SUPPLEMENTAL MATERIALS:

Table S1: Baseline and week 8 estimates of dietary intakes in the sub-sample who completed the stable isotope tracers protocol to assess hepatic *de novo* lipogenesis (n=29)

		Control (n=13)		Treatment (n=16)		
Variable	**Time**	**LS-Mean[A]**	**95% CI**	**LS-Mean[A]**	**95% CI**	**Adj. Week 8 Mean Difference (95% CI)[B]**
Total Energy Intake (kcal/d)	Baseline	1952	1114	1472	422	
	Week 8	1763	626	1761	384	206 (-58 to 469)
Total Fat Intake (% TEI/d)	Baseline	33.5	4.3	31.1	4.9	
	Week 8	32.9	5.1	36.1	7.7	3.8 (-1.2 to 8.7)
Total Protein Intake (% TEI/d)	Baseline	17.8	3.7	19.9	3.3	
	Week 8	17.6	3.6	22.6	3.8	4.5 (1.5 to 7.6)
Total CHO Intake (% TEI/d)	Baseline	46.8	8.6	49.9	4.9	
	Week 8	50.6	6.0	42.8	9.9	-8.1 (-14.6 to -1.5)
Free Sugar Intake (% TEI/d)	Baseline	13.1	8.0	9.9	5.2	
	Week 8	11.8	6.8	1.1	0.9	-10.2 (-13.8 to -6.5)

[A] Estimated from mixed models adjusted for study site. Degrees of freedom were estimated using the Kenward-Roger method and standard errors were estimated by an unstructured covariance structure.

[B] Estimated from mixed models adjusted for study site and baseline. Week 8 mean difference is calculated as predicted hepatic DNL in the treatment group at week 8 – control group at week 8.

Abbreviations: kcal, kilocalories; TEI, total energy intake; CHO, carbohydrate.

Table S2: Baseline and week 8 estimates of secondary variables in the sub-sample who completed the stable isotope tracers protocol to assess hepatic *de novo* lipogenesis (n=29)

		Control (n=13)		Treatment (n=16)		
Variable	**Time**	**LS-Mean[A]**	**95% CI**	**LS-Mean[A]**	**95% CI**	**Adj. Week 8 Mean Difference (95% CI)[B]**
Hepatic Fat (MRI-PDFF)	Baseline	19.5	(14.0, 25.1)	25.5	(20.6, 30.4)	
	Week 8	18.8	(13.1, 24.5)	17.9	(12.8, 22.9)	-6.3 (-10.1 to -2.6)
ALT (U/L)	Baseline	83.3	(43.3, 123.4)	125.3	(89.5, 161.1)	
	Week 8	83.3	(49.3, 117.2)	77.7	(48.1, 107.3)	-34.9 (-61.3, -8.3)
AST (U/L)	Baseline	47.5	(25.8, 69.1)	62.4	(43.0, 81.8)	
	Week 8	45.6	(29.7, 61.4)	39.6	(25.7, 53.4)	-15.1 (-27.0, -3.3)
GGT (mg/dL)	Baseline	46.2	(29.4, 63.0)	51.8	(36.7, 66.8)	
	Week 8	47.7	(36.1, 59.3)	35.7	(25.5, 45.9)	-15.4 (-22.9, -7.8)
Glucose (mg/dL)	Baseline	86.7	(81.5, 91.8)	91.2	(86.6, 95.8)	
	Week 8	91.9	(87.2, 96.6)	85.1	(81.2, 89.1)	-8.7 (-14.3, -3.0)
Insulin (uIU/mL)	Baseline	35.5	(25.5, 45.5)	44.3	(35.3, 53.3)	
	Week 8	37.0	(29.2, 44.7)	34.7	(28.1, 41.3)	-7.4 (-14.1, -0.7)
Triglycerides (mg/dL)	Baseline	150.3	(109.6, 191.1)	145.9	(109.5, 182.4)	
	Week 8	161.8	(129.3, 194.4)	117.9	(89.3, 146.4)	-41.0 (-0.63, -18.4)
Total Cholesterol (mg/dL)	Baseline	164.0	(143.0, 185.0)	163.6	(144.9, 182.3)	
	Week 8	166.5	(147.0, 186.1)	145.6	(128.5, 162.7)	-20.6 (-33.8, -7.5)
LDL Cholesterol (mg/dL)	Baseline	102.5	(86.1, 118.9)	101.8	(87.2, 116.4)	
	Week 8	102.7	(86.7, 118.8)	89.1	(75.1, 103.0)	-13.1 (-26.1, -0.2)
HDL Cholesterol (mg/dL)	Baseline	39.1	(35.2, 43.1)	40.2	(36.7, 43.7)	
	Week 8	39.0	(34.7, 43.3)	38.3	(34.6, 42.1)	-1.7 (-4.6, 1.3)
Weight (kg)	Baseline	83.3	(70.7, 96.9)	91.1	(79.9, 102.3)	
	Week 8	83.9	(71.5, 96.3)	89.7	(78.6, 100.8)	-1.9 (-3.7, -0.1)

