# INPLASY PROTOCOL

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**Support:** **None.**

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

**Conflicts of interest:**
**None declared.**

# Circulating growth differentiation factor-15 concentration and hypertension risk: A dose-response meta-analysis

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**Review question / Objective:** **GDF-15 is also referred to as macrophage inhibitory cytokine-1, and is a member of the superfamily of transforming growth factors. It has been shown that GDF-15 regulates appetite, body weight, glycolipid metabolism, and infection protection. In several prospective studies, increased circulating GDF-15 levels were found to be an excellent predictor of adverse clinical outcomes, including cardiovascular events and all-cause mortality. However, GDF-15 hasn't been studied extensively to determine its ability to predict hypertension risks in the current studies. The objective of this meta-analysis was to evaluate systematically the dose-response relationship between GDF-15 and hypertension prevalence.**
**Information sources:** **Information sources will be found by searching the electronic databases Pubmed, EMBASE, and Web of Science.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 March 2023 and was last updated on 23 March 2023 (registration number INPLASY202330082).

## INTRODUCTION

**Review question / Objective:** **GDF-15 is also referred to as macrophage inhibitory cytokine-1, and is a member of the superfamily of transforming growth factors. It has been shown that GDF-15 regulates appetite, body weight, glycolipid metabolism, and infection protection. In several prospective studies, increased circulating GDF-15 levels were found to be an excellent predictor of adverse clinical outcomes, including cardiovascular events and all-cause mortality. However, GDF-15**

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hasn't been studied extensively to determine its ability to predict hypertension risks in the current studies. The objective of this meta-analysis was to evaluate systematically the dose-response relationship between GDF-15 and hypertension prevalence.

**Condition being studied:** Although no prospective studies have examined whether circulating GDF-15 contributes to hypertension, many studies have been conducted in the past decade examining the prevalence of hypertension in different populations based on the distribution of GDF-15.

## METHODS

**Participant or population:** No matter what population was studied, studies were eligible if they reported the percentage of hypertension in at least three GDF-15 categories.

**Intervention:** Circulating GDF-15 will be main Exposure/Interventions.

**Comparator:** Comparing the high versus low, or per 1 ng/mL increase in GDF-15 concentration.

**Study designs to be included:** Any study design.

**Eligibility criteria:** At least three categories of GDF-15 hypertension were required for studies to be eligible.

**Information sources:** Information sources will be found by searching the electronic databases Pubmed, EMBASE, and Web of Science.

**Main outcome(s):** The combined effects were estimated using odds ratios (ORs) and 95% confidence intervals (CIs). Furthermore, all studies included in the analysis will have dose-response curves plotted.

**Quality assessment / Risk of bias analysis:** Study quality of the included studies will be assessed using the Newcastle-Ottawa Scale (NOS) for the included studies.

**Strategy of data synthesis:** Based on heterogeneity among studies, fixed-effects or random-effects models will be used to estimate the pooled effect size.

**Subgroup analysis:** There will be a subgroup analysis based on the study region, sample size, sample types, and GDF-15 detection method used in the study.

**Sensitivity analysis:** By removing one study at a time, sensitivity analyses will be conducted to confirm the stability of the overall pooled OR.

**Country(ies) involved:** China.

**Keywords:** GDF-15; hypertension prevalence; dose-response; meta-analysis.

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