD) of 36.5 ± 12.7 years. Concerning antidepressant-related sexual function, it was found to be impaired with sertraline (50-150 mg/day) and fluoxetine (20-60 mg/day) was evident as early as the second week. For sertraline, it did not get much worse after that, whereas for fluoxetine sexual dysfunction continued to increase up to 6 weeks. Thus, among patients with anxiety or depression, the risk of antidepressant-induced sexual dysfunction at 6 weeks was lower when the drug dose was initially lower and gradually increased. Mirtazapine has been associated with favorable sexual outcomes, while fluoxetine was associated

with impaired sexual outcomes. Baseline dysfunction was independently associated with impaired sexual function. Men may be more likely than women to experience impaired sexual outcomes. For patients with baseline linear dysfunction, the prescription drug mirtazapine may be the first choice, while fluoxetine must be avoided, especially when dose escalation is planned.

Regarding Paula Jacobsen, the sample of N = 361 patients, the mean gender and age group respectively: 123 women (49%) and 185 men (51%), with a mean age of 28.4 years ranging from 18 to 40 years with normal sexual functioning. Regarding the intervention, administered to healthy volunteers, vortioxetine 10 mg QD was associated with a statistically lower TESD compared with paroxetine 20 mg QD. Vortioxetine 20 mg was also associated with fewer TESDs compared with paroxetine, but the difference did not reach statistical significance. Furthermore, no significant TESD was observed with vortioxetine dose compared to placebo, while paroxetine was significantly worse than placebo.

According to Laforgue, the sample of N = 70 patients were included, it is evident that the patients were between 31 and 50 years old, one in five was between 51 and 65 years old and about 10% were between 18 and 29 years old. Of the groups it appears, 8% of euthymic patients had sexual dysfunction (mean ASEX score = 12.4) compared with 56% of untreated patients (mean ASEX total score = 17.7) and 62% (34/55) de The patient has sexual dysfunction. Treated patients (mean total ASEX score = 18.5) ($P < 0.001$). Sexual function in treated men was not significantly different from men who did not receive antidepressants, although those who received antidepressants reported that their mood was better than those who did not receive antidepressants.

The results showed that in the studies selected from the inclusion and exclusion criteria. References 1-2 demonstrate the association of antidepressant use with interfering sexual function in men with depression or another psychiatric disorder. Only in article 3 does it show that there is no impact on sexual function between men who received the treatment and those who did not.

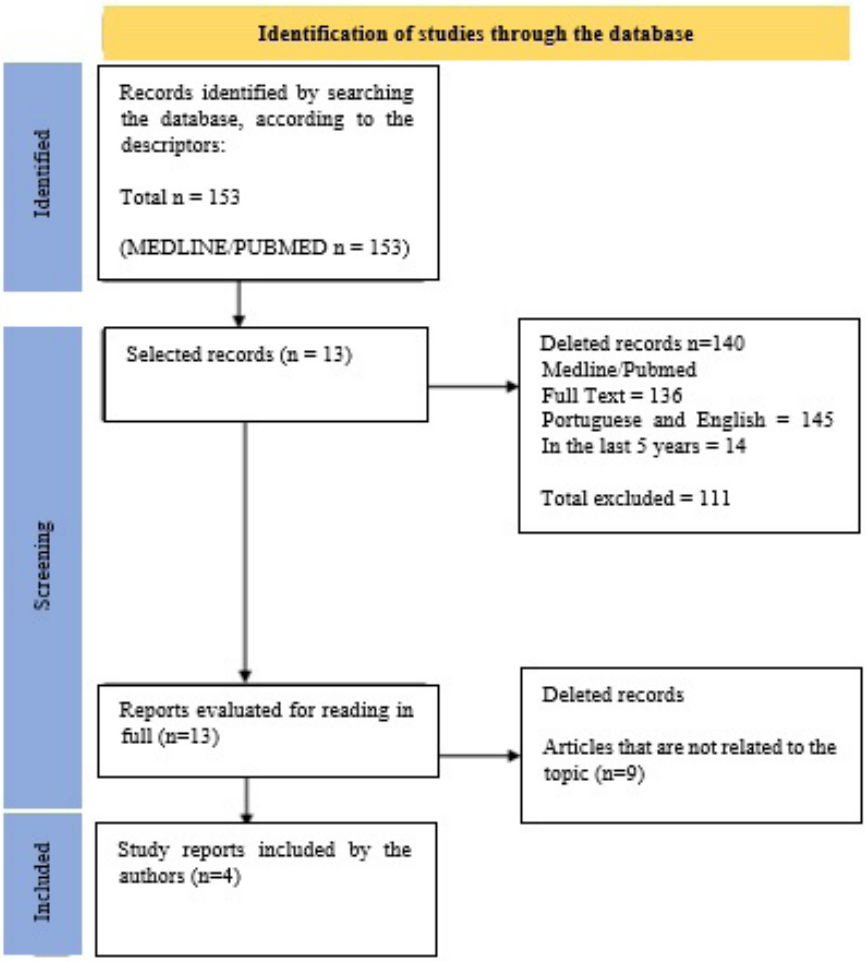


Figure 1:Flowchart for selection process, identification, screening, eligibility and included.

