INTRODUCTION
- Polypharmacy is common among patients with nonalcoholic fatty liver disease (NAFLD).
- Relationships among polypharmacy, potential drug induced liver injury (DILI), elevated liver enzymes, and severity of liver disease are unclear.

OBJECTIVE
- This study evaluated patterns of medication use by liver disease severity and the association between medication use and serum ALT elevation.

METHODS
Cohort
- TARGET-NASH is an ongoing longitudinal, observational cohort of >3,700 patients with NAFLD managed according to local practice standards at 55 academic and community sites in the United States.
- Patient narratives, laboratory, pathology, and imaging data are extracted and stored in a secure database. Patient reported outcomes (PRO) measures as well as blood samples were collected annually.

Study Population
- 3,284 patients ≥ 18 years enrolled in TARGET-NASH between August 2016 and October 2018 were included in the study.

Variable Definitions
- Patients were classified by:
  - Severity of liver disease (NAFLD Cirrhosis, NASH, NAFL).
  - Serum ALT levels ≤ 50 U/L or >50 U/L at enrollment.
  - Medication use: Any use of medications by at least 10% of patients within one year of enrollment.

Statistical Methods
- Patterns of medication use were estimated within severity of liver disease using hierarchical cluster analysis.
- The odds of ALT elevation and 95% confidence intervals were estimated by medication class.

RESULTS
Patient Characteristics at enrollment
- 3,284 patients ≥ 18 years
  - 39% NAFLD cirrhosis, 40% NASH, and 21% NAFL
  - Median age was 56.9 years, and median BMI was 33.2 kg/m²
  - 59% were female
  - 66% were receiving treatment at academic sites
  - 59% had private insurance, 32% had Medicare, and 13% had Medicaid
  - 74% were White, 5% were African American, and 12% were Hispanic.
- Multiple medications were associated with a decrease in the odds of having an ALT > 50 U/L (Figure 1).
  - Users of statins were 38% less likely to have an ALT > 50 U/L.
  - Vitamin D was also associated with a 27% decrease in the odds of higher ALT level.

CONCLUSIONS
- Understanding the association between medication use and ALT levels may allow the identification of subtle and otherwise unappreciated effects of medications on NAFLD.
- Among patients with NAFLD, statins and anti-diabetic medications reduced the odds of having an ALT > 50%.
- Further research is needed to determine causality and the direction of the associations among specific medications and ALT levels.

Figure 2: Hierarchical Clustering of Medication Use Among People with NAFLD Cirrhosis

A) NAFLD Cirrhosis with ALT ≤ 50
- Two distinct clusters:
  - Beta blockers, vitamin D, PPI, aldosterone and non-aldosterone diuretics.
  - Ace inhibitors, salicylates, statins, insulin, and metformin.

B) NAFLD Cirrhosis with ALT > 50
- Four distinct clusters:
  - Pain medications/mental health medications.
  - Medications for portal hypertension (beta-blockers and diuretics).
  - Medications for the metabolic syndrome.
  - Anti-oxidants.