[A] Estimated from mixed models adjusted for study site. Degrees of freedom were estimated using the Kenward-Roger method and standard errors were estimated by an unstructured covariance structure.

[B] Estimated from mixed models adjusted for study site and baseline. Week 8 mean difference is calculated as predicted hepatic DNL in the treatment group at week 8 – control group at week 8.

Abbreviations: MRI-PDFF, magnetic resonance imaging-proton density fat fraction; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, g-glutamyl transferase; LDL, low density lipoprotein; HDL, high density lipoprotein.

Table S3: Percent changes in key variables during the 8 week intervention in the sub-sample who completed the stable isotope tracers protocol to assess hepatic *de novo* lipogenesis (n=29), overall and by treatment group

	Full Sample (n=26)		Control (n=10)[a]		Treatment (n=16)		p-value [b] (Control vs. Treatment)
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Hepatic DNL	-19.89	39.42	-3.47	42.50	-30.15	34.84	0.094
Free sugar (% TEI/d)	-54.61	59.01	0.19	64.12	-88.86	9.09	0.002
Hepatic fat (MRI-PDFF)[c]	-19.98	27.10	-2.77	21.74	-31.46	24.55	0.007
ALT (U/L)	-20.10	41.31	8.93	49.71	-38.25	21.18	0.016
AST (U/L)	-19.93	31.87	-1.86	38.73	-31.23	20.95	0.047
GGT (mg/dL)	-12.17	26.07	6.11	28.47	-23.59	16.85	0.003
Glucose (mg/dL)	-1.80	10.12	5.01	4.22	-6.07	10.48	0.001
Insulin (uUI/mL)[d]	-5.04	35.40	12.15	36.86	-16.50	30.39	0.045
Triglycerides (mg/dL)	-5.09	25.90	8.86	28.61	-13.81	20.40	0.027
Total-Cholesterol (mg/dL)	-6.84	10.69	-0.56	12.53	-10.76	7.31	0.015
LDL-Cholesterol (mg/dL)	-8.15	16.41	-1.65	19.36	-12.21	13.35	0.112
HDL-Cholesterol (mg/dL)	-3.54	8.22	-2.28	8.66	-4.33	8.13	0.547
Weight (kg)	-0.54	2.73	0.85	1.67	-1.42	2.94	0.037

[a] In the control group, n=2 participants were missing DNL at week 8 and n=1 had an outlier value for % change DNL (+480%) and were excluded from all analyses.
[b] p-values calculated using Student's t-test comparing the mean percent change for each variable in the control vs. treatment group.
[c] In the treatment group, n=1 participant was missing hepatic fat at week 8 and was excluded from analyses in this row.
[d] In the treatment group, n=1 was missing insulin at week 0 and was excluded from analyses in this row.

Abbreviations: TEI, total energy intake; MRI-PDFF, magnetic resonance imaging-proton density fat fraction; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, g-glutamyl transferase; LDL, low density lipoprotein; HDL, high density lipoprotein.

