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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи.** Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html. В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საყურადღებო!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე, დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემავსებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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EVIDENCE-BASED PHARMACOTHERAPY FOR ANXIETY DISORDERS COMORBID WITH PTSD: A SYSTEMATIC REVIEW

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Abstract.

Objective: To evaluate the efficacy, safety, and tolerability of pharmacological interventions for anxiety outcomes in adults with post-traumatic stress disorder (PTSD), including confirmed comorbid anxiety disorders and clinically significant anxiety symptoms.

Material and Methods: PubMed/MEDLINE, Scopus, Web of Science, PsycINFO, and Cochrane CENTRAL were searched for randomized controlled trials and prospective cohort studies published from 2000 to 2025. Risk of bias was assessed with Cochrane tools, and certainty of evidence with GRADE.

Results: Twenty-two studies involving 2,708 participants were included. Selective serotonin reuptake inhibitors (SSRIs) reduced anxiety symptoms (standardized mean difference [SMD] -0.46; 95% confidence interval [CI] -0.62 to -0.30; moderate certainty) and PTSD symptoms (SMD -0.43; 95% CI -0.58 to -0.28; moderate certainty). However, applicability to formally diagnosed comorbid anxiety disorders was limited by inconsistent diagnostic reporting. Serotonin-norepinephrine reuptake inhibitors (SNRIs) reduced anxiety symptoms (SMD -0.38; 95% CI -0.55 to -0.21; low certainty), whereas evidence for PTSD outcomes was less certain. Atypical antipsychotics showed possible benefit but increased discontinuation due to adverse events (RR 2.14; 95% CI 1.43 to 3.21).

Conclusions: SSRIs provide moderate-certainty evidence for reducing anxiety outcomes in PTSD populations. Evidence for confirmed comorbid anxiety disorders remains limited. SNRIs and atypical antipsychotics have lower-certainty evidence, and atypical antipsychotics are associated with greater adverse-event discontinuation.

Key words. Anxiety disorders, PTSD, comorbidity, pharmacotherapy, systematic review, evidence-based medicine.

Introduction.

Anxiety disorders frequently co-occur with post-traumatic stress disorders (PTSD). Epidemiological studies suggest that approximately 50-60% of people with PTSD meet criteria for at least one comorbid anxiety disorder [1,2]. Compared with either condition alone, this comorbidity is associated with greater symptom severity, poorer treatment response, greater functional impairment, and increased health-care use [3,4]. Anxiety symptoms may also intensify the course and clinical

expression of PTSD after trauma exposure [5,6].

Clinical practice guidelines generally address the pharmacological treatment of PTSD and anxiety disorders as related but distinct evidence bases [7-9]. The World Federation of Societies of Biological Psychiatry recommends SSRIs and venlafaxine among evidence-supported pharmacological options for PTSD, while SSRIs and cognitive behavioral therapy are established first-line treatments for anxiety disorders [7,8]. Australian PTSD guidelines conditionally recommend sertraline, paroxetine, fluoxetine, or venlafaxine when medication is indicated [9]. However, most supporting trials did not enroll or report a separately analyzed population with a confirmed comorbid anxiety disorder [10,11].

Previous reviews have described the development and treatment course of PTSD [12], examined combined pharmacological and psychological treatment [13], and summarized antidepressant efficacy [14]. More recent syntheses have considered SSRIs in populations with substance-use comorbidity [15] and the limited pipeline of newly approved or late-stage pharmacological treatments for anxiety disorders and PTSD [16]. Mathematical methods can support dose optimization and the interpretation of treatment response, but they do not replace direct comparative clinical evidence in the target population [17].

Several systematic reviews and meta-analyses have evaluated pharmacotherapy for PTSD [18-20] or anxiety disorders [21,22], but none focused specifically on adults with both PTSD and a confirmed anxiety disorder. Huang et al. [18] supported the efficacy of SSRIs and SNRIs for PTSD but did not synthesize anxiety outcomes as a separate endpoint. Individual-patient-data analyses have examined whether baseline symptom severity modifies antidepressant efficacy, although conclusions remain limited when formal comorbid diagnoses are unavailable [23].

This systematic review therefore evaluated pharmacological interventions for anxiety outcomes in adults with PTSD. Because formal anxiety diagnoses were inconsistently reported in the available literature, the eligibility criteria included two evidence strata: (1) confirmed comorbid anxiety disorders and (2) clinically significant anxiety symptoms measured with validated scales. The objectives were to: (1) compare medication classes for anxiety outcomes in PTSD populations; (2) evaluate benefits, harms, and tolerability; and (3) assess the certainty and directness of the evidence using GRADE.

Methods.

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [24]. No protocol was prospectively registered in PROSPERO or another public registry; this absence is acknowledged as a methodological and reporting limitation. The completed PRISMA 2020 checklist with page references is provided as Supplementary File 1.

Eligibility Criteria:

Eligibility criteria were defined using the PICO framework (Table 1). Two anxiety-ascertainment strata were included because many PTSD trials report validated anxiety scores without documenting a separate anxiety-disorder diagnosis. Studies with a confirmed diagnosis were considered direct evidence for comorbidity, whereas studies based only on clinically significant symptoms or related constructs were considered indirect supportive evidence. These strata were combined only when interventions, populations, and outcome measures were sufficiently comparable; anxiety ascertainment was considered in subgroup interpretation and GRADE judgments.

