

Supplementary Table 1 Search strategies

Database	Search	Items Found
Pubmed	(((((((Non-alcoholic Fatty Liver Disease [Mesh]) OR (Non alcoholic Fatty Liver Disease)) OR (Fatty Liver, Nonalcoholic)) OR (Fatty Livers, Nonalcoholic)) OR (Fatty Livers, Nonalcoholic)) OR (Liver, Nonalcoholic Fatty)) OR (Nonalcoholic Steatohepatitis)) OR (Steatohepatitides, Nonalcoholic)) AND (“AKR-001” [Supplementary Concept]) OR (Efruxifermin))	20
Embase	('Non-alcoholic Fatty Liver Disease'/exp OR 'Non-alcoholic Fatty Liver Disease' OR 'Fatty Liver, Nonalcoholic' OR 'Fatty Livers, Nonalcoholic' OR 'Liver, Nonalcoholic Fatty' OR 'Nonalcoholic Steatohepatitis' OR 'Steatohepatitides, Nonalcoholic') AND ('AKR-001'/exp OR 'Efruxifermin')	68
Scopus	TITLE-ABS-KEY(“Non-alcoholic Fatty Liver Disease” OR “Non alcoholic Fatty Liver Disease” OR “Fatty Liver, Nonalcoholic” OR “Fatty Livers, Nonalcoholic” OR “Liver, Nonalcoholic Fatty” OR “Nonalcoholic Steatohepatitis” OR “Steatohepatitides, Nonalcoholic”) AND TITLE-ABS-KEY(“AKR-001” OR “Efruxifermin”)	70

Efruxifermin compared to Placebo for Metabolic Dysfunction-associated steatohepatitis.

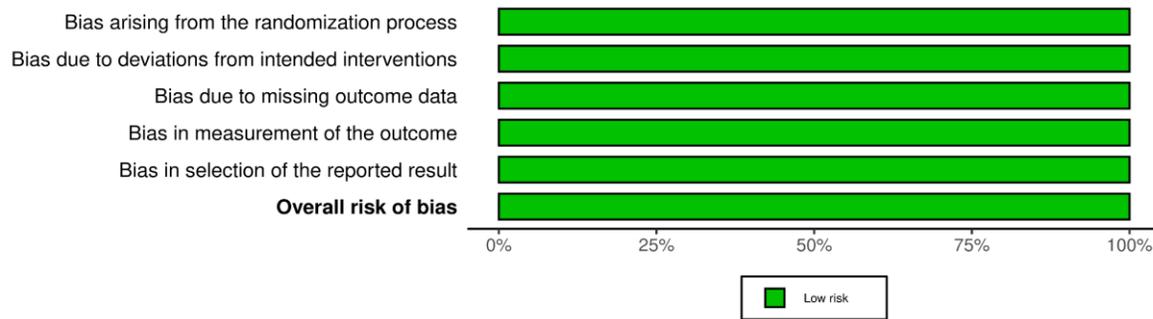
Supplementary Table 2 GRADE summary of findings: Efruxifermin vs placebo for metabolic dysfunction-associated steatohepatitis

Outcome	Participants (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty	Study event rates (%)		Relative effect (95% CI)	Anticipated effects	absolute
								Placebo	Efruxifermin			
≥ 1-stage improvement in fibrosis (RR)	353 (4 RCTs)	Not serious	Not serious	Not serious	Serious ¹	Strong association	⊕⊕⊕⊕ High ¹	19/109 (17.4%)	92/244 (37.7%)	RR 2.24 (1.46–3.44); 216 more per 1,000 (from 80 more to 425 more)		
MASH resolution without worsening fibrosis (RR)	314 (4 RCTs)	Not serious	Not serious	Not serious	Serious ¹	Strong association	⊕⊕⊕⊕ High ¹	20/93 (21.5%)	150/221 (67.9%)	RR 3.00 (2.05–4.38); 430 more per 1,000 (from 226 more to 727 more)		
Normalized liver fat > 5% (RR)	209 (3 RCTs)	Not serious	Not serious	Not serious	Serious ¹	Very strong association	⊕⊕⊕⊕ High ¹	3/72 (4.2%)	68/137 (49.6%)	RR 11.33 (3.74–34.28); 430 more per 1,000 (from 114 more to 1,000 more)		
ALT change (MD)	232 (4 RCTs)	Not serious	Serious ^b	Not serious	Not serious	None	⊕⊕⊕○ Moderate ²	Mean 83	Mean 149	MD 15.32 lower (22.82 lower to 7.81 lower)		
AST change (MD)	235 (4 RCTs)	Not serious	Serious ^b	Not serious	Not serious	None	⊕⊕⊕○ Moderate ²	Mean 83	Mean 152	MD 12.80 lower (20.98 lower to 4.62 lower)		
Enhanced Liver Fibrosis (ELF) score (MD)	384 (4 RCTs)	Not serious	Not serious	Not serious	Not serious	None	⊕⊕⊕⊕ High	Mean 134	Mean 250	MD 0.72 lower (0.81 lower to 0.62 lower)		
Liver Stiffness Measurement (LSM) (MD)	327 (3 RCTs)	Not serious	Not serious	Not serious	Not serious	None	⊕⊕⊕⊕ High	Mean 113	Mean 214	MD 2.74 lower (3.13 lower to 2.34 lower)		

¹Sample size did not meet prespecified optimal information size criteria.

²High heterogeneity among studies.

CI: Confidence interval; MD: Mean difference; RR: Risk ratio; RCT: Randomized controlled trial.



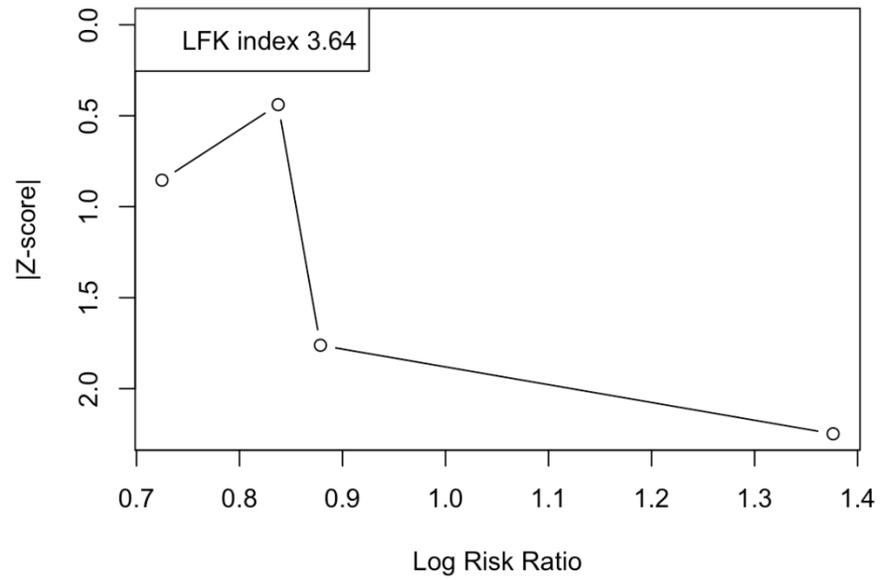
Supplementary Figure 1 Summary of quality assessment.

