# INPLASY PROTOCOL

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Conflicts of interest: None declared.

## Optical coherence tomography in depression: A protocol of systematic review and meta-analysis

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**Review question / Objective:** Optical coherence tomography is a noninvasive approach to detect changes in the retinal layers, which may reflect brain structure and function changes. Depression is the leading cause of disability worldwide, yet the relation between OCT and depression remains unknow. To address above issue, this study aims to conduct a systematic review and meta-analysis to explore ocular biomarkers and their role in depression.

Eligibility criteria: 1) cohort and cross-sectional human studies; (2) studies recruited adult depression participants diagnosed according to operationalized criteria such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), as well as healthy controls; (3) study outcomes were measured by OCT, including retinal nerve fiber layer (RNFL), ganglion cell complex (GCC), macular thickness, macular volume or other related indicators.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 May 2022 and was last updated on 25 May 2022 (registration number INPLASY202250142).

#### INTRODUCTION

**Review question / Objective:** Optical coherence tomography is a noninvasive approach to detect changes in the retinal layers, which may reflect brain structure and function changes. Depression is the leading cause of disability worldwide, yet

the relation between OCT and depression remains unknow. To address above issue, this study aims to conduct a systematic review and meta-analysis to explore ocular biomarkers and their role in depression.

Condition being studied: Depression has been the second leading cause of years

lived with disability since 2010 in China and is now a common public health problem with a huge burden. The pathophysiology of depression includes genetic factors, environmental factors and central nervous system (CNS) involvement, especially abnormal neurotransmission. Neuroimaging study indicated that depression could lead to altered brain neuroplasticity. The retina is considered part of the CNS and shares the same embryologic origin. The axons of retinal ganglion cells (RGCs) form the optic nerve, which extends to the thalamus and the midbrain. Emerging evidence suggests a link between retina and depression. Peripapillary retinal nerve fiber layer (RNFL) thinning is associated with neuronal cell and axonal loss. In addition, several studies demonstrated a reduction in the thickness of retinal layers in depression patients. Optical coherence tomography (OCT) is a noninvasive approach to detect changes in the retinal layers, which may visualize the processes of neurodegeneration, neuroprotection and, potentially, even neurorepair. Recently, OCT has been increasingly used in the research of neurodegenerative diseases, and changes of retinal layers has been shown to be associated with disease severity. In addition, OCT shows potential as a diagnostic tool for psychiatric disorders such as schizophrenia and major depression.

### **METHODS**

Participant or population: Adult depression participants diagnosed according to operationalized criteria such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), as well as healthy controls.

Intervention: No intervention will be involved.

**Comparator:** No comparator will be involved.

Study designs to be included: Cohort and cross-sectional human studies.

Eligibility criteria: (1) cohort and crosssectional human studies; (2) studies recruited adult depression participants diagnosed according to operationalized criteria such as the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), as well as healthy controls; (3) study outcomes were measured by OCT, including retinal nerve fiber layer (RNFL), ganglion cell complex (GCC), macular thickness, macular volume or other related indicators.

Information sources: We will conduct comprehensive search of China National Knowledge Infrastructure (CNKI), Chinese **Biomedical Literature Database (CBM)**, Chinese Science and Technology Periodical Database (VIP), WanFang Database, PubMed, EMBASE and Web of Science (WoS) from their inception onwards, using the combination of text words and medical subject headings (MeSH) terms. Table 1 shows the details of the search strategy in the PubMed. Corresponding retrieval strategies will be applied in other electronic databases according to respective retrieval rules. Furthermore, the reference lists and gray literature will be manually searched for additional potential studies.

Main outcome(s): Study outcomes were measured by OCT, including retinal nerve fiber layer (RNFL), ganglion cell complex (GCC), macular thickness, macular volume or other related indicators.

Quality assessment / Risk of bias analysis: We will use the adaptations for cohort and cross-sectional studies of the Newcastle-Ottawa Scale (NOS) recommended by the Cochrane Collaboration (http:// w w w. o h r i.ca/programs/ clinical\_epidemiology/oxford. asp) to assess the risk of bias and methodological quality of the included studies.

Strategy of data synthesis: We will perform statistical analyses by Review Manager (version 5.4.1) and STATA (version 12.0) software. Means and standard deviations (SD) will be used to assess the standardized mean difference (SMD) and the weighted mean difference (WMD), with respective 95% CIs. P < 0.05 will be considered statistically significant. We will use Chi-square test and I2 statistic to test the heterogeneity. For acceptable heterogeneity, the fixed effects model will be used, otherwise the random effects model will be used. When meta-analysis is not possibly carried out, results will be described qualitatively.

Subgroup analysis: We will perform subgroup analyses according to age, severity of depression and type of OCT, as well as the quality of included studies.

Sensitivity analysis: Sensitivity analyses (excluding study one by one ) will be performed to test the stability of result.

Country(ies) involved: China.

Keywords: Optical coherence tomography; Depression; Systematic review; Metaanalysis; Protocol.

#### Contributions of each author:

Author 1 - Xili Xiao. Author 2 - Rong Fan. Author 3 - Huan Liu. Author 4 - Chengzhi Jiang. Author 5 - Li Wan.