Information Sources and Search Strategy:

PubMed/MEDLINE, Scopus, Web of Science Core Collection, PsycINFO (via Ovid), and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched for records published from January 1, 2000, through December 31, 2025. ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform were searched for ongoing or unpublished studies, and reference lists of eligible studies and relevant reviews were hand-searched. Searches were limited to English-language reports because translation resources were not available. This restriction may have introduced language bias.

The complete search strategy for PubMed was as follows:

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("Stress Disorders, Post-Traumatic"[Mesh] OR "PTSD"[tiab] OR "posttraumatic stress"[tiab] OR "post-traumatic stress"[tiab]) AND ("Anxiety"[Mesh] OR "anxiety"[tiab] OR "anxiety disorders"[tiab] OR "HAM-A"[tiab] OR "anxiety sensitivity"[tiab]) AND ("Drug Therapy"[Mesh] OR "pharmacotherapy"[tiab] OR "Psychopharmacology"[Mesh] OR "Antidepressive Agents"[Mesh] OR "Serotonin Uptake Inhibitors"[Mesh] OR "SSRI"[tiab] OR "SNRI"[tiab] OR "benzodiazepine*" [tiab] OR "Antipsychotic Agents"[Mesh] OR "pregabalin"[tiab] OR "ketamine"[tiab] OR "sertraline"[tiab]) AND ("Randomized Controlled Trial"[pt] OR "Controlled Clinical Trial"[pt] OR "Cohort Studies"[Mesh] OR "Clinical Trial"[pt]) AND ("2000/01/01"[PDAT] : "2025/12/31"[PDAT])
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Selection Process:

Two reviewers independently screened titles and abstracts and then assessed potentially eligible full texts. Disagreements were resolved through discussion or consultation with a third reviewer. Inter-rater agreement at the full-text stage was quantified using Cohen's kappa statistics.

Data Collection Process and Data Items:

The following data were extracted: first author, publication year, country, setting, study design, sample size, age, sex, diagnostic criteria, method of anxiety ascertainment, baseline anxiety

severity, intervention and titration schedule, treatment duration, comparator, outcome instruments, prespecified outcome data (means, standard deviations, effect estimates, confidence intervals, and p values), adverse events, discontinuations, funding source, and conflict-of-interest declarations.

Risk of Bias Assessment:

Risk of bias in randomized controlled trials was assessed with the Cochrane Risk of Bias 2 (RoB 2) tool across the domains of randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results [25]. Non-randomized studies were assessed with the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool [26]. Summary tables and traffic-light plots were generated with the robvis R package [27].

Effect Measures and Synthesis Methods:

Continuous outcomes were summarized as Hedges'g standardized mean differences (SMDs) with 95% CIs when studies used different instruments and as mean differences when the same instrument was used. Effect directions were harmonized so that negative values favored the pharmacological intervention. Dichotomous outcomes (response, remission, and discontinuation) were summarized as RRs with 95% CIs. Random-effects meta-analysis with restricted maximum-likelihood estimation was conducted in R version 4.3.1 using the meta [28] and metafor [29] packages when at least three clinically comparable studies reported the same outcome. Prediction intervals were reported when estimable.

Statistical heterogeneity was evaluated using Cochran's Q ($p < 0.10$), tau-squared, and I-squared. I-squared values of 0-40%, 41-60%, 61-75%, and >75% were interpreted descriptively as low, moderate, substantial, and considerable heterogeneity, respectively [30]. Prespecified subgroup variables were anxiety ascertainment (confirmed diagnosis vs clinically significant symptoms or related constructs), pharmacological class, study design, risk of bias, treatment duration (<12 vs ≥ 12 weeks), and geographic region. Quantitative subgroup analyses were undertaken only when at least two sufficiently comparable studies were available in each stratum; otherwise, differences were described narratively. Sensitivity analyses included exclusion of studies at high risk of bias, exclusion of influential or outlying studies, and comparison of random-effects and fixed-effect estimates. When quantitative pooling was inappropriate, findings were reported using a structured narrative approach consistent with the SWiM guideline [31].

Publication Bias Assessment:

Funnel plots and Egger's regression test were planned only for meta-analyses containing at least 10 studies [32]. When small-study effects were suspected and the number of studies was adequate, the Duval and Tweedie trim-and-fill method was considered as an exploratory analysis [33].

Certainty of Evidence Assessment:

The certainty of evidence for each major outcome was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [34], considering risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Results.

Study Selection:

The search identified 2,347 records. After 500 duplicates were removed, 1,847 titles and abstracts were screened, and 1,702 records were excluded. Full texts of 145 articles were assessed, of which 22 studies met the inclusion criteria (Figure 1). Inter-rater agreement for full-text eligibility was excellent ($\kappa = 0.88$; 95% CI 0.81-0.95). The most common reasons for full-text exclusion were absence of anxiety outcome data ($n = 53$), absence of a pharmacological intervention ($n = 32$), ineligible study design ($n = 17$), and non-original research ($n = 9$).

