# INPLASY PROTOCOL

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# The prevalence of depression and its association with the risk of mortality in patients with cancer: a protocol for systematic review and meta analysis

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Review question / Objective: 1. Types of studies: Crosssectional, cohort and case-control studies will be included, while the case reports, reviews, editorials, abstracts of conferences, and letter to the editors will be excluded. 2. Types of participants: Participants of adults (18 years old or older) of either gender with primary diagnosis of cancer. 3. Types of diagnosis: Depression should be diagnosed by validated methods and instruments including WHO International Classification of Diseases codes (WHO ICD codes), or scales such as Hamilton Rating Scale for Depression (HAMD), Patient Health Questionnaire-9 (PHQ-9), Hospital Anxiety and Depression Scale (HADS), etc. The studies with improper methodology and incomplete data will be excluded. 4. Types of outcome measures: Prevalence of depression among cancer patients. Risk factors associated with depression in cancer patients measured by univariate and multivariate Cox proportional hazards models.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 July 2021 and was last updated on 20 July 2021 (registration number INPLASY202170065).

### INTRODUCTION

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Condition being studied: Cancer is a global health concern of with a rising mortality and prevalence rate, currently ranked as the second most common cause of death in the worldwide. With the development of social economy, the risk factors of cancer are plentiful but most prominently include genetic factors, lifestyle, diet structure, and environmental conditions. Once contracted, evidence has shown that the prognosis of cancer is closely associated with the development of psychiatric symptoms. The major symptoms of depression are melancholia, low mood, and anhedonia. One study reported that the prevalence of depression in patients with cancer is common, including major depression (15%) and minor depression (10%). Depression has profound effects on the prognosis of patients with cancer leading to complications such as suicide, reduced treatment compliance, worsened quality of life, extended hospital stays and increased familial burden. It is through these means that depression can negatively impact the survival rates of cancer patients. Several systematic reviews and meta-analysis have investigated the effectiveness of psychotherapy for depression in patients with cancer, but there is a lack of literature focusing specifically on the prognosis of these patients, meaning the prevalence of depression and correlating risk of mortality. The primary objective of this protocol is to build up an explicit methodology for conducting a systematic review and metaanalysis which could effectively investigate the prevalence of depression in cancer patients and clarify the associations

between depression and cancer mortality. The data of this review will help better the understanding and management of cancer patients affected with comorbid depression.

### **METHODS**

Search strategy: A literature search will be conducted on Pubmed, Medline, Embase, Web of Science databases, the Cochrane Library (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews), and all published articles will be searched from 1 January 1975 to 1 May 2021 in English. The terms will be searched in Medical Subject Heading (MeSH) database, the keywords include ("depression" OR "depressive" OR "depressions" OR "depressive disorder" OR "psychiatry" OR "psychological" OR "psychology" OR "psychiatric" OR "mental" OR AND ("cancer" OR "tumor" OR "neoplasm" OR "carcinoma" OR "malignant" ) AND ("mortality" OR "survival" OR "death") AND ("observational study" OR "prospective study" OR "cohort study" OR "longitudinal study" OR "follow up"). The search will be limited to Title/ Abstract. The reference list of the retrieved articles and the related reviews will be manually searched for additional sources.

Participant or population: Participants of adults (18 years old or older) of either gender with primary diagnosis of cancer.

Intervention: Depression should be diagnosed by validated methods and instruments including WHO International Classification of Diseases codes (WHO ICD codes), or scales such as Hamilton Rating Scale for Depression (HAMD), Patient Health Questionnaire-9 (PHQ-9), Hospital Anxiety and Depression Scale (HADS), etc.

**Comparator: Not available.** 

Study designs to be included: Crosssectional, cohort and case-control studies will be included, while the case reports, reviews, editorials, abstracts of conferences, and letter to the editors will be excluded.

Eligibility criteria: 1. Types of studies: Cross-sectional, cohort and case-control studies will be included, while the case reports, reviews, editorials, abstracts of conferences, and letter to the editors will be excluded. 2. Types of participants: Participants of adults (18 years old or older) of either gender with primary diagnosis of cancer. 3. Types of diagnosis: Depression should be diagnosed by validated methods and instruments including WHO International Classification of Diseases codes (WHO ICD codes), or scales such as Hamilton Rating Scale for Depression (HAMD), Patient Health Questionnaire-9 (PHQ-9), Hospital Anxiety and Depression Scale (HADS), etc. The studies with improper methodology and incomplete data will be excluded. 4. Types of outcome measures: Prevalence of depression among cancer patients. Risk factors associated with depression in cancer patients measured by univariate and multivariate Cox proportional hazards models.

Information sources: Pubmed, Medline, Embase, Web of Science databases, the Cochrane Library (Cochrane Central Register of Controlled Trials, Cochrane Database of SystematicReviews).

Main outcome(s): Prevalence of depression among cancer patients. Risk factors associated with depression in cancer patients measured by univariate and multivariate Cox proportional hazards models.

## Quality assessment / Risk of bias analysis:

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) will be used to evaluate the quality of evidence for all outcomes. 5 domains of risk of bias, consistency, directness, precision and publication bias will be assessed. The strength of evidence will be adjudicated as high, moderate, low, or very low.

Strategy of data synthesis: The HRs of mortality will be selected as our primary outcomes for this systematic review and meta-analysis. A pre-designed

standardized data extraction form will be used to summarize the characteristics of all included studies. Reviewers (SSL and ZQW) will conduct a meta-analysis if there are more than 6 observational studies investigating the prevalence of depression and the risk of mortality. If it is possible to conduct a meta-analysis, we will use a random-effects model with the extracted HRs of mortality with 95% CIs.

Subgroup analysis: Subgroup analysis and meta-regression will be performed to clarify particular factors which may influence the primary outcomes. According to the mean age, male proportion of study, depression severity, definition of the depression, bias score and causes of mortality (depression-related or all-cause).

Sensitivity analysis: We will conduct a sensitivity analysis of the primary outcomes to ensure the review quality, assessing the impact of methodological quality, sample size, the missing data and the analysis methods on the result of this meta-analysis.

Country(ies) involved: China.

Keywords: depression; mortality; cancer; systematic review.

### Contributions of each author:

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