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Harrison 2021	+	+	+	+	+	+
Harrison 2023	+	+	+	+	+	+
Harrison 2023*	+	+	+	+	+	+
Harrison 2025	+	+	+	+	+	+
Noureddin 2025	+	+	+	+	+	+

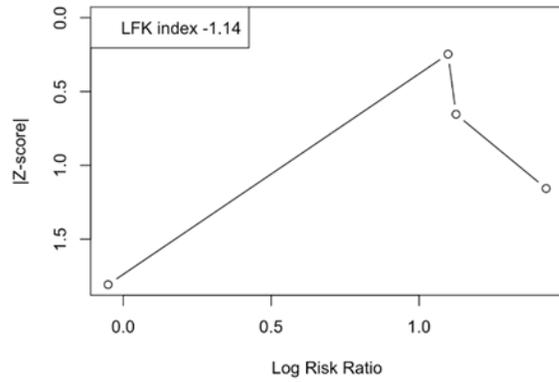
Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
+ Low

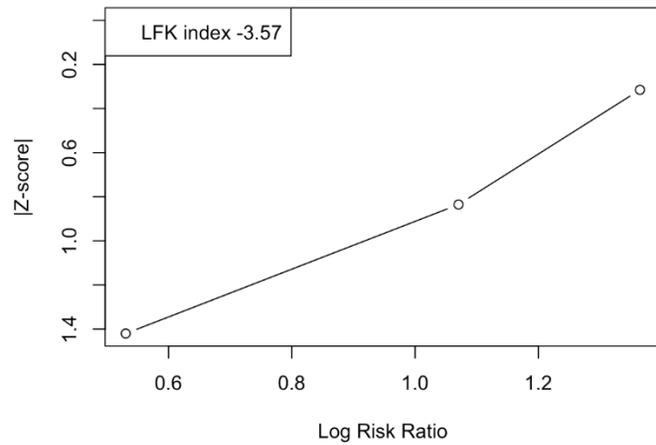
Supplementary Figure 2 Traffic plot of quality assessment.



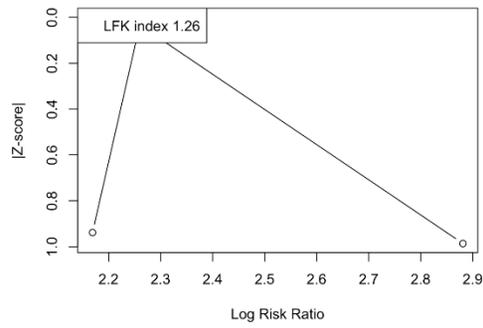
Supplementary Figure 3 Doi plot of Achieving at least one stage of improvement in fibrosis without worsening of MASH.



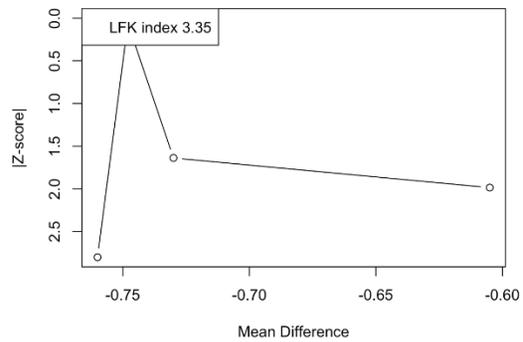
Supplementary Figure 4 Doi plot of MASH resolution without worsening fibrosis.



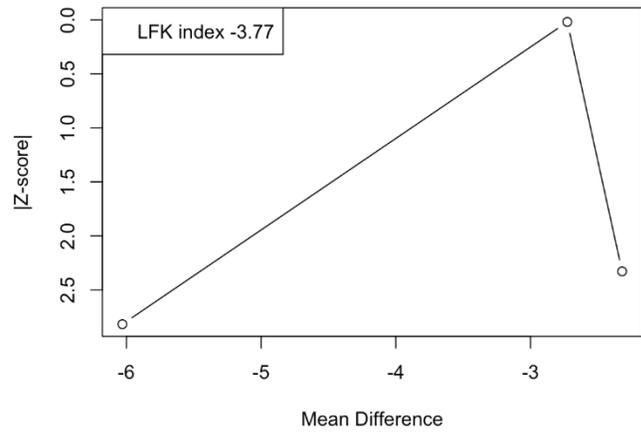
Supplementary Figure 5 Doi plot of At least a Two-point improvement in the MASLD activity score (NAS) with no worsening of fibrosis.



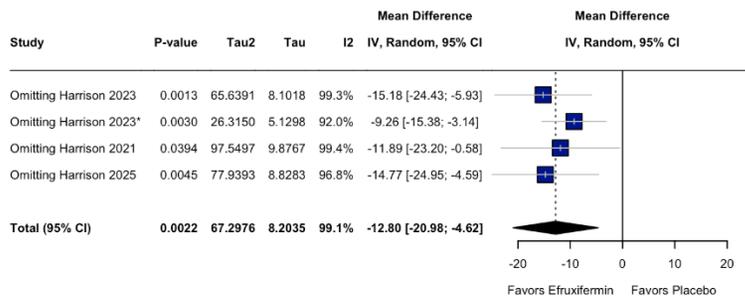
Supplementary Figure 6 Doi plot of Normalized Liver Fat (> 5%).



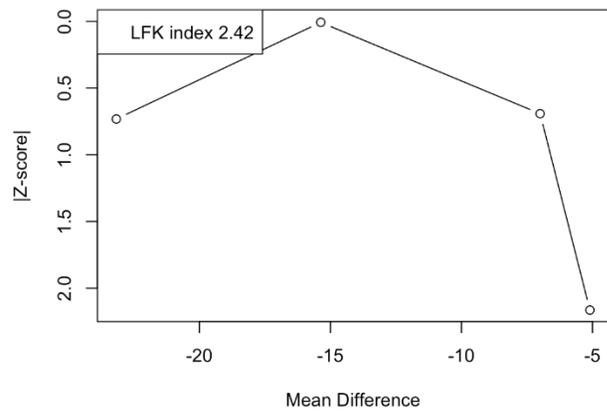
Supplementary Figure 7 Doi plot of Enhanced Liver Fibrosis Test Score.



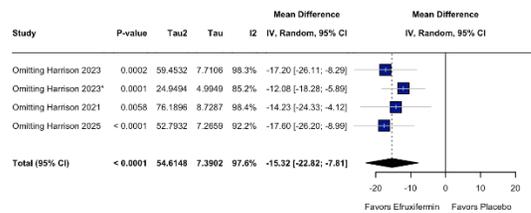
Supplementary Figure 8 Doi plot of Liver stiffness measurement score (kPa).