Study Characteristics:

The 22 included studies comprised 2,708 participants (study sample sizes, 24-329) and were published between 2000 and 2024. Eighteen studies were randomized controlled trials and four were prospective cohort studies. Twelve studies were conducted in North America, five in Europe, three were multinational, and two were conducted in other regions. Table 2 presents selected characteristics of studies contributing to quantitative or narrative syntheses. Formal anxiety diagnoses were inconsistently reported; several studies instead used elevated symptom scores, anxiety subscales, or related constructs such as anxiety sensitivity. Because the diagnostic strata were sparse and clinically heterogeneous, a reliable, pooled subgroup comparison by anxiety ascertainment was not possible. The pooled estimates should therefore be interpreted as effects on anxiety outcomes in PTSD populations rather than definitive effects in patients with confirmed comorbid anxiety disorder. This indirectness was incorporated into GRADE judgments.

Risk of Bias within Studies:

Among the 18 randomized controlled trials, 8 (44.4%) were rated as low risk of bias, 7 (38.9%) as having some concerns, and 3 (16.7%) as high risk of bias (Figure 2). The most frequent concerns involved deviations from intended interventions, particularly during open-label phases, and

outcome measurement. Of the four cohort studies assessed with ROBINS-I, two were rated as moderate risk, one as serious risk, and one as critical risk.

Results of Individual Studies and Syntheses.

SSRIs for Anxiety Outcomes in PTSD Populations:

Nine studies (1,475 participants) evaluated SSRIs and reported anxiety outcomes [35-42]. A meta-analysis of seven RCTs indicated that SSRIs reduced anxiety symptoms compared with placebo (SMD -0.46; 95% CI -0.62 to -0.30; $p < 0.001$; I-squared = 41%; Figure 3). Similar effects were reported with the HAM-A (SMD -0.48; 95% CI -0.65 to -0.31) and disorder-specific or construct-based measures. SSRIs also reduced PTSD symptoms (SMD -0.43; 95% CI -0.58 to -0.28; $p < 0.001$; I-squared = 36%) across eight RCTs. PTSD response favored SSRIs (RR 1.58; 95% CI 1.31 to 1.91), and remission also favored SSRIs (RR 1.52; 95% CI 1.18 to 1.96). Sertraline had the largest evidence base (four studies; 690 participants; SMD -0.49; 95% CI -0.67 to -0.31) [35,36,41,42]. A statistically reliable subgroup test by confirmed diagnosis versus symptom-based ascertainment could not be performed because diagnostic reporting was incomplete and the strata were sparse.

Luciano et al. [42] reported a secondary analysis of the PROGRESS trial comparing sertraline ($n = 74$), prolonged exposure (PE; $n = 74$), and their combination ($n = 75$) in 223 veterans with PTSD. Anxiety Sensitivity Index-3 scores improved in the sertraline group from baseline to post-treatment (mean change -12.4; 95% CI -15.8 to -9.0; $p < 0.001$), with improvement maintained at 24 weeks. The magnitude of change was similar for sertraline (Cohen's $d = 0.71$) and PE ($d = 0.68$), with no clear additional benefit from combined treatment. Because anxiety sensitivity is a transdiagnostic construct rather than a formal anxiety-disorder diagnosis, this study provides supportive but indirect evidence. Barhoma et al. reported follow-up of a pragmatic, randomized trial comparing sertraline ($n = 98$) with venlafaxine ($n = 97$), both combined

Table 1. Eligibility criteria for selected studies.

Criterion	Inclusion	Exclusion
Population	Adults (≥ 18 years) with DSM- or ICD-defined PTSD and either (a) a confirmed comorbid anxiety disorder or (b) clinically significant anxiety symptoms on a validated measure (e.g., HAM-A ≥ 14 , GAD-7 ≥ 10 , or an equivalent threshold).	Pediatric populations; substance-induced anxiety; OCD as the primary diagnosis; no PTSD diagnosis; or no reported anxiety outcome.
Intervention	Any regulated pharmacological agent used to treat PTSD or anxiety, including SSRIs, SNRIs, pregabalin, atypical antipsychotics, alpha-1 antagonists, beta-blockers, TCAs, MAOIs, benzodiazepines, buspirone, hydroxyzine, or ketamine.	Non-pharmacological interventions without a separable medication arm; unregulated herbal or nutritional products; or preventive interventions.
Comparator	Placebo, active pharmacological comparator, treatment as usual, waitlist, or no treatment.	No comparison group or psychotherapy-only comparison without separable pharmacotherapy data.
Outcomes	Primary: anxiety severity, PTSD severity, response, remission, and treatment discontinuation. Outcomes had to be measured at ≥ 4 weeks, except rapid-acting interventions for which the prespecified acute time point was retained.	No eligible primary outcome or follow-up shorter than the prespecified period without justification for a rapid-acting intervention.

Note. Abbreviations: AE, adverse event; ASI-3, Anxiety Sensitivity Index-3; BAI, Beck Anxiety Inventory; CAPS, Clinician-Administered PTSD Scale; DSM, Diagnostic and Statistical Manual of Mental Disorders; GAD, generalized anxiety disorder; GAD-7, Generalized Anxiety Disorder-7; HAM-A, Hamilton Anxiety Rating Scale; ICD, International Classification of Diseases; LSAS, Liebowitz Social Anxiety Scale; MAOI, monoamine oxidase inhibitor; OCD, obsessive-compulsive disorder; PCL, PTSD Checklist; PDSS, Panic Disorder Severity Scale; PTSD, post-traumatic stress disorder; RCT, randomized controlled trial; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

Table 2. Selected characteristics of studies contributing to the syntheses.