| N° | Title/Author | publication year | Study design | Goals | Methodology | Main results |
|---|---|---|---|---|---|---|
| 1 | Antidepressant-induced sexual dysfunction during treatment with fluoxetine, sertraline, and trazodone; a randomized controlled trial / Habibolah Khazaie | 2015 | clinical trial | Objective was to evaluate sexual dysfunction in patients with MDD who received fluoxetine, sertraline and trazodone. | In a randomized, single-blind, controlled trial in Kermanshah, Iran, during 2009-2010, 195 patients who met DSMIV-IR criteria for MDD were enrolled. Patients completed the Hamilton Depression Rating Scale (HAM-D) and sexual function questionnaire. (SFQ) | There were 102 men and 93 women in the three groups that received fluoxetine (n=64), sertraline (n=67) and trazodone (n=64). There was no significant difference in the sexual dysfunction of patients in the three groups at baseline (Ph.05). |
| 2 | Sexual Dysfunction in Patients with Anxiety or Depressive Disorders Treated with Antidepressants: A Pragmatic Multivariate Longitudinal Study / S. Preeti | 2018 | observational study | To investigate the early course, tolerability and predictors of emergent sexual dysfunction of antidepressants in patients with anxiety or depressive disorder. | Patients with anxiety or depressive disorders who received monotherapy with antidepressants (mirtazapine, sertraline, desvenlafaxine, escitalopram or fluoxetine) at the discretion of the attending physician were recruited from July 2012 to June 2014 in a hospital outpatient clinic. All were free of psychotropic medication for at least 1 month. | Of the 230 patients recruited, 209 were assessed at baseline, of whom 184 were assessed at week 2; of these, 154 were also evaluated at week 6. At baseline, 138 (66%) of 209 patients were diagnosed with depressive disorder and 71 (34%) with anxiety disorder; 29% of patients had sexual dysfunction (in any domain of the PRSexDQ). |

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|---|---|---|---|---|---|---|
| 3 | Paroxetine, but not vortioxetine, impairs sexual functioning compared with placebo in healthy adults: a randomized controlled trial / Paula Jacobsen | 2019 | clinical trial | To assess sexual functioning in healthy volunteers given vortioxetine compared to paroxetine, an antidepressant known to cause sexual dysfunction, and placebo | This phase 4, multicenter, randomized, double-blind, placebo-controlled, 4-arm fixed-dose, direct study compared sexual functioning in healthy volunteers administered vortioxetine (10 and 20 mg once daily [QD]), paroxetine (20 mg QD) or placebo for 5 weeks. | Of the 361 enrolled subjects (mean age 28.4 years), approximately 57% were white, 34% black/African-American, and 4% Asian. Vortioxetine 10 mg was associated with significantly less TESD than paroxetine (mean difference, +2.74 points; P = 0.009). Although vortioxetine 20 mg was numerically associated with less TESD than paroxetine (mean difference, +1.05 points), the difference did not reach statistical significance. |
| 4 | Evolution of men's sexual functioning through treated and untreated depression / E-J Laforque | 2022 | clinical trial | The main objective of the SADD study (for sexuality, antidepressants and depression) is to evaluate sexual dysfunctions in depressed men treated or not with antidepressants. | Participants in this cross-sectional observational study were men aged over 18 years, with unipolar major depressive disorder and treated by a psychiatrist, with or without antidepressants. | Seventy patients were included. Eight percent of euthymic patients had sexual dysfunction (mean ASEX score=12.4), while 56% of untreated patients had sexual dysfunction (mean ASEX total score=17.7) and 62% (34/55) of patients treated with antidepressants (mean ASEX total score=18,5) (P<0.001). |

Table 1: Description of the articles selected with the variables: Title of study/Author, year of publication, objectives, methodology and main results.

## CONCLUSION

This review corroborates that there is an impact on the sexual function of patients who use antidepressants to treat depressive disorder and generalized anxiety disorder. However, the drugs that had a direct influence on sexual dysfunction were paroxetine, fluoxetine and sertraline, although Trazodone and Mirtazapine were shown to be protective factors during the 6-month follow-up. Therefore, the risk factors associated with this class of drugs need to be investigated more closely in order to obtain a possible effective intervention.

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