

## INTRODUCTION

- Among NAFLD patients with metabolic syndrome, the most common cause of death is arteriosclerotic cardiovascular disease (ASCVD)
- Although statins are considered safe in liver disease and even potentially beneficial in cirrhosis, many patients are not prescribed a statin due to concerns of hepatic enzyme elevations.
- We aim to determine whether statins are under prescribed in NAFLD patients with indications for lipid-lowering agents and whether this effect is modified in patients with cirrhosis.

## METHODS

### Cohort

- TARGET-NASH is an ongoing longitudinal, observational cohort of > 3,700 patients with NASH managed according to local practice standards at 55 academic and community sites in the United States.
- Participating clinics provided redacted medical records (structured and unstructured data) from consented patients. Patient narratives, laboratory, pathology, and imaging data were extracted and stored in a secured database. Patient reported outcome (PRO) measures were also collected on an annual basis at select sites. Patients contributed blood samples to a biospecimen repository for biomarker validation and translational research.

### Patient Population

This sub-cohort included 3,284 patients ≥ 18 years old with a diagnosis of NAFLD enrolled in TARGET-NASH between August 1, 2016 and October 4, 2018.

Patients were stratified into: NAFLD Cirrhosis, NASH, and NAFL.

### Clinical Case Definition of NAFLD

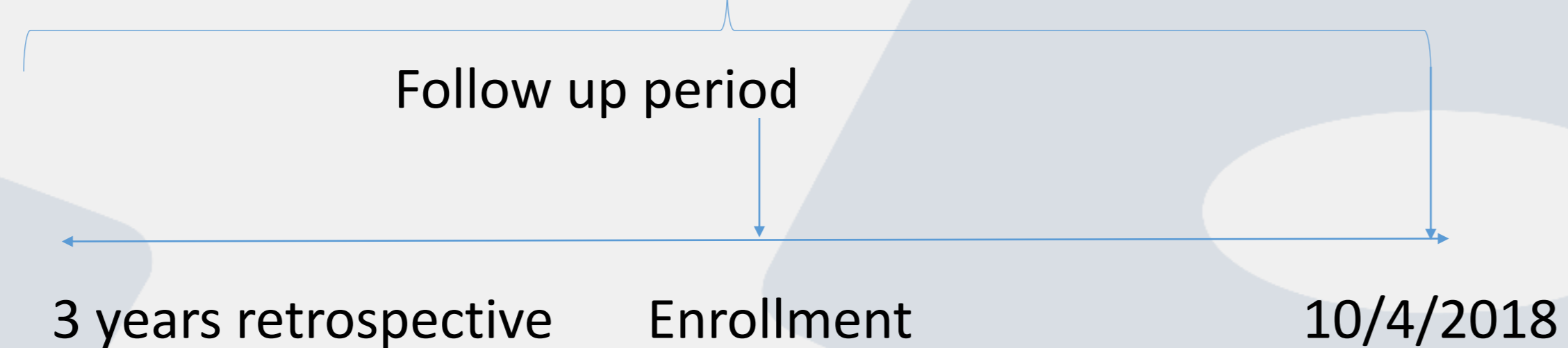
NAFLD Cirrhosis	NASH	NAFL
History of NAFLD with: 1) Liver biopsy with fibrosis stage = 4 OR 2) Liver biopsy with fibrosis stage = 3 and ≥ 1 clinical sign of cirrhosis OR 3) 2 or more clinical signs of cirrhosis OR 4) FibroScan® elastography result ≥11 kPa	Confirmed by biopsy: • Steatohepatitis by Brunt criteria OR NAS total score ≥4 Clinical diagnosis: • ALT > 19 U/L for adult female (22 child), > 30 U/L for adult male (26 child) and; • Hepatic steatosis on biopsy or CT/US/MRI and; • 1 of the following: BMI ≥30, type II diabetes, dyslipidemia	Any participant not meeting criteria for clinical NASH or cirrhosis

## Statistical Analysis

Indication for statin therapy was defined as one or more of the following:

