

USING REAL WORLD DATA TO EXAMINE TRIGLYCERIDES, LDL, AND HDL CHOLESTEROL AS PREDICTORS OF PROGRESSION FROM NASH TO HCC AND LIVER CIRRHOSIS



TriNetX

Seth Kuranz¹, Sierra Luciano¹, Stephan Palm¹

¹TriNetX, Inc., Cambridge, MA, United States

OBJECTIVES

The aims of this study were to:

1. Examine changes in triglycerides (TGs), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol after a diagnosis of nonalcoholic steatohepatitis (NASH).
2. Measure the incidence of liver cirrhosis (LC) and hepatocellular cancer (HCC) by lipid type.

METHODS

Patients with a laboratory measure for triglycerides, LDL-, or HDL-cholesterol in the year prior to their first diagnosis of NASH (ICD-10 code K75.81; defined as baseline period) were identified through TriNetX, a large electronic medical record network (Figure 1). Mean values for each lipid were assessed in the 1st, 2nd, and 3rd year after the first NASH diagnosis. LC and HCC incidence were measured in patients with consistently abnormal and normal baseline values. Risk ratios (95 CIs) compared triglyceride (150+ vs <150 mg/dL), HDL (<60 vs 60+ mg/dL), and LDL (130+ vs <130 mg/dL) values, adjusting for confounding using a 1:1 matched greedy-nearest-neighbor propensity score model. ICD-10/9, RxNorm and LOINC codes captured all variables.

RESULTS

Patients with and LDL, HDL, and/or TG lab measures at baseline did not differ by age or gender (Table 1). After the incident diagnosis of NASH, the mean TG values increased monotonically, LDL values decreased monotonically, and HDL values remained stable (Figure 2). In each lipid category, 20% of patients had a lipid measure after three years. Patients in highest categories decreased most across all three lipids (Figures 3).