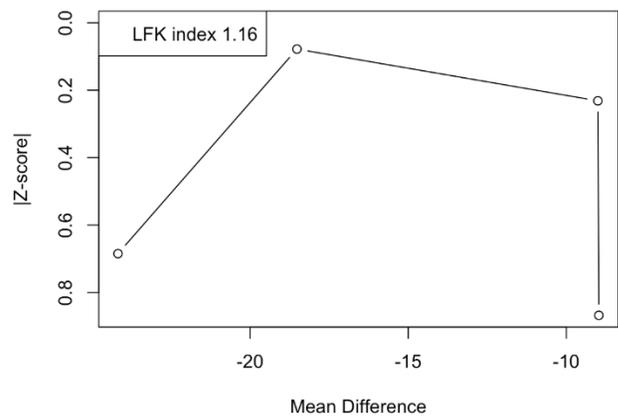
Supplementary Figure 9 Sensitivity analysis of change in AST.



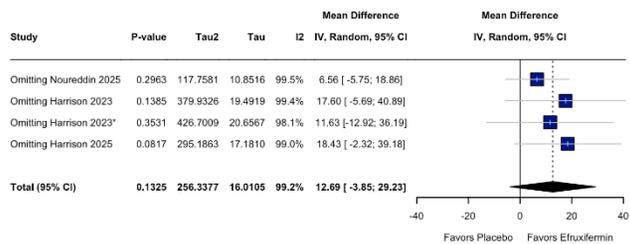
Supplementary Figure 10 Doi plot of change in AST.



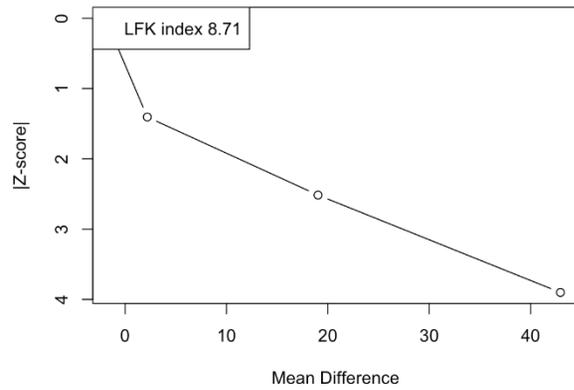
Supplementary Figure 11 Sensitivity analysis of change in ALT.



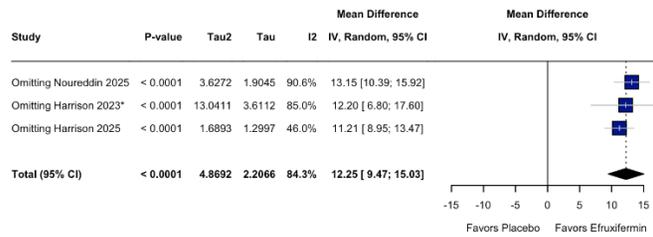
Supplementary Figure 12 Doi plot of change in ALT.



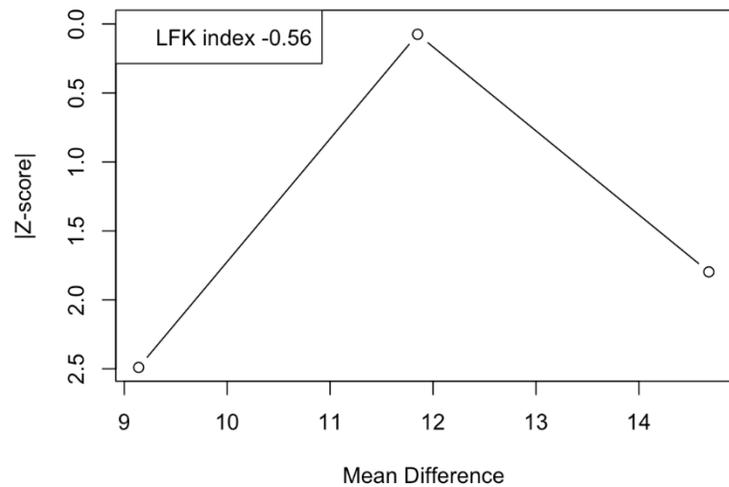
Supplementary Figure 13 Sensitivity analysis of percentage change in adiponectin.



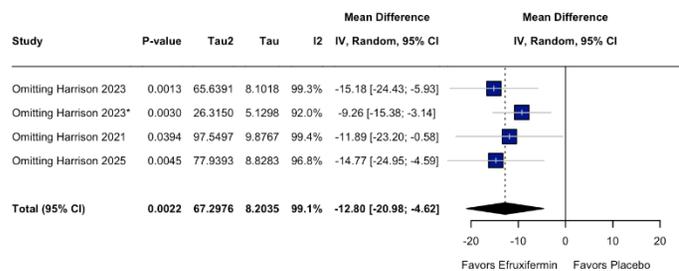
Supplementary Figure 14 Doi plot of percentage change in adiponectin.



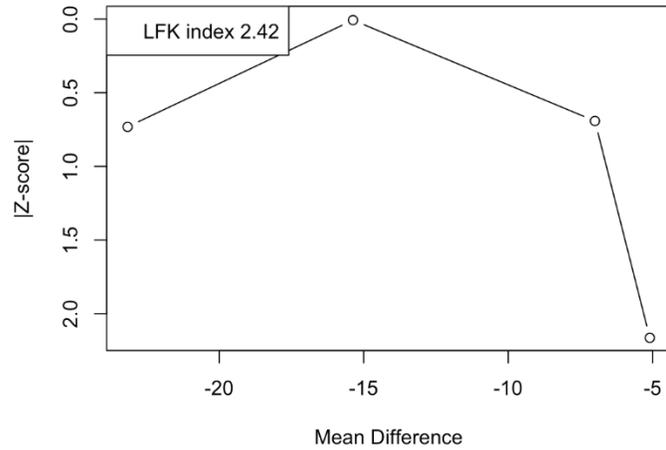
Supplementary Figure 15 Sensitivity analysis of HDL cholesterol.



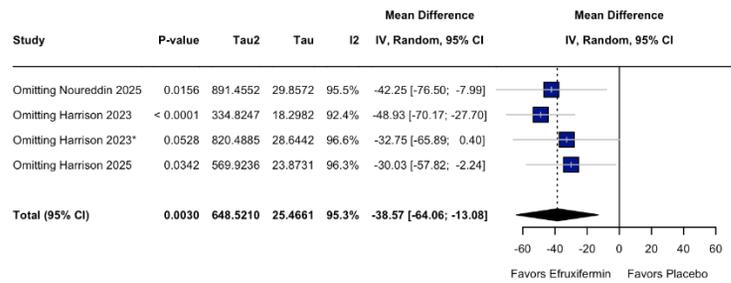
Supplementary Figure 16 Doi plot of HDL cholesterol.



