INTRODUCTION

Review question / Objective: Which studies on the prediction models for the development of diabetic retinopathy applicable to patients with T2DM are eligible to be included in the systematic review of the literature, and what is the accuracy and quality of them?

Condition being studied: Type 2 diabetes mellitus and diabetic retinopathy.

METHODS

Search strategy: The literature was searched for all studies reporting the development of a prediction model for the risk of retinopathy applicable to people with T2DM.
with T2D. The search was performed on March 1st, 2022 in PubMed and Embase, using a search string containing synonyms of the terms type 2 diabetes, retinopathy, blindness, and prediction modelling. A manual retrieval of references cited in key articles was also applied in order not to miss potentially eligible articles, and all relevant articles will also be included in the screening process.

**Participant or population:** Patients with type 2 diabetes mellitus.

**Intervention:** Prediction models for the development of diabetic retinopathy, applicable to patients with T2DM.

**Comparator:** Not applicable.

**Study designs to be included:** Studies on the prediction models for the development of diabetic retinopathy applicable to patients with T2DM.

**Eligibility criteria:** 1) The prediction model has been developed in patients with T2DM or in the general population. 2) The outcome of the prediction model is any stage of retinopathy or blindness. 3) The follow-up period of the development study was at least one year.

**Information sources:** The literature was searched for all studies reporting the development of a prediction model for the risk of DR applicable to patients with T2DM. The search was performed on March 1st, 2022 in PubMed and Embase, using a search string containing synonyms of the terms type 2 diabetes mellitus, diabetic retinopathy, blindness, and prediction modelling. A manual retrieval of references cited in key articles was also applied in order not to miss potentially eligible articles, and relevant articles will also be included in the screening process.

**Main outcome(s):** Any stage of diabetic retinopathy.

**Data management:** Two reviewers will independently review the titles, abstracts and full texts of the results obtained from the searches, and will exclude studies that do not meet the inclusion criteria. Any disagreements between the two reviewers will be resolved by consulting a third reviewer. Data extraction will then be performed on the studies selected for inclusion independently by two reviewers, with any disagreements arising between them being resolved by discussion. The Checklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS), which is a form that includes the following eleven key domains: source of data, participants, outcome to be predicted, candidate predictors, sample size, missing data, model development, model performance, model evaluation, results, and interpretation and discussion, will be completed.

**Quality assessment / Risk of bias analysis:** Risk of bias assessment will be performed using the Checklist for critical Appraisal and data extraction for systematic Reviews of prediction Modelling Studies (CHARMS). The assessment will be performed by rating the first nine domains of the CHARMS checklist as being of 'high' or 'low' risk of bias, or 'unclear' if the description regarding the specific domain of the study is insufficient. Two reviewers will independently assess the risk of bias for the included studies, with any disagreements arising between them being resolved by discussion.

**Strategy of data synthesis:** We will provide a narrative synthesis of the included studies focusing on the development of the prediction models, based on the CHARMS checklist. We will evaluate the population, the sample sizes, the selection methods for the predictors, the developmental methods, and the validation methods. We will also compare performances of the models in terms of their discrimination and calibration.

**Subgroup analysis:** None planned.

**Sensitivity analysis:** None planned.

**Country(ies) involved:** China.
Keywords: type 2 diabetes mellitus; diabetic retinopathy; prediction models; systematic review.

Contributions of each author:
Author 1 - Wei Wang.
Email: zoc_wangwei@yahoo.com
Author 2 - Yi Wu.
Email: wuyi68@mail.sysu.edu.cn