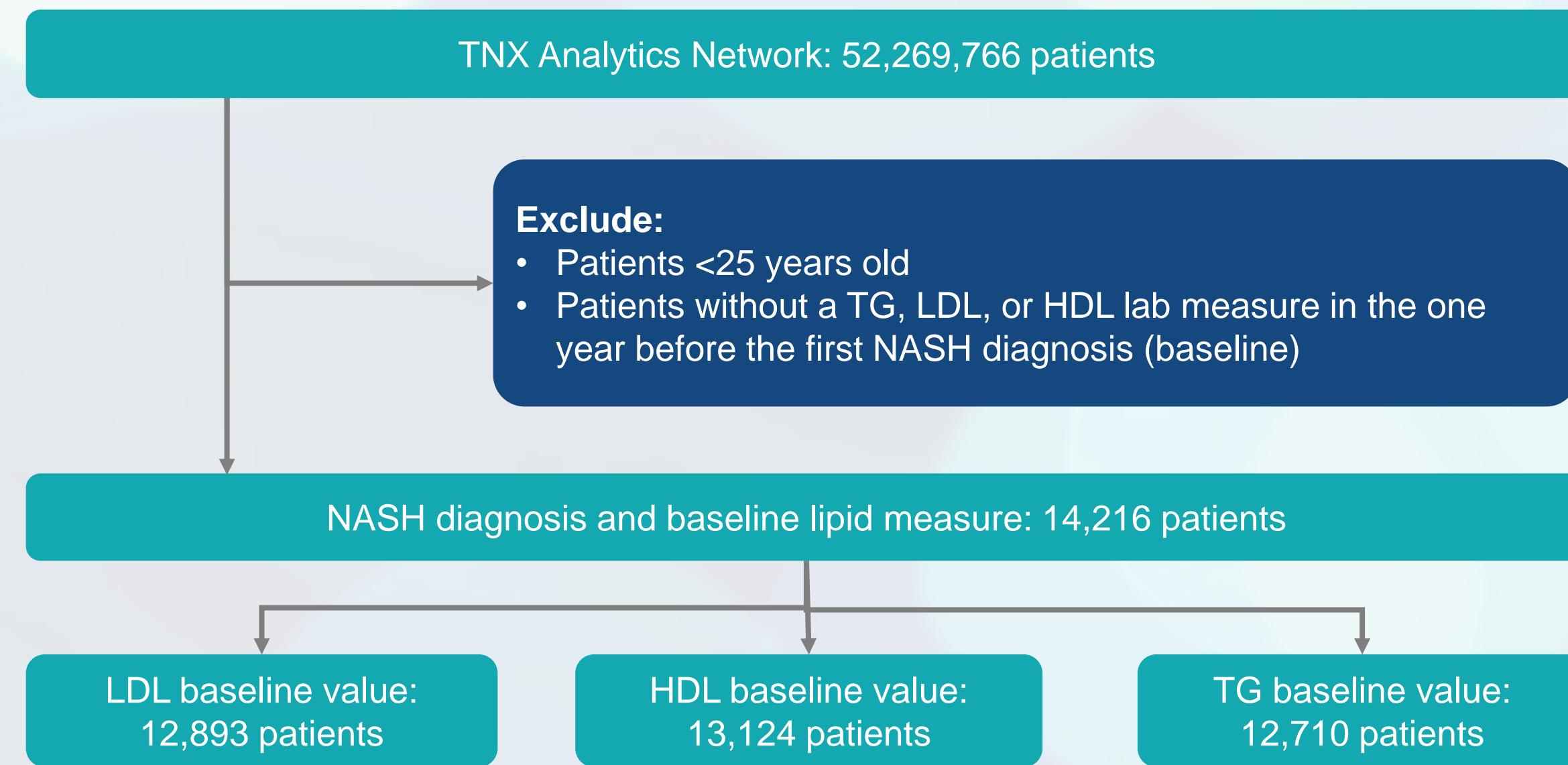


Figure 1. Patient flow diagram

Table 1. Demographics at time of incident NASH diagnosis, by lipid

	Age		Female
	Mean	SD	Percentage
LDL	56.8	12.7	55
HDL	56.7	12.7	55
TGs	56.6	12.7	55

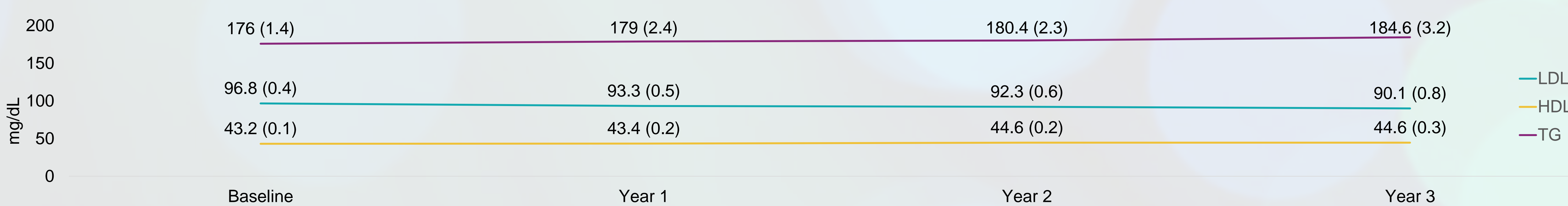


Figure 2. Changes in mean (SE) lipid levels from baseline to years 1, 2, and 3 following the incident NASH diagnosis