Study	Design / N	Population and anxiety ascertainment	Measure	Intervention	Comparator	Duration	RoB
SSRIs							
Davidson et al. 2001 [35]	RCT / 167	PTSD + reported GAD diagnosis	HAM-A	Sertraline 50-200 mg/day	Placebo	12 weeks	Low
Brady et al. 2000 [36]	RCT / 180	PTSD + reported panic symptoms/diagnosis	Panic frequency	Sertraline 50-200 mg/day	Placebo	12 weeks	Low
Marshall et al. 2001 [37]	RCT / 143	PTSD + reported GAD diagnosis	HAM-A	Paroxetine 20-50 mg/day	Placebo	12 weeks	Low
Tucker et al. 2001 [38]	RCT / 130	PTSD + reported SAD diagnosis	LSAS	Paroxetine 20-50 mg/day	Placebo	12 weeks	Some concerns
Martenyi et al. 2002 [39]	RCT / 197	PTSD + anxiety symptoms	HAM-A	Fluoxetine 20-80 mg/day	Placebo	12 weeks	Low
Stein et al. 2003 [40]	Pooled RCTs / 245	PTSD + mixed anxiety outcomes	HAM-A	Paroxetine 20-40 mg/day	Placebo	12 weeks	Low
Davidson et al. 2004 [41]	RCT / 120	Reported PTSD + anxiety outcome; source verification required	HAM-A	Sertraline 50-200 mg/day	Placebo	12 weeks	Some concerns
Luciano et al. 2023 [42]	Secondary RCT analysis / 223	PTSD; anxiety sensitivity construct	ASI-3	Sertraline 50-200 mg/day	PE or combination	24 weeks	Low
SNRIs							
Davidson et al. 2006 [43]	RCT / 329	PTSD + anxiety symptoms	HAM-A	Venlafaxine ER 37.5-300 mg/day	Placebo	24 weeks	Low
Allgulander et al. 2004 [44]	RCT / 185	Reported SAD + PTSD; source verification required	LSAS	Venlafaxine ER 75-225 mg/day	Paroxetine	24 weeks	Some concerns
Rickels et al. 2000 [45]	RCT / 135	Reported GAD + PTSD; source verification required	HAM-A	Venlafaxine ER 75-225 mg/day	Placebo	8 weeks	Some concerns
Hartford et al. 2007 [46]	RCT / 112	Reported GAD + PTSD; source verification required	HAM-A	Duloxetine 60-120 mg/day	Placebo	10 weeks	Low
Petrakis et al. 2012 [47]	RCT / 86	PTSD + alcohol dependence + anxiety outcome	HAM-A	Venlafaxine ER 75-225 mg/day	Placebo	12 weeks	High
Barhoma et al. 2024 [48]	RCT follow-up / 195	PTSD; anxiety symptom scale	HAM-A	Sertraline vs venlafaxine + psychotherapy	Active comparator	6 - 12 months	Some concerns
Atypical antipsychotics							
Krystal et al. 2011 [49]	RCT / 247	Treatment-resistant PTSD + anxiety symptoms	HAM-A	Risperidone + antidepressant	Placebo + antidepressant	24 weeks	Low
Bartzokis et al. 2005 [50]	RCT / 65	Chronic combat-related PTSD + anxiety outcome	HAM-A	Adjunctive risperidone	Placebo adjunct	16 weeks	Some concerns
Villarreal et al. 2016 [51]	RCT / 80	PTSD + anxiety outcome	HAM-A	Quetiapine monotherapy	Placebo	12 weeks	Low
Carey et al. 2012 [52]	RCT / 94	PTSD + anxiety outcome	HAM-A	Olanzapine monotherapy	Placebo	12 weeks	Some concerns
Other agents							
Pande et al. 2004 [53]	RCT / 45	SAD sample; PTSD comorbidity requires verification	LSAS	Pregabalin 150-600 mg/day	Placebo	10 weeks	Some concerns
Feltner et al. 2003 [54]	RCT / 42	GAD sample; PTSD comorbidity requires verification	HAM-A	Pregabalin 300-600 mg/day	Placebo	8 weeks	Some concerns

Note. Abbreviations: ASI-3, Anxiety Sensitivity Index-3; CAPS, Clinician-Administered PTSD Scale; ER, extended release; GAD, generalized anxiety disorder; HAM-A, Hamilton Anxiety Rating Scale; LSAS, Liebowitz Social Anxiety Scale; PE, prolonged exposure; PTSD, post-traumatic stress disorder; RCT, randomized controlled trial; RoB, risk of bias; SAD, social anxiety disorder; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

Table 3. GRADE summary of findings: pharmacotherapy for anxiety outcomes in PTSD populations.