- Clinical ASCVD
- LDL ≥ 160 mg/dL
- Diabetes
- 10-year ASCVD risk at enrollment ≥ 7.5%

Statin use was defined as any use documented in the electronic medical record during the follow up period:



## RESULTS

- 58.6% of NAFLD patients had one or more indications for lipid lowering therapy
- 61.1% of patients with an indication were prescribed a lipid lowering medication
- Men (65.6% vs 59.9%), patients ≥ 40 (64.0% vs 31.3%), those with any CV disease history (74.4% vs 59.3%) and those with a CV event (79.7% vs 59.4%) were more likely to be prescribed a statin.
- Similar proportions of patients managed in academic and community centers, 62.4% and 61.5%, of those with indications were prescribed a statin.
- Statins were used in 65% of those prescribed lipid lowering therapy.

Figure 1. Characteristics of Patients with NAFLD Receiving a Statin

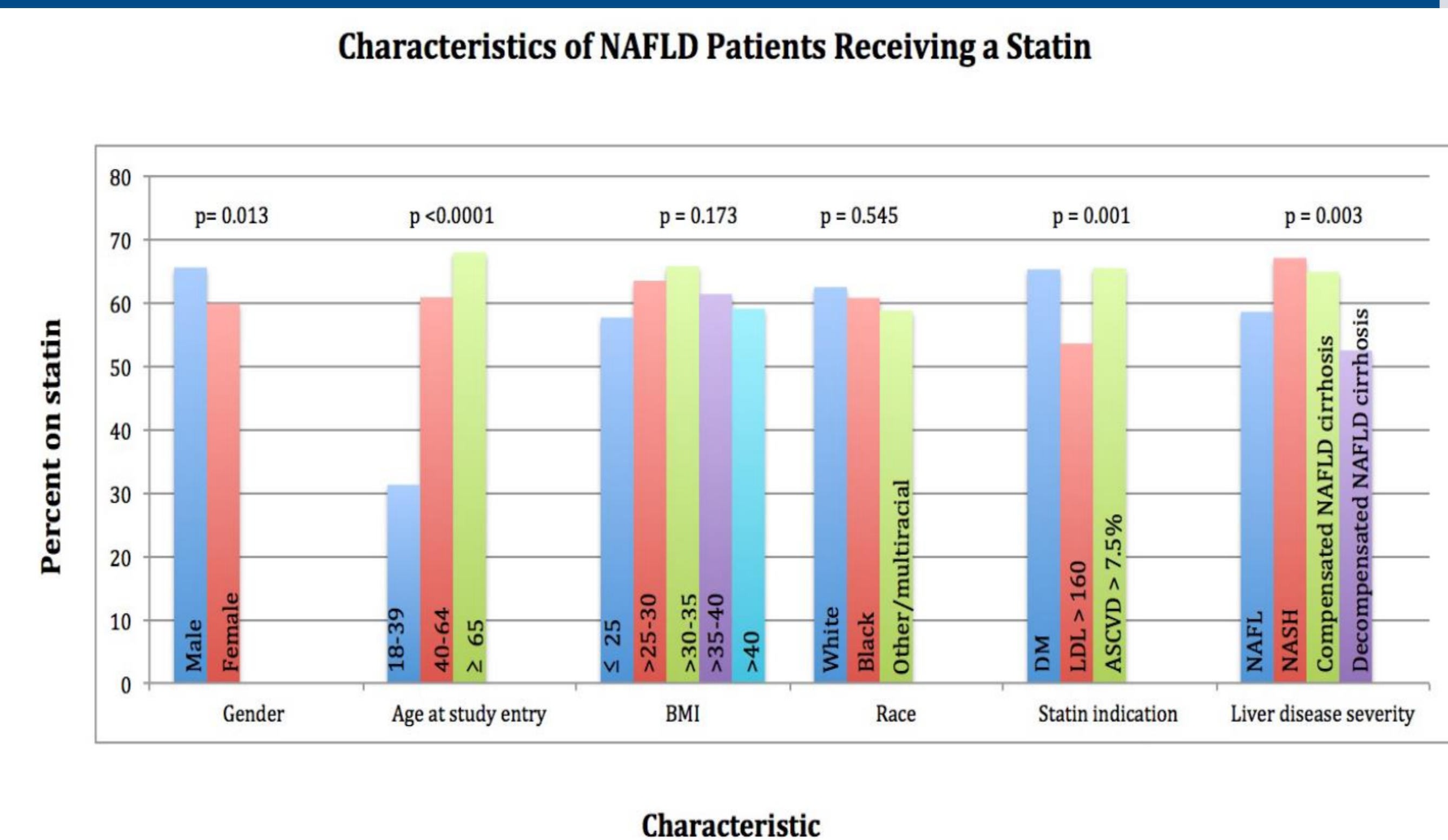


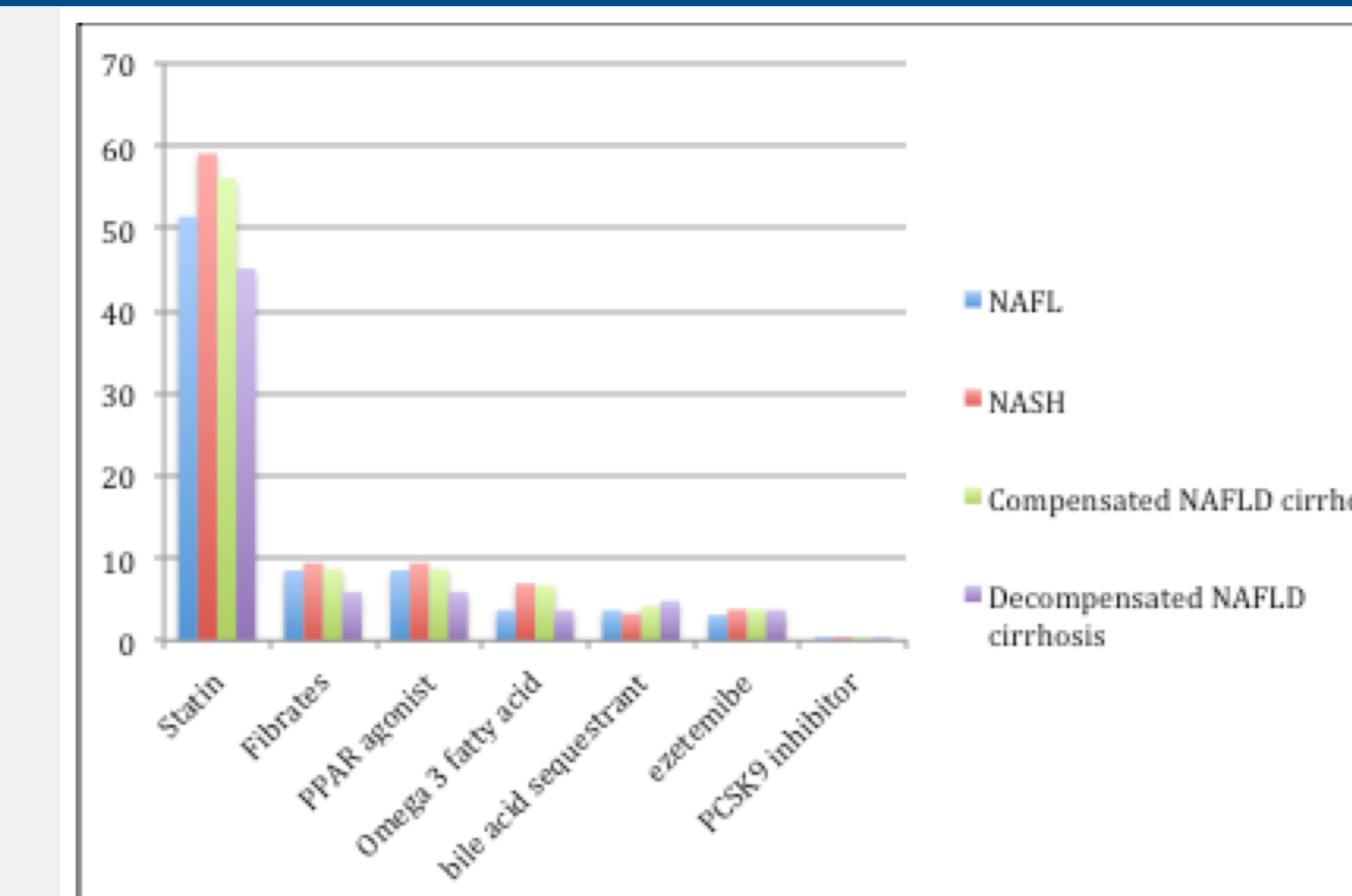
Table 1. Descriptive characteristics of the patients with NAFLD