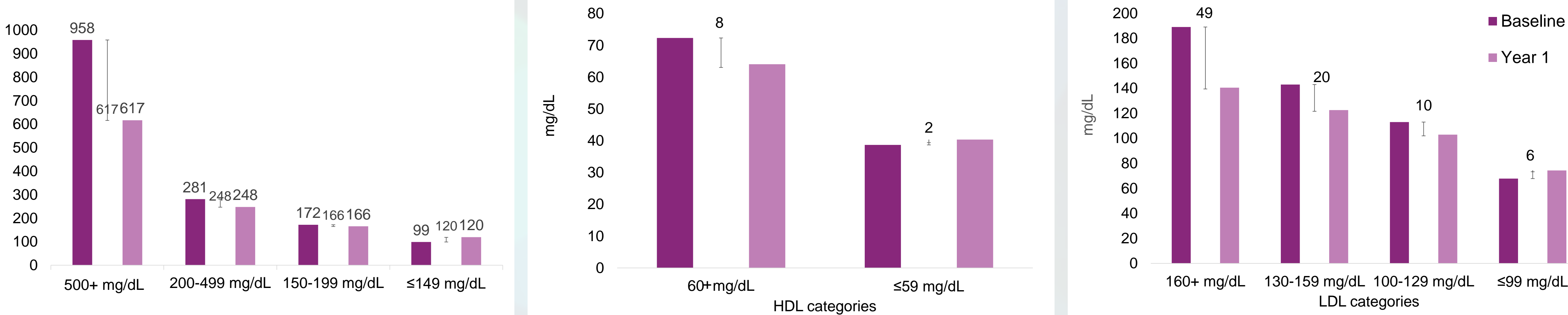


Figure 3. Changes in mean lipid values between baseline and year 1 after incident NASH diagnosis, by lipid categories

Note: p<0.01 for all baseline-to-year-1 comparisons

Table 2. Baseline patient characteristics before and after matching for each set of normal and abnormal lipids

Note: standardized mean differences <10% after matching for all comparisons except mean ALT.

	LDL				HDL				TG			
	Before Matching		After Matching		Before Matching		After Matching		Before Matching		After Matching	
	130+ mg/dL	<130 mg/dL	130+ mg/dL	<130 mg/dL	<60 mg/dL	60+ mg/dL	<60 mg/dL	60+ mg/dL	150+ mg/dL	<150 mg/dL	150+ mg/dL	<150 mg/dL
Total (N)	2,305	10,588	2,303	2,303	11,744	1,380	1,378	1,378	5,766	6,944	2,086	2,086
Digestive system surgery (%)	38	42	38	36	41	41	42	41	39	42	43	43
Antilipemic agents (%)	42	48	42	40	48	47	47	47	54	40	54	53
Diuretics (%)	40	50	40	39	45	45	44	44	44	50	48	46
Antiarrhythmics (%)	39	45	39	37	49	40	38	40	44	44	46	45
Beta blockers (%)	32	43	32	31	42	38	36	38	41	42	43	42
ACE inhibitors (%)	27	36	27	26	35	32	32	32	37	31	39	38
Overweight/obesity (%)	47	50	47	45	54	41	42	41	55	49	52	51
Diabetes mellitus (%)	35	56	35	34	52	40	42	40	51	47	48	47
Abnormal glucose (%)	23	23	23	22	34	34	34	34	25	42	27	27
Fibrosis and cirrhosis of liver (%)	21	37	21	22	24	21	20	21	25	20	27	26
Hyperglycemia (%)	6	7	6	6	7	6	5	6	7	6	7	7
History of metabolic disease (%)	3	3	3	3	3	4	4	4	3	2	3	3
Mean ALT (U/L) / (SD)	71.9 (81.5)	53.6 (65.7)	72.0 (81.5)	60.1 (65.8)	57.6 (68.8)	54.9 (65.8)	53.1 (48.8)	54.9 (65.9)	64.7 (71.1)	51.1 (70.0)	62.0 (72.6)	56.2 (78.0)
Mean AST (U/L) / (SD)	57.2 (60.1)	50.2 (131.0)	57.2 (60.1)	51.1 (75.6)	51.0 (23.0)	55.6 (92.6)	50.2 (43.9)	55.6 (92.7)	51.9 (57.0)	52.5 (163.6)	51.5 (63.6)	51.5 (93.7)