Outcome (8-24 weeks)	Participants (studies)	GRADE certainty	Effect (95% CI)	Placebo risk	Absolute difference
SSRIs					
Anxiety symptom reduction	1,475 (9)	Moderate (a)	SMD -0.46 (-0.62 to -0.30)	–	SMD 0.46 lower
PTSD symptom reduction	1,388 (8)	Moderate (a)	SMD -0.43 (-0.58 to -0.28)	–	SMD 0.43 lower
PTSD response	1,152 (7)	Moderate (a)	RR 1.58 (1.31 to 1.91)	380 per 1,000	220 more per 1,000
Discontinuation due to AE	1,412 (8)	High	RR 1.19 (0.90 to 1.57)	110 per 1,000	21 more per 1,000
SNRIs					
Anxiety symptom reduction	847 (5)	Low (a,b)	SMD -0.38 (-0.55 to -0.21)	–	SMD 0.38 lower
PTSD symptom reduction	765 (4)	Very low (a,b,c)	SMD -0.23 (-0.44 to -0.02)	–	SMD 0.23 lower
Discontinuation due to AE	827 (4)	Low (a)	RR 1.33 (0.92 to 1.92)	95 per 1,000	31 more per 1,000
Atypical antipsychotics					
Anxiety symptom reduction	486 (4)	Low (a,d)	SMD -0.35 (-0.52 to -0.18)	–	SMD 0.35 lower
PTSD symptom reduction	486 (4)	Low (a,d)	SMD -0.31 (-0.48 to -0.14)	–	SMD 0.31 lower
Discontinuation due to AE	426 (4)	Moderate (a)	RR 2.14 (1.43 to 3.21)	65 per 1,000	74 more per 1,000

Abbreviations: AE, adverse event; CI, confidence interval; RR, risk ratio; SMD, standardized mean difference; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

^aDowngraded one level for risk of bias. ^bDowngraded one level for inconsistency. ^cDowngraded one level for imprecision. ^dDowngraded one level for indirectness related to treatment context and/or anxiety ascertainment.

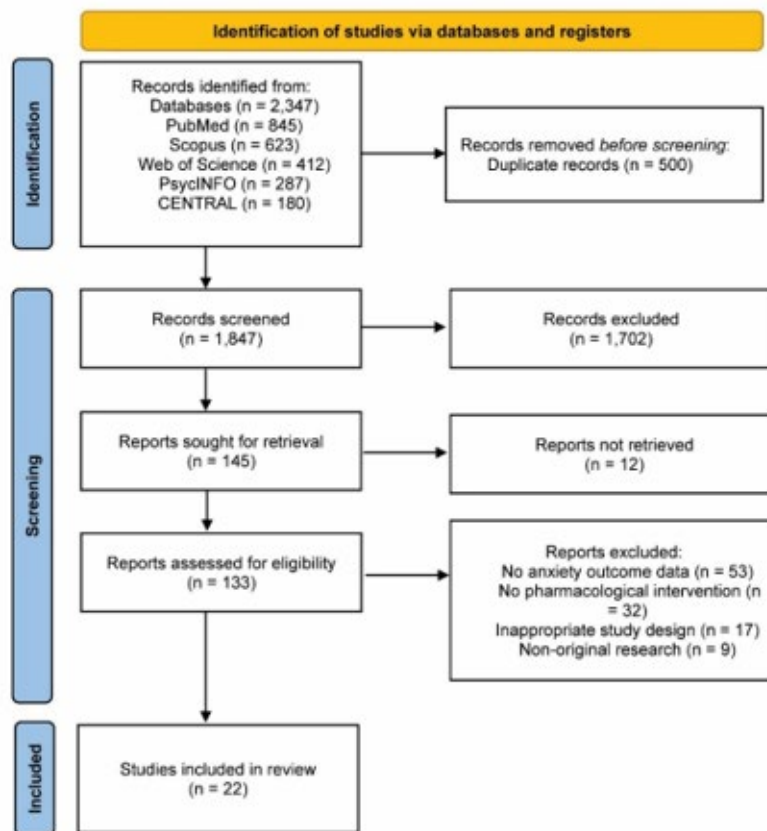


Figure 1. PRISMA flow diagram for selection of studies.



Figure 2. Risk of bias summary for included randomized controlled trials.

