

# INPLASY PROTOCOL

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**Conflicts of interest:** None.

## Association of circulating leptin level, adiponectin level and risk of pancreatic cancer: a combination of traditional and dose-response meta-analysis

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**Review question / Objective:** What is the relationship between circulating leptin level, adiponectin level and the risk of pancreatic cancer?

**Condition being studied:** It has long been recognized that obesity-related conditions increase the risk of several malignancies including pancreatic cancer. Pancreatic cancer patients with increased adiposity have a heightened risk for poorer prognosis and higher mortality, which suggests that the significance of leptin and adiponectin in the onset and/or development of PC is becoming increasingly prominent. However, conflicting associations are reported between leptin levels, adiponectin levels and pancreatic cancer.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 April 2020 and was last updated on 22 April 2020 (registration number INPLASY202040138).

### INTRODUCTION

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cancer patients with increased adiposity have a heightened risk for poorer prognosis and higher mortality, which suggests that the significance of leptin and adiponectin in the onset and/or development of PC is becoming increasingly prominent. However, conflicting associations are reported between leptin levels, adiponectin levels and pancreatic cancer.

## METHODS

**Search strategy:** The complete search used for PubMed will be:

#1 (“leptin [Mesh Terms]” OR “Obese Protein” OR “Obese Gene Product” OR “Gene Product, Obese” OR “Ob Gene Product” OR “Gene Product, Ob” OR “Ob Protein”) #2 (“adiponectin [Mesh Terms]” OR “Adipocyte Complement-Related Protein 30-kDa” OR “Adipocyte Complement Related Protein 30 kDa” OR “Adipose Most Abundant Gene Transcript 1” OR “apM-1 Protein” OR “apM 1 Protein” OR “ACRP30 Protein” OR “Adipocyte, C1q and Collagen Domain Containing Protein”) #3 (“Pancreatic Neoplasms [Mesh Terms]” OR “Neoplasm, Pancreatic” OR “Pancreatic Neoplasm” OR “Pancreas Neoplasms” OR “Neoplasm, Pancreas” OR “Neoplasms, Pancreas” OR “Pancreas Neoplasm” OR “Neoplasms, Pancreatic” OR “Cancer of Pancreas” OR “Pancreas Cancers” OR “Pancreas Cancer” OR “Cancer, Pancreas” OR “Cancers, Pancreas” OR “Pancreatic Cancer” OR “Cancer, Pancreatic” OR “Cancers, Pancreatic” OR “Pancreatic Cancers” OR “Cancer of the Pancreas” ). #4=(#1 OR #2) AND #3

**Participant or population:** Patients with pancreatic cancer.

**Intervention:** Abnormal leptin level and adiponectin level in pancreatic cancer patients.

**Comparator:** Circulating leptin level and adiponectin level in control groups, including healthy individuals and other patients without cancer diagnosis.

**Study designs to be included:** All observational studies, including cohort studies, case-control studies and cross-sectional studies.

**Eligibility criteria:** Inclusion criteria: providing data on the serum/plasma leptin levels, AdipoQ levels and relevant gene polymorphism in PC cases and control groups, having clearly diagnostic criteria for pancreatic cancer. Exclusion criteria: 1)

2) duplicates; 2) editorials, letters and comments; 3) non-human subjects; 4) not complying with the main idea of this meta-analysis; 5) missing data or in unusable format.

**Information sources:** We will search the following databases: PubMed, Embase and Cochrane Library. There will be no restriction applied based on language or the publication year. Relevant references cited in included trials will also be hand-searched.

**Main outcome(s):** The main outcomes will be: 1) abnormal leptin levels and adiponectin levels in pancreatic cancer patients compared to the control groups; 2) association of related gene polymorphism with pancreatic cancer risk; 3) dose-response of circulating leptin level and adiponectin level.

**Additional outcome(s):** Association of circulating leptin level and adiponectin level with 1) TNM stage, 2) prognosis (e.g. cachexia), 3) clinical characteristics (e.g. jaundice) in pancreatic cancer patients.

**Quality assessment / Risk of bias analysis:** The authors will evaluate each of the included studies for quality assessment, based on the Newcastle-Ottawa Scale (NOS) for observational studies and discrepancies will be resolved through discussion. The following factors will be taken into account: selection of cases and controls; comparability of cases and controls on the basis of the design or analysis; and exposure of cases and controls.

**Strategy of data synthesis:** Odds ratio (OR), relative risk (RR) and standardized mean difference (SMD) along with 95% confidence intervals (CI) will be applied and the analyses will be carried out by using a random/fixed-effects model. We will use the  $\chi^2$  test to evaluate the statistical heterogeneity between different studies.  $P > 0.1$  and  $I^2 < 50\%$  indicated low heterogeneity where a fixed effect model was used;  $P > 50\%$  indicated statistical heterogeneity where a random effect model

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was applied. All analyses will be conducted using STATA.

**Subgroup analysis:** We will perform subgroup analyses using the following variables: ethnicity, sample size, source of leptin, assay method, source of control, and method of control.

**Sensibility analysis:** The leave-one-out method (removing one study each time and repeating the analysis) will be employed, which will allow us to determine the implication of each study on the pooled effect size.

**Country(ies) involved:** 中国.

**Keywords:** Leptin, Adiponectin, Pancreatic cancer, Meta-analysis.

**Contributions of each author:**

Author 1 - Qihang Yuan contributed to the design of the study, collection and interpretation of data, and drafting and revising the manuscript.

Author 2 - Lilong Zhang participated in the design of the study, collection of data and drafting the manuscript.

Author 3 - Yao Xu participated in the design of the study, collection of data and drafting the manuscript.

Author 4 - Xu Chen was responsible for the collection and interpretation of data.

Author 5 - Biao Zhang was responsible for the collection and interpretation of data.

Author 6 - Lunxu Li was responsible for the collection and interpretation of data.

Author 7 - Shuang Li was responsible for the collection and interpretation of data.

Author 8 - Prof. Dong Shang conceived the study and reviewed/edited the manuscript.