Patient Characteristics	NAFLD Cirrhosis (N=1279)	NASH (N=1317)	NAFL (N=688)	p-value
	N(%)	N(%)	N(%)	
Statin Status				
Statin Use	480 (37.5)	510 (38.7)	196 (28.5)	
No Statin use	799 (62.5)	807 (61.3)	492 (71.5)	
Not Available	-	-	-	<0.0001
Age at Study Entry; Mean (SD)	60.8 (10.2)	53.6 (14.0)	56.1 (13.7)	<0.001
Gender				
Male	523 (40.9)	816 (62.0)	363 (52.7)	
Not Available	5 (0.39)	6 (0.46)	2 (0.29)	0.0003
Race				
White	1117 (87.3)	941 (71.5)	374 (54.4)	
Black	34 (26.6)	89 (6.8)	50 (72.6)	
Other	89 (7.0)	222 (16.9)	224 (32.6)	
Not Available	39 (3.0)	65 (4.9)	40 (5.8)	<0.0001
BMI (kg/m <sup>2</sup> ); Mean (SD)	34.7 (7.5)	33.5 (7.4)	30.3 (7.4)	<0.0001
History of Coronary Artery Disease				
Yes	122 (9.5)	66 (5.0)	31 (4.5)	
Not Available	-	-	-	<0.0001
Diabetes Mellites				
Yes	875 (68.4)	548 (41.6)	169 (24.6)	<0.0001
Not Available	-	-	-	
On ASA				
Yes	349 (27.3)	334 (25.4)	147 (21.4)	
Not Available	-	-	-	0.0157
Smoking Status				
Never	99 (7.7)	94 (7.1)	52 (7.6)	
Current	634 (49.6)	771 (58.5)	403 (58.6)	
Former	376 (29.4)	320 (24.3)	134 (19.5)	
Not Available	170 (13.3)	132 (10.0)	99 (14.4)	<0.0001

Table 2. Median Laboratory values of patients with NAFLD

Patient Characteristics	NAFLD Cirrhosis (N=1279)	NASH (N=1317)	NAFL (N=688)	p-value
Total cholesterol	162	182	183	<0.0001
HDL	43.0	44.0	48.0	<0.0001
LDL	90.0	103.0	105.0	<0.0001
Triglycerides	129.0	148.0	125.0	<0.0001
AST	38.0	30.0	23.0	<0.0001
ALT	33.0	41.0	26.0	<0.0001
HBA1c	6.5	6.2	6.0	0.0007

Figure 2. Percent of patients treated with Lipid lowering agents used in TARGET-NASH Participants with Indications for Treatment



## CONCLUSIONS

- Statins and other lipid-lowering agents are underprescribed in adult patients with NAFLD despite clear indications, particularly in those with decompensated cirrhosis.
- Underprescribing is common among women and younger patients.
- A shift in treatment paradigm is essential to ensure optimal use of statins and other lipid lowering agents in patients with NAFLD to reduce cardiovascular outcomes.
- For practitioners who still have reservations about statin use, alternative lipid lowering agents may be considered as above.

## ACKNOWLEDGEMENTS

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