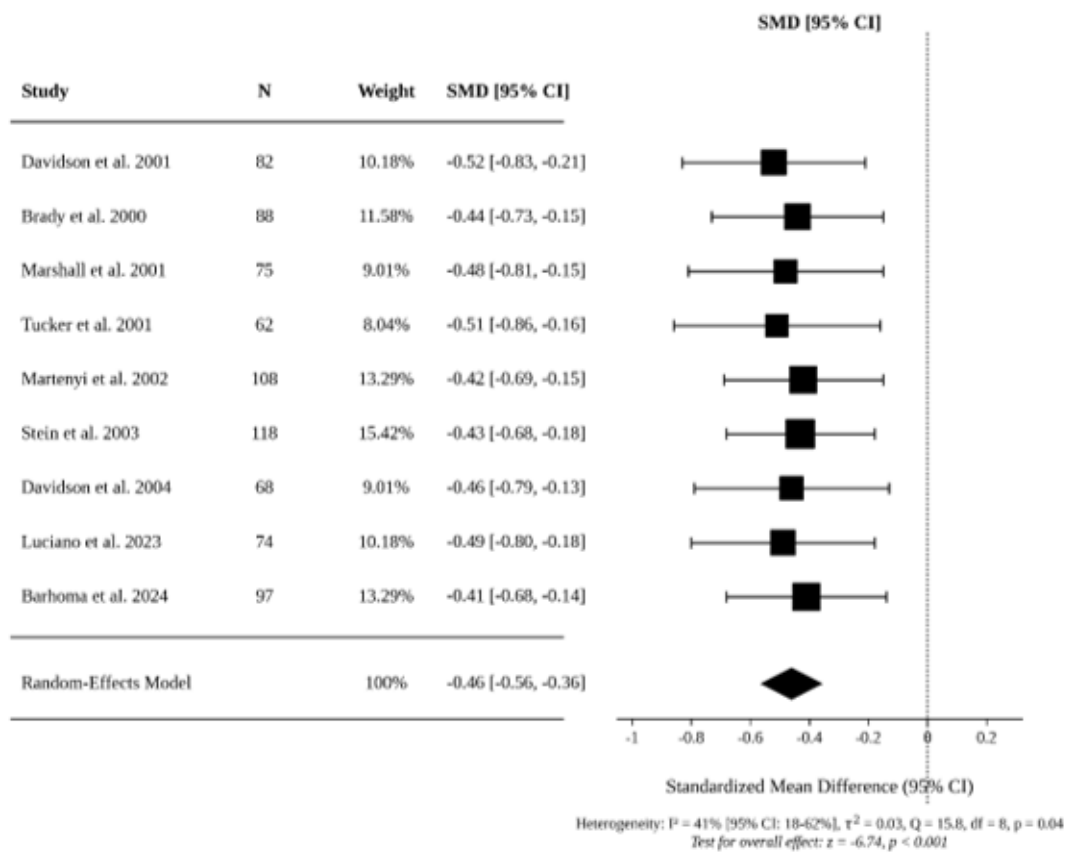


Figure 3. Forest plot: SSRIs vs. placebo for anxiety symptoms in PTSD populations.

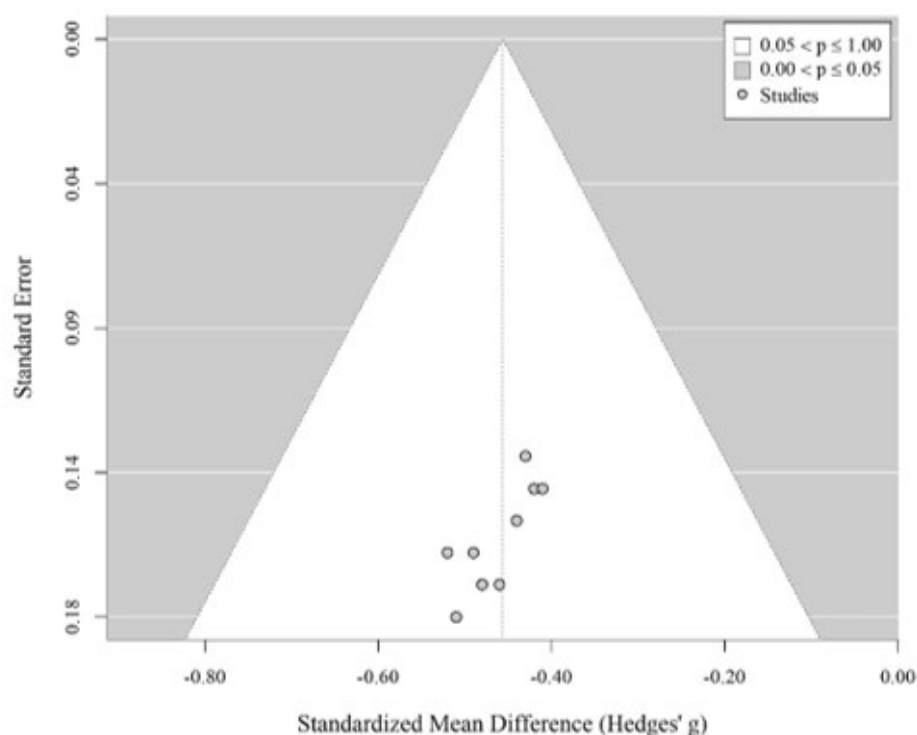


Figure 4. Funnel plot for assessment of publication bias across studies examining SSRI efficacy for anxiety outcomes in PTSD populations.

with psychotherapy, in 195 trauma-affected refugees with PTSD. Both groups improved on HAM-A scores at 6 months, and the difference between-group difference was not significant ($p = 0.48$).

SNRIs for Anxiety Outcomes in PTSD Populations:

Five studies (847 participants) evaluated SNRIs and reported anxiety outcomes [43-48]. Meta-analysis of four RCTs indicated a reduction in anxiety compared with placebo (SMD -0.38; 95% CI -0.55 to -0.21; $p < 0.001$; I-squared = 36%). Estimates were similar for venlafaxine (SMD -0.39; 95% CI -0.57 to -0.21) and duloxetine (SMD -0.35; 95% CI -0.58 to -0.12). The pooled effect on PTSD symptoms was smaller and less certain (SMD -0.23; 95% CI -0.44 to -0.02; $p = 0.03$; I-squared = 46%). One study in veterans with alcohol dependence [47] did not demonstrate benefit; excluding it reduced heterogeneity (SMD -0.31; 95% CI -0.47 to -0.15; $p < 0.001$; I-squared = 28%). PTSD response favored SNRIs (RR 1.33; 95% CI 1.02 to 1.73), although the certainty of this evidence was low.

