INPLASY PROTOCOL

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Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
None declared.

Serotonin syndrome with dextromethorphan alone and in combination with other serotonergic drugs. a systematic review

Deng, JH[1]; Zhang, JX[2]; Zhang, QX[3]; Zhong, GW[4].

Review question / Objective: **To assess the evidence for serotonin syndrome occurring in the context of dextromethorphan administration. To assess concurrent medication to see if there are associations with 1) other serotonergic medication.**
Condition being studied: **It is uncertain whether use of dextromethorphan alone or in therapeutic doses can cause Serotonin syndrome (SS). Also, SS by dextromethorphan has not previously been systematically reviewed. Therefore, the main aim is to present a systematic review and summary of these studies.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 May 2022 and was last updated on 12 May 2022 (registration number INPLASY202250079).

INTRODUCTION

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METHODS

Search strategy: searched MEDLINE, EMBASE, the Cochrane Library, China National Knowledge Infrastructure (CNKI), VIP, WANFANG and Sinomed database using keyword "serotonin syndrome" or "serotonin toxicity" AND "dextromethorphan".

Participant or population: Patients of all ages in any setting.

Intervention: Dextromethorphan either alone or in combination with other medications for any indication.

Comparator: Any control or no control.

Study designs to be included: All studies included including but not limited to Case studies, Cohort studies.

Eligibility criteria: Dextromethorphan induced SS patients (as defined by the author) will be included in the study.

Information sources: Electronic databases(MEDLINE, EMBASE, the Cochrane Library, China National Knowledge Infrastructure (CNKI), VIP, WANFANG and Sinomed). Additionally, we also conducted citation searches from key articles and conference abstracts.

Main outcome(s): Serotonin Syndrome in the context of dextromethorphan administration.

Additional outcome(s): Assessment of concurrent medication.

Data management: Two independent reviewers will select the included articles. First, in phase-one, both reviewers will read titles and abstracts independently while applying the eligibility criteria. Second, in phase-two, the same two reviewers will perform a full-text reading while applying the election criteria. In both phases, all the retrieved information will be crosschecked by the third review. Final selection will be always based on the full-text of the publication. Data management with Endnote.

Quality assessment / Risk of bias analysis: We will assess accuracy of diagnosis by comparing with standardised criteria (Hunter criteria) and use the Naranjo's Adverse Drug Reaction Probability Scale to assess likelihood of dextromethorphan being causal in serotonin syndrome.

Strategy of data synthesis: Where patient level information about concurrent medication is available, data will be pooled and analysed for associations with other serotonergic medication and CYP inhibitors. We will summarise results from epidemiological studies. We suspect a formal meta-analysis will not be feasible.

Subgroup analysis: None planned.

Sensitivity analysis: None planned.

Language: English and Chinese.

Country(ies) involved: China.

Keywords: serotonin syndrome; serotonin toxicity; dextromethorphan.

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