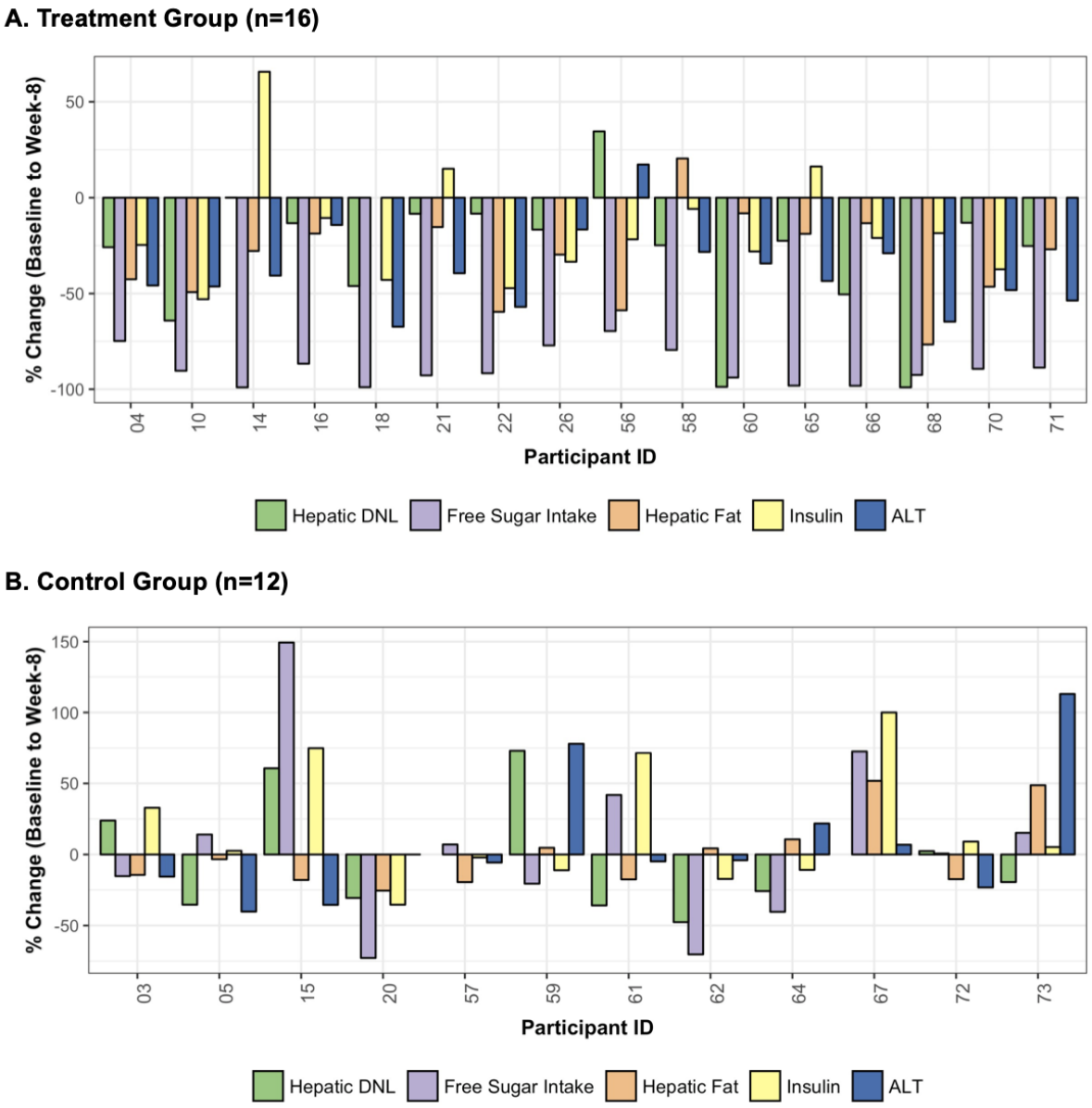

Figure S1: Percent changes in hepatic DNL, free sugar intake, hepatic fat (MRI-PDFF), fasting insulin, and ALT after the 8-week dietary intervention. (A) Treatment Group. (B) Control Group. In the figure, 2 participants in the control group were missing % change DNL (#57 and #67); 1 participant in the treatment group was missing % change in MRI-PDFF (#18); and 1 participant in the treatment group was missing % change in insulin (#71) due to missing values at baseline or week 8 for each variable. One outlier participant in the control group with a +480% change in hepatic DNL was excluded from the figure. Abbreviations: DNL, *de novo* lipogenesis; MRI-PDFF, magnetic resonance imaging-proton density fat fraction; ALT, alanine aminotransferase.