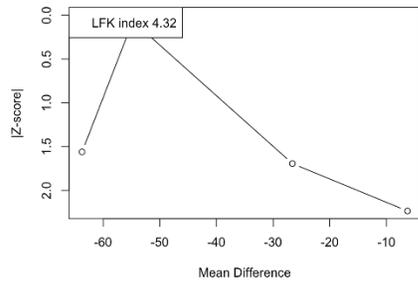
Supplementary Figure 17 Sensitivity analysis of LDL cholesterol.



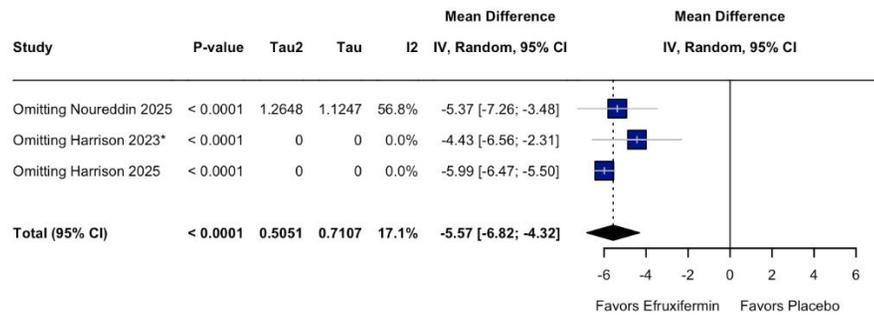
Supplementary Figure 18 Doi plot of LDL cholesterol.



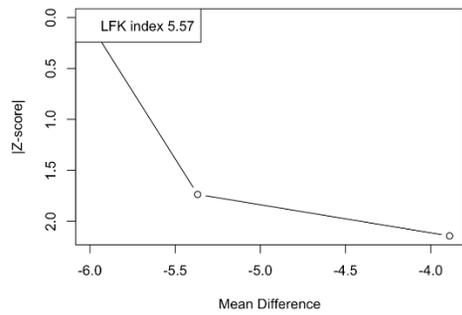
Supplementary Figure 19 Sensitivity analysis of change in triglycerides.



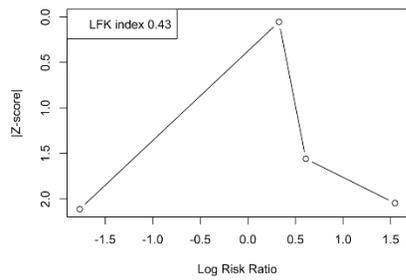
Supplementary Figure 20 Doi plot of triglycerides change.



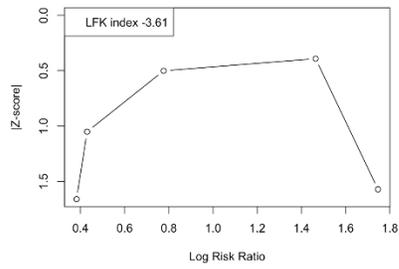
Supplementary Figure 21 Sensitivity analysis of HOMA index.



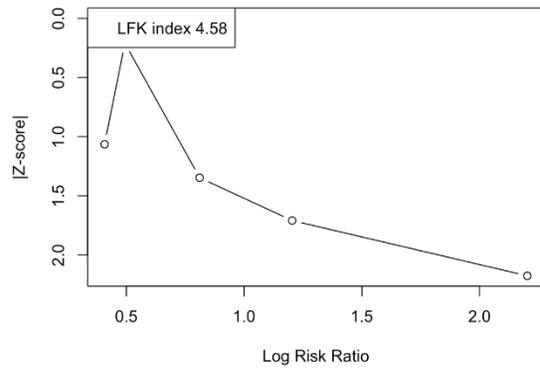
Supplementary Figure 22 Doi plot of HOMA index.



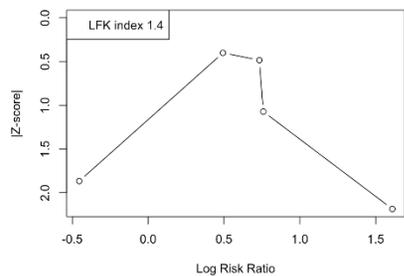
Supplementary Figure 23 Doi plot of serious adverse events.



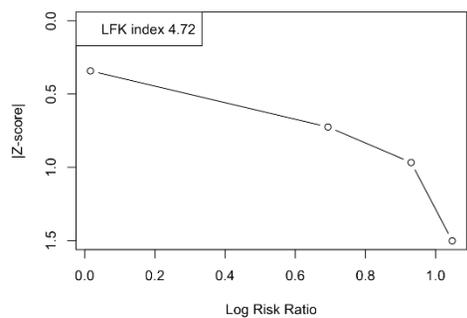
Supplementary Figure 24 Doi plot of adverse events leading to discontinuation.



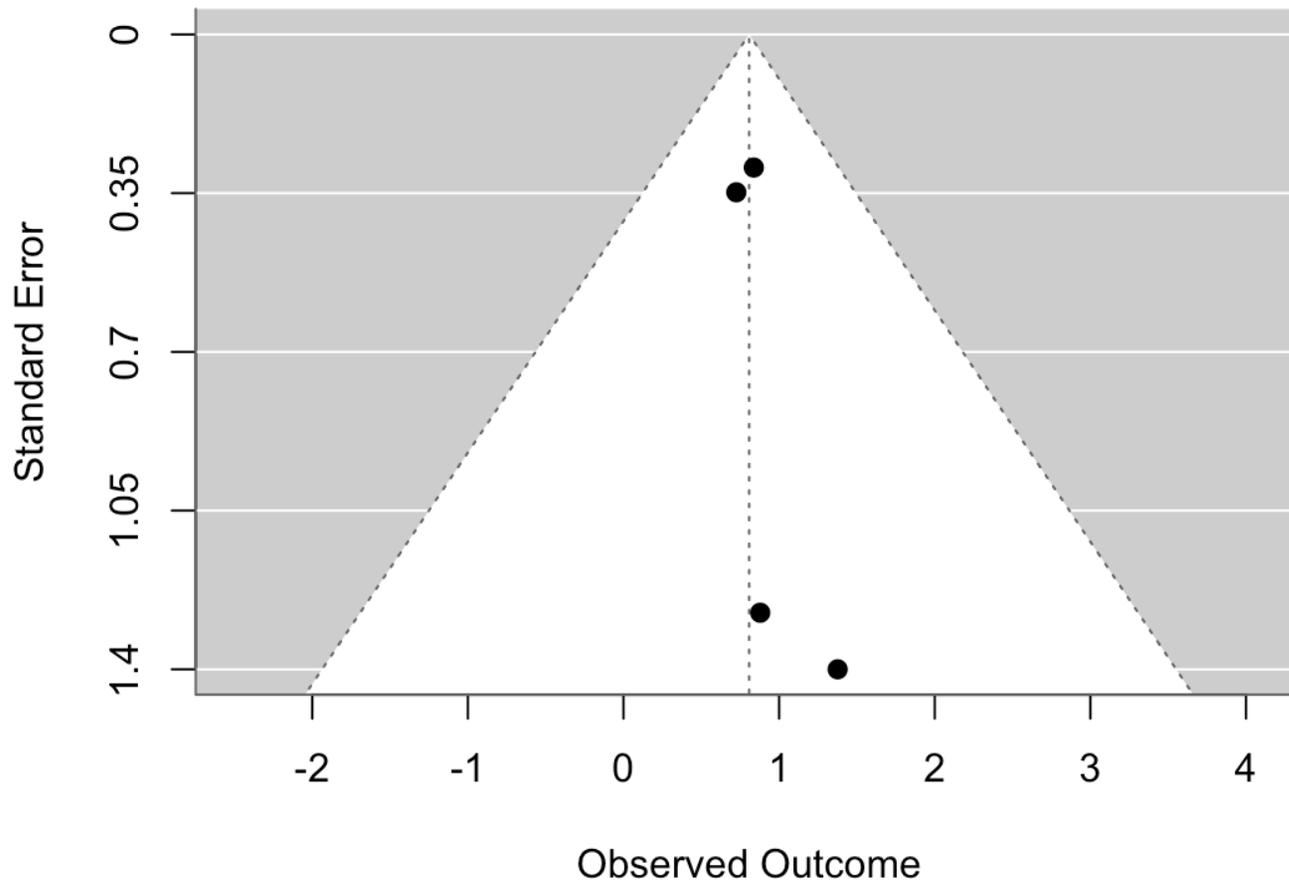
Supplementary Figure 25 Doi plot of nausea.