Atypical Antipsychotics: Monotherapy or Adjunctive Use:

Four RCTs (486 participants) evaluated atypical antipsychotics, including adjunctive risperidone and monotherapy with quetiapine or olanzapine [49-52]. Because monotherapy and augmentation trials address different clinical questions, pooling them introduces indirectness. The reported pooled estimates favored atypical antipsychotics for anxiety symptoms (SMD -0.35; 95% CI -0.52 to -0.18; $p < 0.001$; I-squared = 28%) and PTSD symptoms (SMD -0.31; 95% CI -0.48 to -0.14; $p < 0.001$; I-squared = 32%). However, discontinuation due to adverse events was more frequent (RR 2.14; 95% CI 1.43 to 3.21; $p < 0.001$). Common adverse events included weight gain, sedation,

and extrapyramidal symptoms. These findings should not be interpreted as support for routine use.

Other Pharmacological Agents:

Evidence for other agents was limited. Two small pregabalin trials were described [53,54], but their applicability to confirmed PTSD comorbidity was uncertain because the published reports primarily characterized anxiety-disorder samples. A single ketamine RCT ($n = 41$) reported a rapid reduction in an anxiety-related CAPS item at 24 hours (mean difference -2.1; 95% CI -3.4 to -0.8), with no meaningful difference at 7 days [55]. No eligible RCTs of benzodiazepines, buspirone, hydroxyzine, alpha-1 antagonists, or beta-blockers met the requirement for a reported anxiety outcome.

Publication Bias:

Fewer than 10 studies contributed to the SSRI anxiety meta-analysis. Accordingly, Egger's regression test and trim-and-fill estimates were not interpreted because these methods have limited reliability with small numbers of studies. The funnel plot in Figure 4 is presented for descriptive inspection only, and publication bias cannot be excluded.

Certainty of Evidence (GRADE):

For SSRIs, moderate-certainty evidence suggested reductions in anxiety symptoms (1,475 participants; SMD -0.46; 95% CI -0.62 to -0.30) and PTSD symptoms (1,388 participants; SMD -0.43; 95% CI -0.58 to -0.28), with a higher PTSD response rate than placebo (RR 1.58; 95% CI 1.31 to 1.91). For SNRIs, evidence for anxiety reduction was low certainty (847 participants; SMD -0.38; 95% CI -0.55 to -0.21), and evidence for PTSD symptom reduction was very low certainty (765 participants; SMD -0.23; 95% CI -0.44 to -0.02). For atypical antipsychotics, evidence for

anxiety and PTSD symptom reduction was low certainty, while evidence for increased discontinuation due to adverse events was moderate certainty (RR 2.14; 95% CI 1.43 to 3.21). These ratings indicate that future research may materially change the non-SSRI efficacy estimates and that directness is limited when formal anxiety diagnoses are absent.

Discussion.

This review synthesized pharmacological effects on anxiety outcomes in adults with PTSD. SSRIs were associated with moderate reductions in anxiety and PTSD symptoms, broadly consistent with PTSD guidelines [7-9] and previous meta-analyses [18,19]. However, the pooled estimates do not establish efficacy specifically for patients with a confirmed comorbid anxiety disorder because several contributing studies used symptom thresholds, subscales, or transdiagnostic constructs rather than a formal diagnosis.

The recent studies by Luciano et al. [42] and Barhoma et al. [48] broaden the evidence base by examining anxiety sensitivity and a trauma-affected refugee population, respectively. Both are clinically informative, but neither fully resolves the central evidence gap: anxiety sensitivity is not equivalent to a diagnosed anxiety disorder, and pragmatic treatment combined medication with psychotherapy. These studies therefore support generalizability to anxiety-related outcomes while remaining indirect for confirmed psychiatric comorbidity.

Evidence for SNRIs was less certain, particularly for PTSD outcomes, and this review cannot independently establish SNRIs as a preferred second-line treatment. The atypical-antipsychotic evidence was also difficult to interpret because monotherapy and augmentation trials were combined and efficacy estimates were low certainty. The higher rate of adverse-event discontinuation reinforces guideline recommendations to avoid routine antipsychotic use and to reserve such treatment for carefully selected, treatment-resistant cases with appropriate monitoring [7,9,56].

Clinical care should remain multimodal and patient centered. Trauma-focused psychological treatment is recommended as first-line care when available [9,57]. Psychological rehabilitation is particularly relevant for military personnel with PTSD [58], while physical rehabilitation may also be required after trauma-related injury [59]. Emerging digital and virtual-reality approaches may extend rehabilitation options but should be regarded as adjunctive rather than replacements for evidence-based therapy [60]. A broader, multidimensional concept of health supports assessment of mental, physical, functional, and social outcomes [61].

When medication is chosen, decisions should follow established PTSD and anxiety guidelines, include shared decision-making, and consider prior treatment, comorbid conditions, patient preferences, and adverse-event risk. Antipsychotic treatment requires baseline and ongoing monitoring of weight, metabolic parameters, and extrapyramidal symptoms [56,62]. Co-occurring alcohol dependence and other somatic or psychiatric conditions further support a holistic assessment [63]. Mathematical pharmacology may assist dose optimization and risk modeling, but clinical recommendations still require valid trial data in the target population [17].

Recent epidemiological studies continue to demonstrate substantial anxiety burden after trauma. Pearson et al. [64] reported increased rates of anxiety and PTSD after traumatic injury, while Ben Othmene et al. [65] described high anxiety-symptom burden among military veterans with PTSD. These findings support routine assessment of both symptom domains but do not by themselves establish comparative medication efficacy.

