

# INPLASY

## Factors contributing to NAFLD progression in a high-fat/high-fructose diet rodent model: A protocol for systematic review

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### ADMINISTRATIVE INFORMATION

**Support** - Korea Health Industry Development Institute (KHIDI).

**Review Stage at time of this submission** - Formal screening of search results against eligibility criteria.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2023110119

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 November 2023 and was last updated on 30 November 2023.

### INTRODUCTION

**Review question / Objective** The objective of this systematic review is to identify contributing factors to the progression of NAFLD, with the aim of enhancing insights for clinical and preclinical practices. To achieve this goal, the proposed systematic review will address the following questions:

1. What factors contribute to the progression of NAFLD, and what is the magnitude of their effect sizes?
2. Which diet-related factors have the greatest impact on NAFLD progression?
3. Which factor exerts a greater influence on the progression of NAFLD: fat or sugar?

**Rationale** 1. The pathogenesis of NAFLD is multifactorial, involving interindividual variations in genetic, dietary, behavioral, and environmental factors. However, it is unknown which factors have the greatest impact on NAFLD progression or how much each factor affects it.

2. Dietary intervention, including dietary restriction and modification of dietary composition, is considered the cornerstone of NAFLD treatment. Despite diet being recognized as a major contributor to both the development and progression, as well as the treatment of NAFLD, the specific composition of the diet remains insufficiently explored. Moreover, the ongoing debate surrounding high-carbohydrate versus high-fat diets in NAFLD progression continues.

**Condition being studied** NAFLD (Non-alcoholic fatty liver disease), including from simple hepatic steatosis and steatohepatitis (NASH) to liver fibrosis, stage 2.

## METHODS

### Search strategy

1. Pubmed

#1 "Non-alcoholic Fatty Liver Disease"[Mesh] OR "Nonalcoholic Fatty Liver"[TW] OR "Nonalcoholic Steatohepatitis"[TW]

#2 "Liver Cirrhosis"[Mesh] OR "Liver Fibrosis"[TW]

#3 "Diet, High-Fat"[Mesh] OR "High Fat"[TW] OR "High-Fat"[TW]

#4 "Fructose"[Mesh] OR "High Fructose"[TW] OR "High-Fructose"[TW]

Filters applied: Full text, Other animals

#1 OR #2 AND #3 AND #4

2. Cochrane library

#1 MeSH descriptor: [Non-alcoholic Fatty Liver Disease] explode all trees

#2 ("Nonalcoholic Fatty Liver" OR "Nonalcoholic Steatohepatitis"):ab,ti,kw

#3 #1 OR #2

#4 [mh "Liver Cirrhosis"] OR ("Liver Fibrosis"):ab,ti,kw

#5 #3 OR #4

#6 [mh "Diet, High-Fat"] OR ("High Fat") OR ("High-Fat"):ab,ti,kw

#7 [mh "Fructose"] OR ("High Fructose") OR ("High-Fructose"):ab,ti,kw

#8 #5 AND #6 AND #7.

**Participant or population** NAFLD rodent model.

**Intervention** High-fat and High-fructose diet.

**Comparator** N/A.

**Study designs to be included** Research articles.

**Eligibility criteria** 1. For an accurate assessment of NAFLD, articles providing information such as NAFLD activity score, fibrosis stage, increased hepatic triglyceride content, or histological assessment were included. 2. Articles providing information about calories from fats and the amount of fructose supplied.

**Information sources** Pubmed, Cochrane library, hand searching.

**Main outcome(s)** 1. Contributing factors of NAFLD progression, such as inducing period, age, fat, fructose, etc. 2. Relative effect sizes of each contributing factor.

**Quality assessment / Risk of bias analysis** 1. Quality assessment: GRADE system; 2. Risk of bias analysis: SYRCLE's risk of bias tool.

**Strategy of data synthesis** Since meta-analysis is not feasible for addressing the review question, Pearson's correlation analysis and multiple linear regression analysis will be conducted for all outcome measures. ANOVA will be conducted for comparison of 3 groups.

**Subgroup analysis** 1. NAFL, NASH, and fibrosis; 2. One with high fat intake and another with high carbohydrate intake; 3. One with fructose added to the pellet and another with fructose added to the drinking water.

**Sensitivity analysis** N/A.

**Country(ies) involved** Republic of Korea.

**Keywords** Systematic review; Nonalcoholic fatty liver disease; Fibrosis; progression; contributing factor; High fat diet; High fructose diet; rodent model.

### Contributions of each author

Author 1 - Yu-Jin Choi - Author 1 drafted the manuscript, wrote the protocol and review.

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Author 2 - Seung-Ju Hwang - The author provided data collection and management.

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