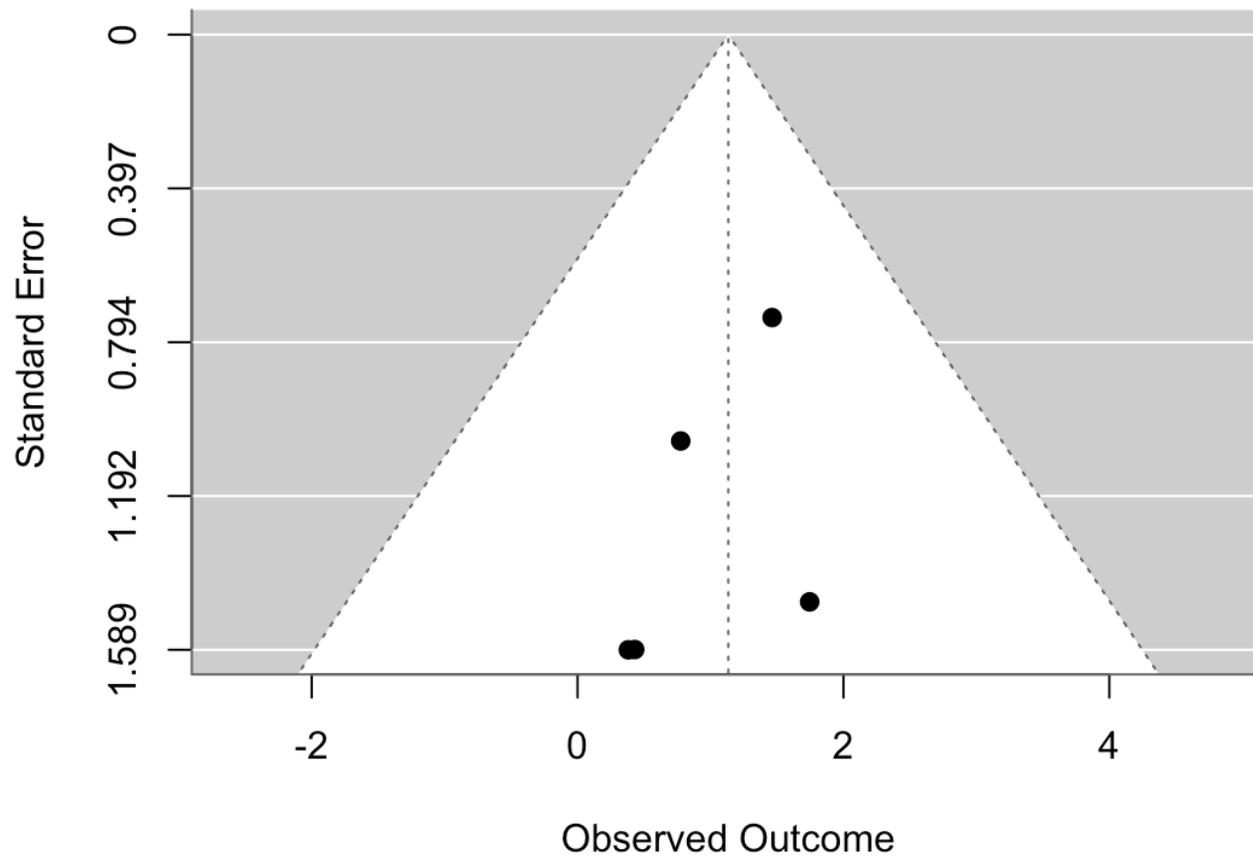
Supplementary Figure 26 Doi plot of diarrhea.



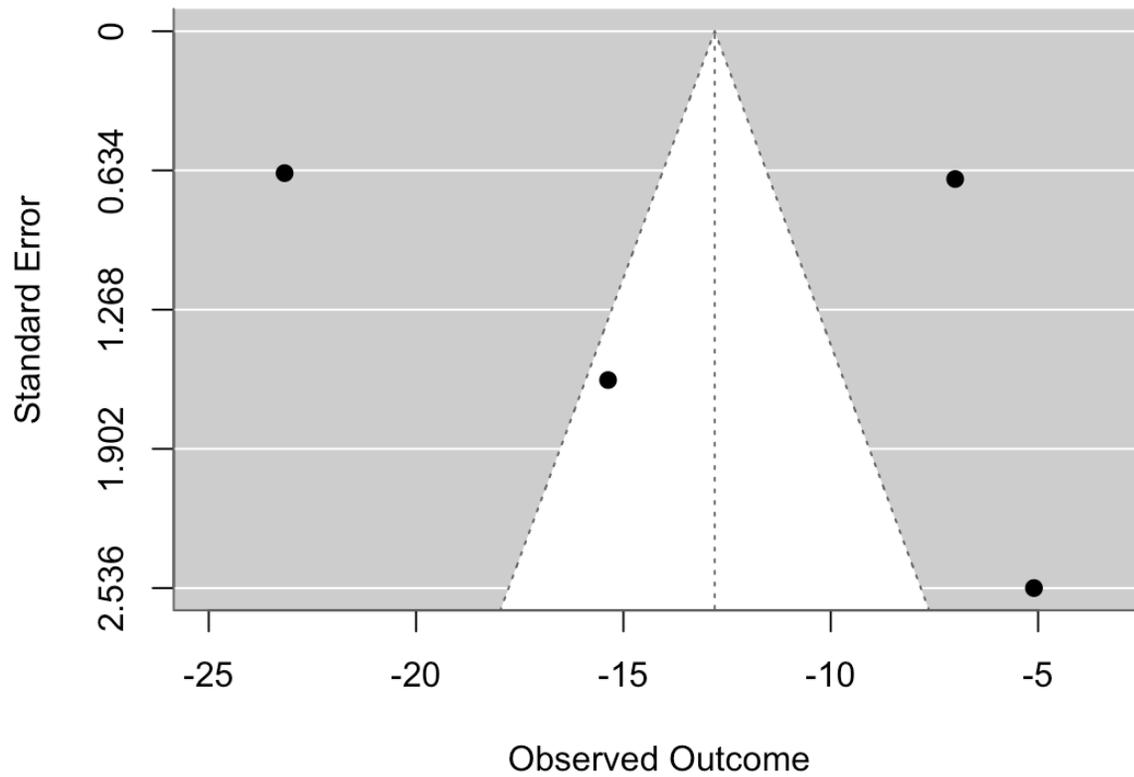
Supplementary Figure 27 Doi plot of injection site bruising.