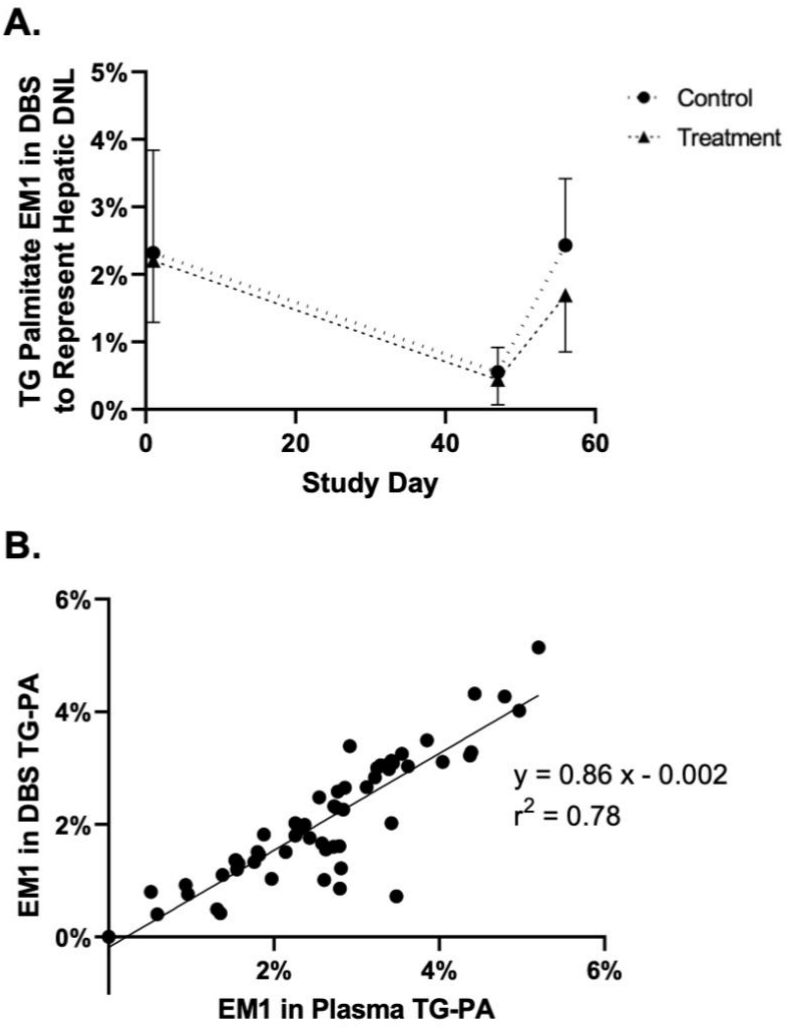

Figure S2: (A) Isotopic enrichment in TG-PA from DBS samples representing hepatic DNL following labeling with heavy water. (B) Scatter plot of the correlation between TG-palmitate enrichment in plasma versus TG-palmitate enrichment in dried blood spots. Abbreviations: DBS=dried blood spot; PA=palmitate; TG=triglyceride; EM1=enrichment of the M1 isotopomer.

