

Relationship of circulating betatrophin in patients with Nonalcoholic Fatty Liver disease (NAFLD): a systematic review and meta-analysis  
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### Citation

Fangping Wu, Yani Ke. Relationship of circulating betatrophin in patients with Nonalcoholic Fatty Liver disease (NAFLD): a systematic review and meta-analysis. PROSPERO 2020 CRD42020159432 Available from: [https://www.crd.york.ac.uk/prospero/display\\_record.php?ID=CRD42020159432](https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020159432)

### Review question

Studies on the relationship between circulating betatrophin and Nonalcoholic Fatty Liver disease

show controversial conclusions, which may confuse researchers. Our systematic review and meta-analysis aim to summarize existing literature and assess the relationship between them. Furthermore, our secondary aim is to analyze the correlation between circulating betatrophin and insulin resistance in patients with Nonalcoholic Fatty Liver disease.

### Searches

We will search some databases including PubMed, Cochrane Library, Cochrane Register of Controlled Trials (CENTRAL), EMBASE, CNKI, WANFANG and CBM, using the terms "fatty liver" (OR "NAFLD" OR "nonalcoholic fatty liver disease") AND "betatrophin" or "ANGPTL8". Furthermore, the reference lists of enrolled studies and publications with citations of included papers will also be reviewed for suitable papers. We will also contact study authors by e-mail to clarify additional studies and ask for missing data. No language limitations will be used.

### Types of study to be included

Case-control studies or cohort studies published report data on circulating betatrophin level in individuals with/without NAFLD will be included.

### Condition or domain being studied

Nonalcoholic fatty liver disease (NAFLD) is a spectrum of liver disorders. It is a condition defined by the presence of steatosis in more than 5% of hepatocytes with little or no alcohol consumption. NAFLD consists of the benign non-alcoholic fatty liver (NAFL), and the more severe non-alcoholic steatohepatitis (NASH). NASH is a more progressive form of NAFLD and is characterized by steatosis, hepatocellular ballooning, lobular inflammation and almost always fibrosis. In an effort to regenerate new cells, NASH progresses to cirrhosis with the hepatocytes replaced by scar tissues of type I collagen produced by stellate cells. Cirrhosis is an end-stage organ failure that requires liver transplantation or may lead to hepatocellular carcinoma.

### Participants/population

?We will include only studies conducted in adults (aged 18 years or older) who were diagnosed as NAFLD either by imaging or by histology.

?We will exclude those including secondary hepatic fat accumulation, such as significant alcohol consumption, use of steatogenic medication, or hereditary disorders, other known causes of liver diseases, eg virus and drugs.

### Intervention(s), exposure(s)

Individuals with NAFLD, Circulating betatrophin level, insulin resistance index.

### Comparator(s)/control

Control cases will be healthy people. In addition, patients with different levels of NAFLD will also be considered.

### Main outcome(s)

Main outcome is circulating betatrophin level in either plasma or serum.

#### \* Measures of effect

None

### Additional outcome(s)

The relationship between circulating betatrophin and insulin resistance in patients with Nonalcoholic Fatty Liver Disease.

#### \* Measures of effect

None

### Data extraction (selection and coding)

Two of the researchers will independently extract data. With the help of one researcher, we will reach a common regarding including first author's last name, publication date, country of origin, the Newcastle-Ottawa Scale (NOS), numbers of cases and controls, betatrophin levels measured method, levels of betatrophin in NAFLD group/ control group, levels of insulin resistance indexes in NAFLD group/ control group.

### Risk of bias (quality) assessment

We will evaluate the quality of the included articles by using Newcastle-Ottawa Scale (NOS) scale. The NOS consists of three dimensions including selection, comparability, and exposure which reflect in eight items. For each item, there are a series of response options. A star system is used to allow a semi-quantitative assessment of study quality. For example, the highest quality studies will be awarded a maximum of one star for each item except for those related to comparability that allows two stars. The NOS ranges from zero to nine stars.

### Strategy for data synthesis

Review manager 5.3 and Stata 15 software will be used for statistical analysis to perform meta-analysis. Heterogeneity will be checked by the  $\chi^2$  test and the  $I^2$  statistic. The criteria for identification of heterogeneity will be a P value less than 0.10 for the  $\chi^2$  test and an  $I^2$  statistic greater than 50%.

### Analysis of subgroups or subsets

Subgroup analyses will be performed by Severity of NAFLD.

### Contact details for further information

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### Organisational affiliation of the review

Zhejiang Chinese Medical University

### Review team members and their organisational affiliations

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### Type and method of review

Meta-analysis, Systematic review

### Anticipated or actual start date

NaN undefined NaN

### Anticipated completion date

NaN undefined NaN

**Funding sources/sponsors**

None

**Conflicts of interest**

None known

**Language**

English

**Country**

China

**Stage of review**

Review Ongoing

**Subject index terms status**

Subject indexing assigned by CRD

**Subject index terms**

MeSH headings have not been applied to this record

**Date of registration in PROSPERO**

28 April 2020

**Date of first submission**

21 November 2019

**Stage of review at time of this submission**

The review has not started

<b>Stage</b>	<b>Started</b>	<b>Completed</b>
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

*The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.*

*The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.*

**Versions**

28 April 2020

PROSPERO

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