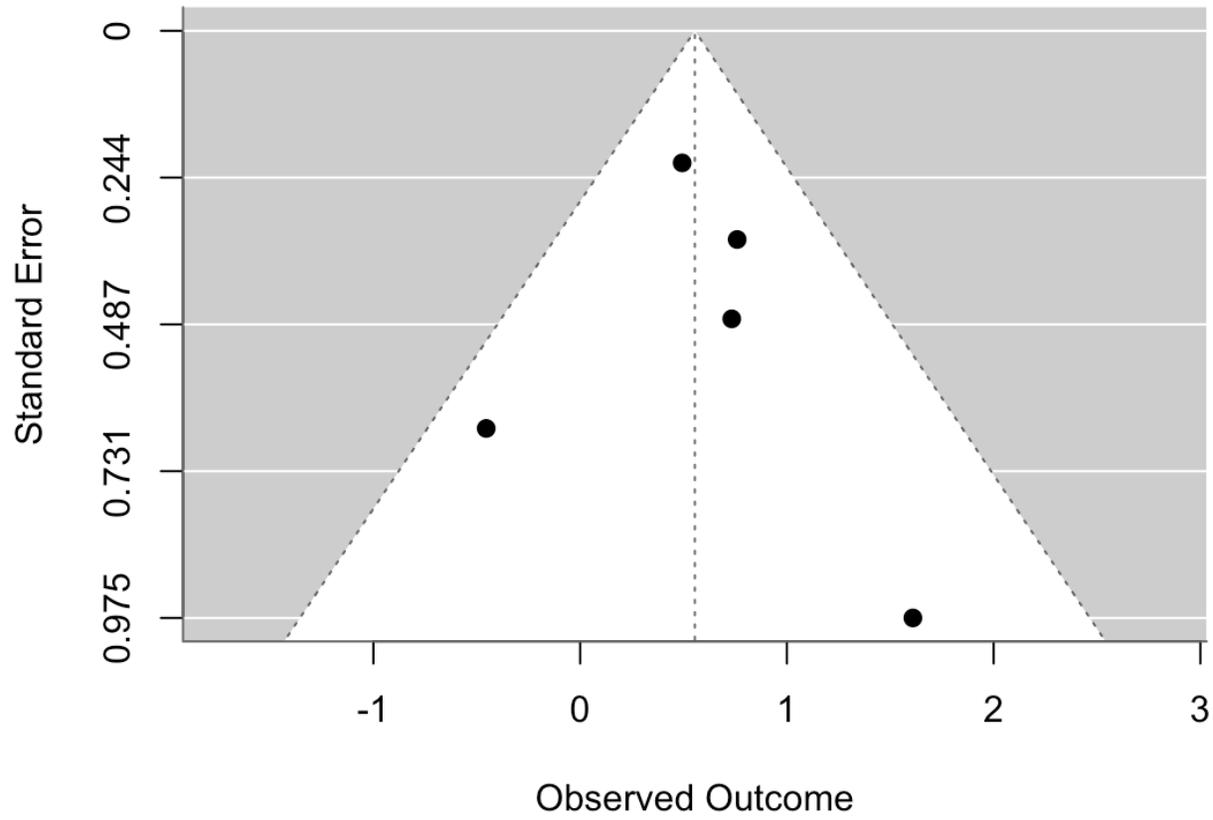
Supplementary Figure 28 Funnel plot of achieving atleast one stage of improvement in fibrosis without worsening of MAS.



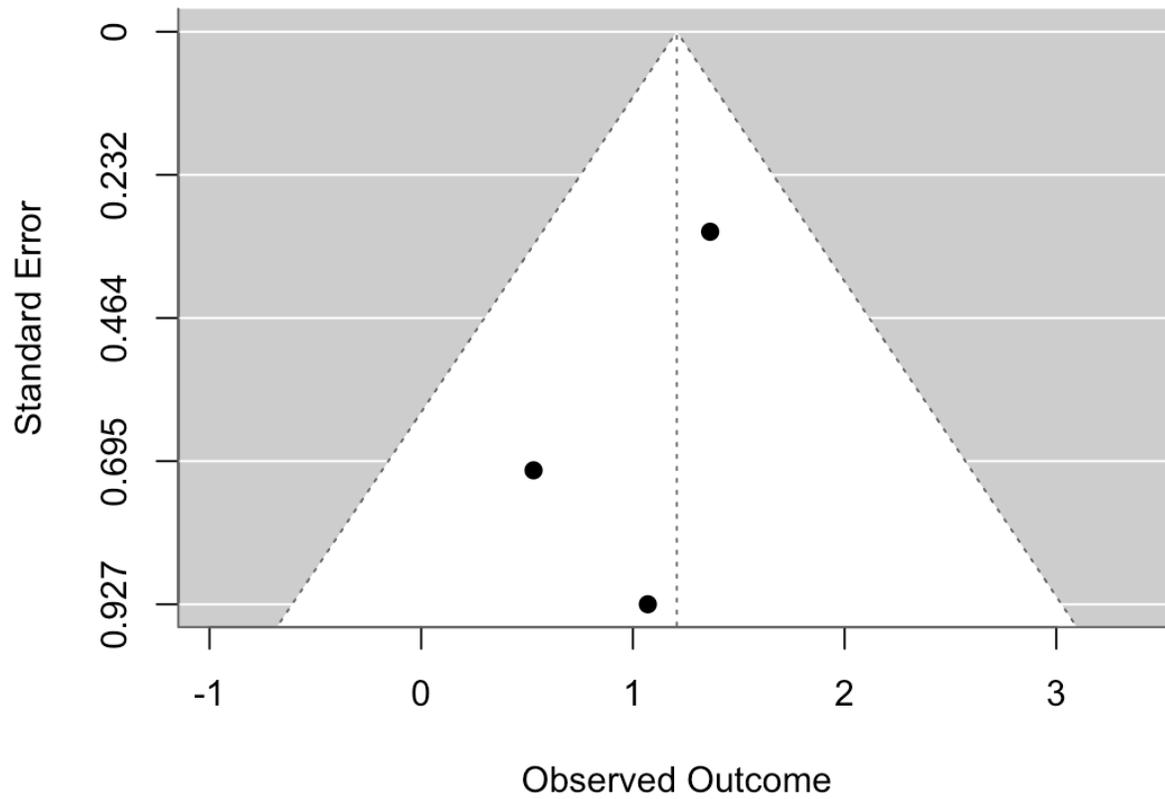
Supplementary Figure 29 Funnel plot of adverse event leading to discontinuation.