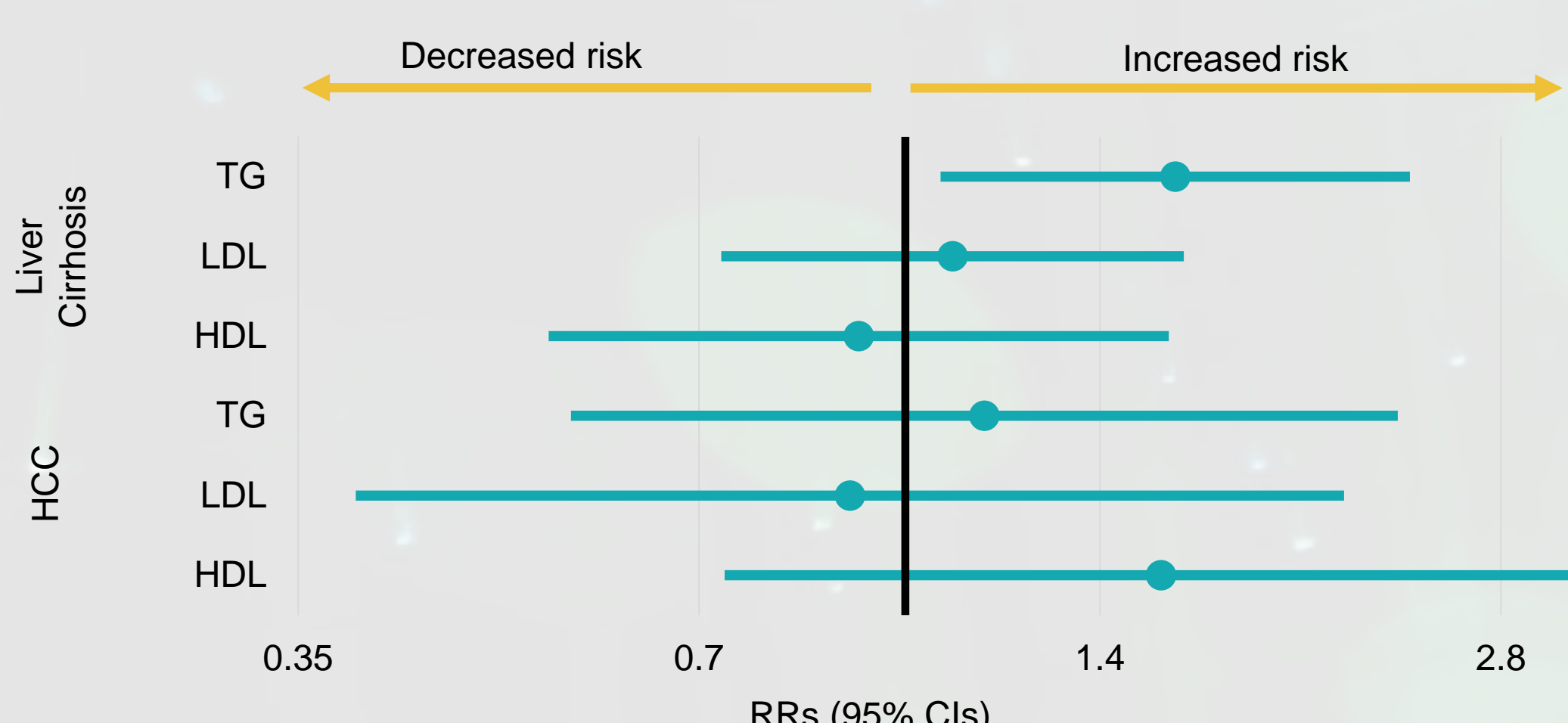


Figure 4. The risk of liver cirrhosis and HCC comparing abnormal to normal lipid levels

RESULTS

After matching, patient characteristics in all three sets of lipid cohorts were similar with a standardized mean differences <10% (Table 2). After adjusting for comorbidities and baseline medications, patients with abnormal TG were 1.6 (1.1-2.4) times as likely to develop LC. Patients with abnormal HDL, were 1.6 (0.7-3.3) times as likely to develop HCC. Other models did not predict progression.

CONCLUSIONS

Mean TG values increased in the 3-years following an incident NASH diagnosis and elevated TG at baseline predicted progression to LC. Although not statistically significant, patients with abnormal HDL had an increased risk of HCC. Robust laboratory data provides real world evidence to support studies demonstrating TG to be a marker for disease progression and interventions in NASH patients.