# INPLASY PROTOCOL

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Corresponding author: Li Wen

aladdin64@163.com

**Author Affiliation:** 

Guizhou University of Traditional Chinese Medicine

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

#### **Conflicts of interest:**

The authors declare that there is no conflict of interest regarding the publication of this review.

## INTRODUCTION

**Review question / Objective:** Is metformin effective in decreasing the risk of asthma exacerbation in concurrent asthma and diabetes patients? Condition being studied: The review has not yet started, but we have already begin preliminary searches. Eleven co-authors were involved in the present study. Nine of them were trained well in systematic review in Medical University of West China

Association of metformin use with asthma exacerbation in patients with concurrent asthma and diabetes: a systematic review and meta-analysis of observational studies

Wen, L<sup>1</sup>; Yihui, C<sup>2</sup>; Zhong, Q<sup>3</sup>; Jie, G<sup>4</sup>; Liancheng, G<sup>5</sup>; Mengzhi, Z<sup>6</sup>; Huaiquan, L<sup>7</sup>; Haiyang, Y<sup>8</sup>; Qingxue, W<sup>9</sup>; Changfu, Y<sup>10</sup>; Yunzhi, C<sup>11</sup>.

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**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 April 2020 and was last updated on 30 April 2020 (registration number INPLASY202040210).

1

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## **METHODS**

Search strategy: We conducted an online search for original researches from inception up to April 2020, in PubMed (www.ncbi.nlm.nih.gov/pubmed), Embase (www.embase.com) and the Cochrane Central Register of Controlled Trials(CENTRAL) ( onlinelibrary.wiley.com/ cochranelibrary/) with the search term "(metformin[Title/Abstract] OR glucophage[Title/Abstract]) AND (asthma[Title/Abstract])" following the demonstration of Cochrane Handbook (LW and CY). In addition, we performed handsearches of the references of all identified articles and relevant reviews (QZ).

Participant or population: Adult concurrent asthma and diabetes patients.

Intervention: Metformin.

Comparator: Non-metformin.

Study designs to be included: Observational studies.

**Eligibility criteria:** 1. Observational studies. 2. Age>18 year. 3. Metformin on concurrent asthma and diabetes. 4. Reported the odds ratio (OR) or Hazard Ratio (HR) of asthma exacerbation compared with metformin user and non-user.

Information sources: Electronic databases.

Main outcome(s): Adjusted risk of asthma exacerbation.

Additional outcome(s): Adjusted risk of asthma hospitalization and emergency room visit.

**Quality assessment / Risk of bias analysis:** The quality of individual records will be assessed according to The Newcastle-Ottawa Scale.

**Strategy of data synthesis:** Review Manager software (version 5.3; Cochrane

Collaboration, Oxford, UK) was used for estimating risks of bias of included studies, data analysis and plotting (WQ, YC and CY). The sensitivity analysis and publication bias test were performed using R language if enough original researches were included. I2 and chi-square tests were used to estimate heterogeneity. If P>0.1 or I2 <40%, the fixed effect model meta-analysis was performed. When there was a high degree of heterogeneity, a random effect analysis was used. Weighted mean difference (WMD) or standard mean difference (SMD) were used for analysis of continuous data and odds ratio (OR) were calculated for dichotomous variable respectively.

Subgroup analysis: No.

Sensibility analysis: No.

Country(ies) involved: China.

Keywords: Metformin, Asthma, Diabetes, Meta-analysis, Systematic review.

## Contributions of each author:

Author 1 - Li Wen. Author 2 - Chai Yihui. Author 3 - Qin Zhong. Author 4 - Gao Jie. Author 5 - Guan Liancheng. Author 6 - Zhang Mengzhi. Author 7 - Liu Huaiquan. Author 8 - Yu Haiyang. Author 9 - Wang Qingxue. Author 10 - Yang Changfu. Author 11 - Chen Yunzhi.