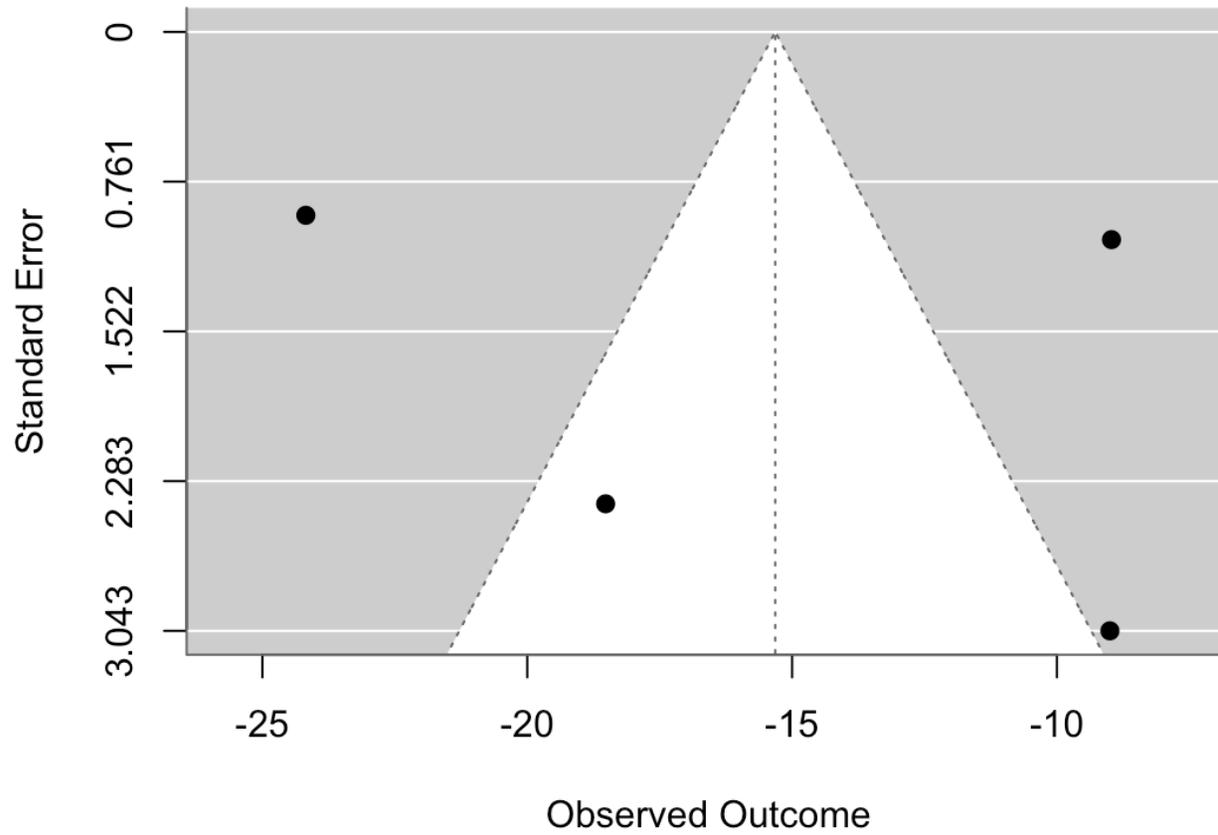
Supplementary Figure 30 Funnel plot of AST.



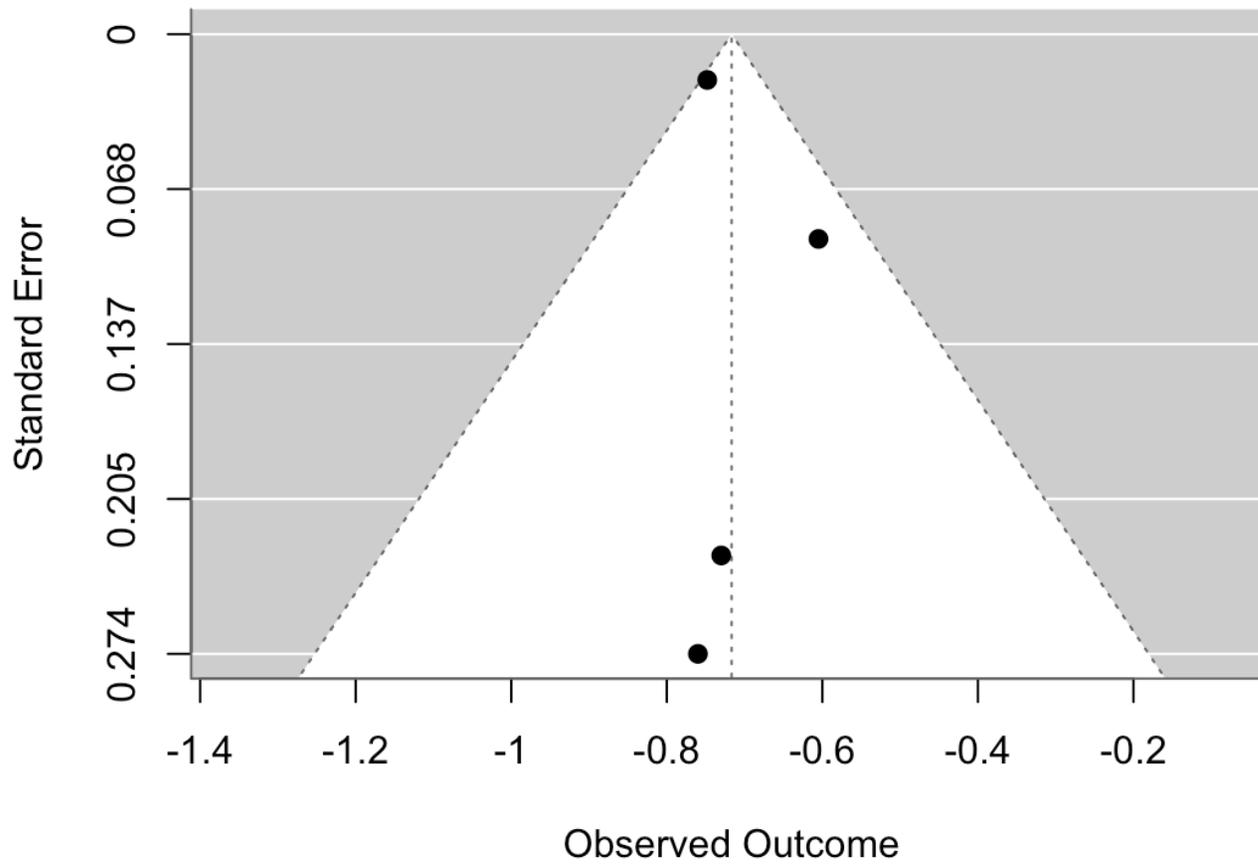
Supplementary Figure 31 Funnel plot of diarrhea.



