Fluvoxamine in Non-Hospitalized Patients with Acute COVID-19 Infection and the Lack of Efficacy in Reducing Rates of Hospitalization, Mechanical Ventilation and Mortality in Placebo-Controlled Trials: A Systematic Review and Meta-Analysis

Supplementary Material

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| --- | --- |
| Title | Page |
| Supplementary Table 1: PRISMA Checklist | 2 |
| Supplementary Table 2: Search strategy | 3 |
| Supplementary Table 3: The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses | 4 |
| Supplementary Figure 1: Quality assessment of the included studies using the Revised Cochrane Risk-of-Bias tool for randomized trials (RoB-2). | 5 |

Supplementary Table 1: PRISMA Checklist

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| --- | --- | --- | --- |
| **Section/topic** | **#** | **Checklist item** | **Reported on page #** |
| **TITLE** | | |  |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | |  |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 3 |
| **INTRODUCTION** | | |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 4-5 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 4-5 |
| **METHODS** | | |  |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | NA |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 5 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 5 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Supplementary page 3 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | Figure 1 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 6 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 6 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 6-7 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 6 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis. | 6-7 |

Supplementary Table 2: Search strategy

|  |  |  |
| --- | --- | --- |
| Database | Search Strategy | Articles Retrieved |
| PubMed/MEDLINE | ("fluvoxamine"[All Fields] OR "SSRI"[All Fields] OR "fluoxetine"[All Fields] OR "citalopram"[All Fields]) AND ("coronavirus"[All Fields] OR "COVID-19"[All Fields] OR "SARS-CoV 2"[All Fields] OR "COVID pneumonia”[All Fields] OR "COVID-19 Pneumonia"[All Fields] OR "Viral COVID pneumonia"[All Fields] OR "Viral Pneumonia"[All Fields]) AND ("clinical deterioration"[All Fields] OR "hospitalization"[All Fields] OR "shortness of breath"[All Fields] OR "supplemental oxygen"[All Fields] OR "hospital stay"[All Fields] OR "emergency stay"[All Fields] OR "extended care"[All Fields]) AND ("dexamethasone"[All Fields] OR "methylprednisolone” [All Fields] OR "ICU"[All Fields] OR "mechanical ventilation"[All Fields] OR "intubated"[All Fields] OR "48 hours"[All Fields]) AND ("mortality” [All Fields] OR "death"[All Fields] OR “tracheostomy"[All Fields] OR "gastric bleed”[All Fields]) | 54 |
| Embase | (‘fluvoxamine'/exp OR 'SSRI') AND ('coronavirus'/exp OR 'COVID-19' OR 'SARS-CoV 2’) AND ('hospitalization' OR 'clinical deterioration') AND ('intensive care unit' OR 'intensive care’ OR ‘mechanical ventilation' OR “intubated’ OR ‘mortality OR ‘death’) | 62 |
| Web of Science | (‘fluvoxamine' OR 'SSRI') AND ('coronavirus' OR 'COVID-19' OR 'SARS-CoV 2’) AND ('hospitalization' OR 'clinical deterioration') | 41 |
| Cochrane CENTRAL | "Hospitalization" in Title Abstract Keyword AND "Coronavirus" in Title Abstract Keyword AND “fluvoxamine” in Title Abstract Keyword AND “clinical deterioration” in Title Abstract Keyword | 23 |

*Dates searched: inception through 2/10/2022*

Supplementary Table 3: The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Selection | | | | | Outcome | | | |
| Study, Year | Representative ness of the exposed cohort | Selection of the non-exposed cohort | Ascertainment of exposure | Outcome not present at baseline | Comparability of the cohort | Assessment of outcome | Enough follow up duration | Adequate follow-up | Total score |
| Seftel 2021 | \* | \* | \* | \* | \* | \* | \* | \* | 8 |
|  |

Each asterisk represents one star in the Newcastle-Ottawa Scaling System (NOS). The maximum stars are 2 for comparability and 1 are for all other categories. Each star counts towards the total score. Score of 5 to 6 considered as moderate quality and 7 to 9 as high quality.

Supplementary Figure 1: Quality assessment of the included studies using the Revised Cochrane Risk-of-Bias tool for randomized trials (RoB-2)

