

**שם:** לורה סול גרינשפן

**שם העבודה:**

The association of ultra-processed food (UPF) consumption with non-alcoholic fatty liver disease (NAFLD), and the role of gut microbiome and genetic predisposition

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## Abstract

### **Background:**

Non-alcoholic fatty liver disease (NAFLD), which is a spectrum of diseases that occur as a result of fat accumulation in the liver, represents the most common chronic liver disease in western countries. Both genetic and environmental factors have been proposed to be implicated in the etiology of NAFLD, and nutrition is a major influencer. As of today, Ultra-processed foods (UPF) represent an important part of the western diet, and therefore studying their potential effects on health is an emerging field of research. Overall, evidence accumulated shows that UPF consumption increases the risk of obesity, several diet-related noncommunicable diseases, and also premature mortality. However, outcomes of NAFLD, liver fibrosis and steatosis were not investigated in the context of UPF consumption as a group. Moreover, the association between the combination of UPF consumption, genetic predisposition, microbiome, and NAFLD has not been investigated yet.

### **Aim:**

To evaluate the association between UPF consumption with NAFLD, and the role of the gut microbiome and genetic predisposition among men and women who live in the center of Israel that were followed for 5 or more years.

### **Methods:**

- a) a prospective cohort study among about 350 participants, men, and women, living in the center of Israel, who underwent a colonoscopy and volunteered to participate in a metabolic screening at the Tel-Aviv medical center (convenient sampling). All the data was gathered at the baseline survey in 2010-2015, and once again at the follow-up survey nowadays. The dependent variables - NAFLD, liver fibrosis and amount of steatosis, will be measured by noninvasive diagnostic methods (serum biomarkers and imaging techniques). The independent variable -UPF consumption, will be measured by a selfreported food frequency questionnaire (FFQ) adapted from the Israeli ministry of the health survey, and classified

according to NOVA food classification. The cohort will include a cumulative incidence of NAFLD and fibrosis. In addition, trajectories in steatosis, fibrosis and UPF consumption will be measured.

- b) a cross-sectional study conducted on the data collected in the follow-up survey for the elaboration of the association (with additional variables - genetics and microbiome). The surveys will also include blood and stool tests (the latter only in follow-up), alongside medical history questionnaires to identify variables that may be confounders, mediators or modifiers. The association between UPF consumption and NAFLD will be analyzed using multiple logistic regression models adjusted for potential confounding factors.

### **Importance of the study:**

To the best of our knowledge, this study will be the first to prospectively test potential associations between UPF consumption and NAFLD. This study may help in understanding relations between diet, microbiome, genetic background and NAFLD. By that, it will provide the basis of knowledge for future research, and support practical nutritional recommendations for the prevention and treatment of highly prevalent liver disease.