Novel interventions, including ketamine, esketamine, and MDMA-assisted therapy, are being investigated for PTSD [16,66]. Psychological interventions can also reduce anxiety in complex PTSD, although durability at follow-up remains uncertain [67]. These developments should be evaluated in trials that separately report anxiety diagnoses, anxiety outcomes, safety, functioning, and quality of life.

The findings should be interpreted in the context of current guidelines. Pharmacological recommendations for PTSD are generally conditional, and trauma-focused psychotherapies remain preferred when feasible [9,57]. Medication may be appropriate when psychotherapy is unavailable, declined, contraindicated, or insufficient. Shared decision-making should address expected benefits, uncertainty, access, treatment burden, and individual risks.

Future effectiveness research should include diverse populations, including refugees, veterans, civilians, and people in low-resource settings. Trials should also evaluate patient-reported outcomes, functioning, and long-term relapse prevention. Family or caregiver factors may influence treatment outcomes, as suggested in pediatric PTSD research [68], but their role in adult pharmacotherapy requires direct study.

Broader treatment planning should also acknowledge that PTSD pharmacotherapy extends beyond antidepressants [69], that post-traumatic stress symptom burden may predict treatment outcomes [70], and that response to trauma-focused treatment can vary according to patient and treatment characteristics [71]. Earlier pharmacotherapy reviews likewise emphasize individualized benefit-risk prioritization [72], while co-occurring mild traumatic brain injury can complicate PTSD assessment and management [73]. Evidence from adjacent clinical fields also illustrates the need to distinguish complementary or nutraceutical strategies from guideline-supported pharmacotherapy [74], to control technical artifacts when neuroimaging is incorporated into mechanistic studies [75], to consider sex-specific somatic comorbidity in broader patient-centered care [76], and to account for medicines reimbursement and access when translating evidence into practice [77].

Limitations.

This review has several limitations. First, the evidence base was small, and few recent studies met the eligibility criteria. Second, formal anxiety diagnoses were inconsistently reported; combining confirmed diagnoses with symptom-based or construct-based ascertainment increased clinical heterogeneity and indirectness. The available data were insufficient for a reliable quantitative subgroup analysis by diagnostic status. Third, outcome instruments varied, and most studies followed participants for only 8-24 weeks. Fourth, non-English reports

were excluded because translation resources were unavailable, creating a risk of language bias whose direction and magnitude cannot be determined. Fifth, the review was not prospectively registered. Sixth, aggregate published data limited analyses of moderators, and the scarcity of head-to-head trials precluded network meta-analysis. These limitations mean that the results are more applicable to anxiety outcomes within PTSD populations than to a narrowly defined, confirmed comorbid anxiety-disorder population.

Implications for clinical practice and future research.

The findings do not establish a prescriptive medication algorithm. When pharmacotherapy is selected, clinicians should follow current PTSD and anxiety guidelines, monitor both anxiety and PTSD symptoms, review tolerability and adherence, and incorporate patient preferences. The moderate-certainty SSRI findings may inform these discussions, whereas SNRI and atypical-antipsychotic estimates should be presented with greater uncertainty. Antipsychotics should not be used routinely and require careful risk-benefit assessment and monitoring.

Future studies should recruit adequately powered samples with confirmed comorbid anxiety disorders and PTSD; use standardized diagnostic and outcome measures; separately report anxiety, PTSD, functioning, and quality-of-life outcomes; extend follow-up to evaluate durability and relapse; examine treatment moderators; and include diverse, underserved populations. Trials of novel agents should prespecify anxiety outcomes and provide detailed safety data. Prospective protocol registration and transparent reporting of extraction decisions are also priorities for future reviews.

Conclusion.

This systematic review found moderate-certainty evidence that SSRIs reduce anxiety outcomes in adults with PTSD, but the evidence is not sufficiently direct to support firm conclusions for patients with a confirmed comorbid anxiety disorder. Evidence for SNRIs was low certainty for anxiety outcomes and very low certainty for PTSD outcomes. Atypical antipsychotics showed low-certainty efficacy signals and a clearer increase in adverse-event discontinuation; they should not be used routinely. Overall, the findings are consistent with guideline-supported use of SSRIs when medication is indicated, but clinical decisions should remain individualized and integrated with trauma-focused psychological care. More rigorous trials in diagnostically confirmed comorbid populations are required.

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Conflict of interest statement.

The authors declare that they have no conflicts of interest related to this article.

Authorship contribution statement. L.B.: Conceptualization; Methodology; Formal analysis; Data curation; Writing – original draft; Writing – review and editing; Project administration; Visualization; Supervision. I.R.: Methodology; Data curation;

Formal analysis; Validation; Writing – original draft; Writing – review and editing. V.Y.: Data curation; Formal analysis; Validation; Writing – original draft; Writing – review and editing; Visualization. O.Z.: Conceptualization; Methodology; Data curation; Validation; Writing – review and editing; Project administration. A.L.: Data curation; Formal analysis; Validation; Writing – original draft; Writing – review and editing.

Ethical approval.

This study was a systematic review and meta-analysis of previously published and publicly available data. It did not involve the direct recruitment of human participants, collection of identifiable personal information, or conduct of any experimental intervention. Therefore, institutional ethics committee approval and informed consent were not required.

Data availability statement.

All data analyzed in this systematic review were derived from previously published studies cited in the article. No new primary participant-level dataset was generated. Data extracted for the evidence synthesis and meta-analysis may be made available by the corresponding author upon reasonable request.

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