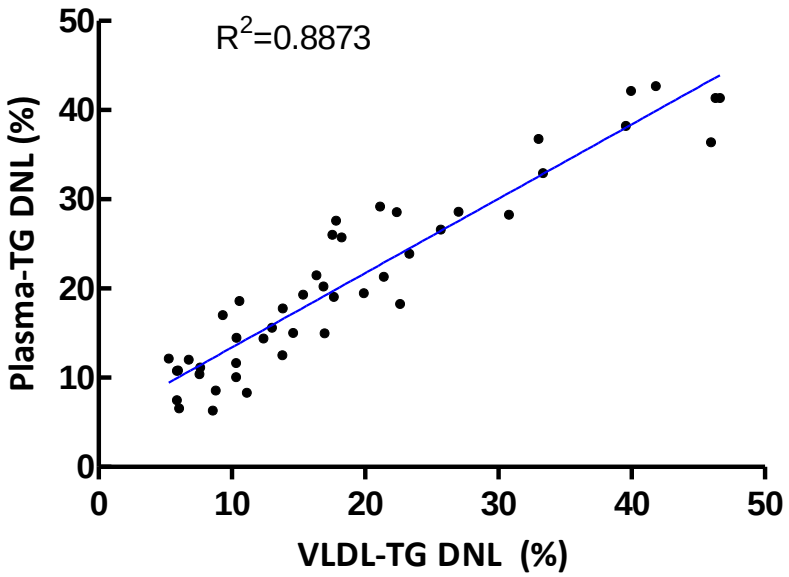

Figure S3: Scatter plot showing correlations between DNL (%) results measured in VLDL-TG and plasma-TG based on n=10 healthy adult participants (50% male; mean age 27.7±5.3 years old) (Hellerstein, Beysen, & Li; unpublished observations). Isolation of VLDL by ultracentrifugation is labor intensive; therefore, in our previous work, we compared the DNL contribution of VLDL-TG to that of total plasma TG (no ultracentrifugation). The two measurements were found to be strongly correlated (correlation coefficient=0.94), supporting the conclusion that DNL measured from fasting state total plasma TG closely resembles DNL measured from VLDL-TG. Abbreviations: DNL, de novo lipogenesis; VLDL, very low density lipoprotein; TG, triglycerides.

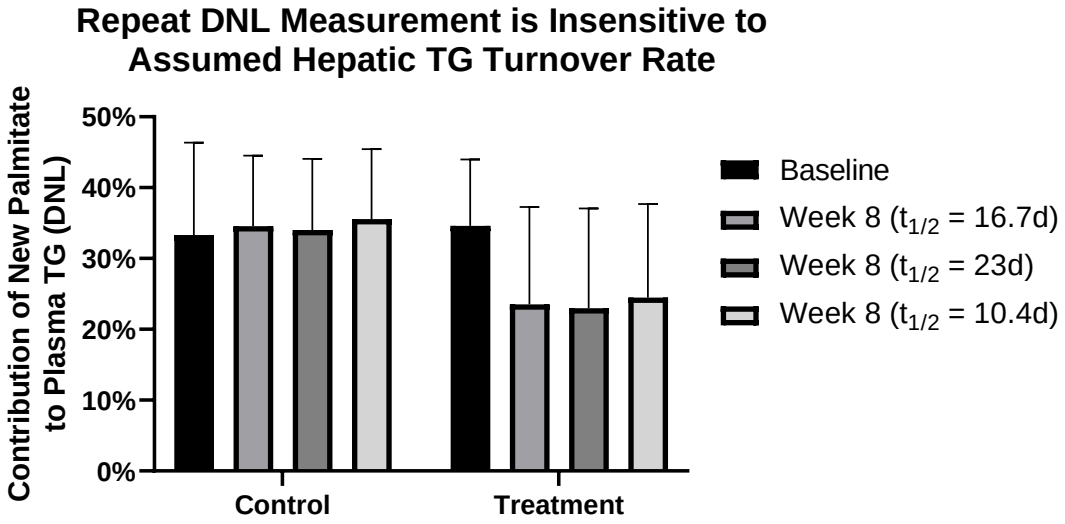

Figure S4: Parameter sensitivity of the repeat DNL calculation on the assumed decay rate ($t_{1/2}$) of the residual label from the previous labeling period. DNL at week 8 was first calculated assuming hepatic TG turns over with a $t_{1/2}$ of 16.7 days, the average value previously observed in adult NASH patients (Smith et al; 2020). DNL at week 8 was calculated again using hepatic TG turnover half-lives that were a standard deviation higher or lower. Despite altering the assumed half-life by 38% in either direction, calculated DNL at Week 8 only changed by 2 to 4% in both the control and treatment groups, indicating that the calculation is relatively insensitive to this particular parameter within the pathophysiological range observed in adult NASH. Abbreviations: DNL, de novo lipogenesis; TG, triglyceride.