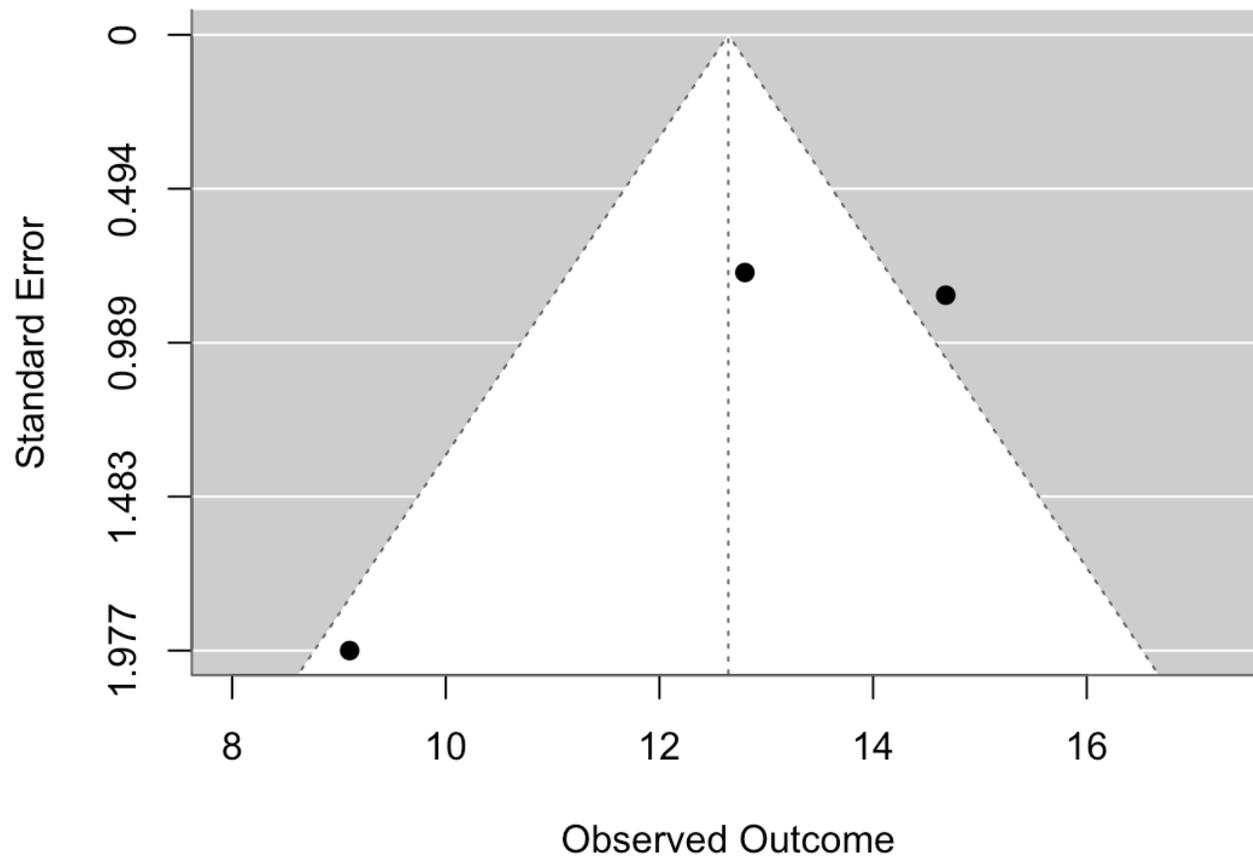
Supplementary Figure 32 Funnel plot of at least a two-point improvement in NAS score without worsening.



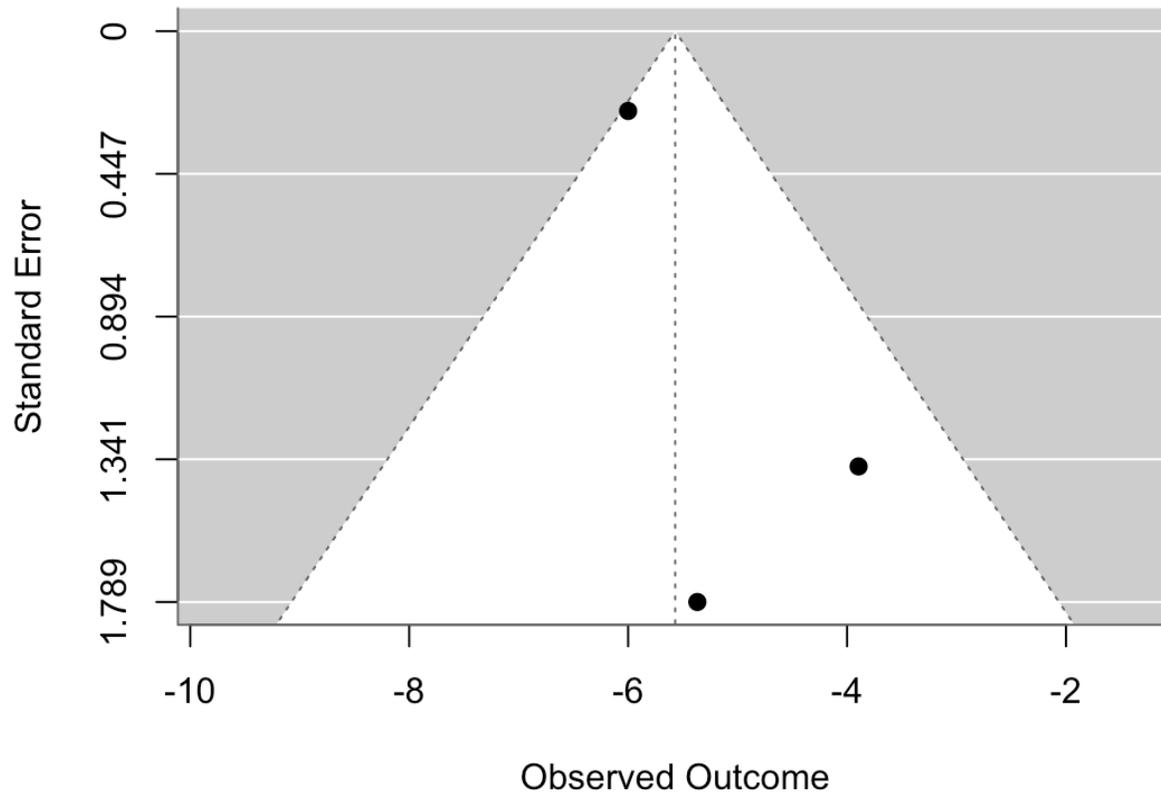
Supplementary Figure 33 Funnel plot of ALT.



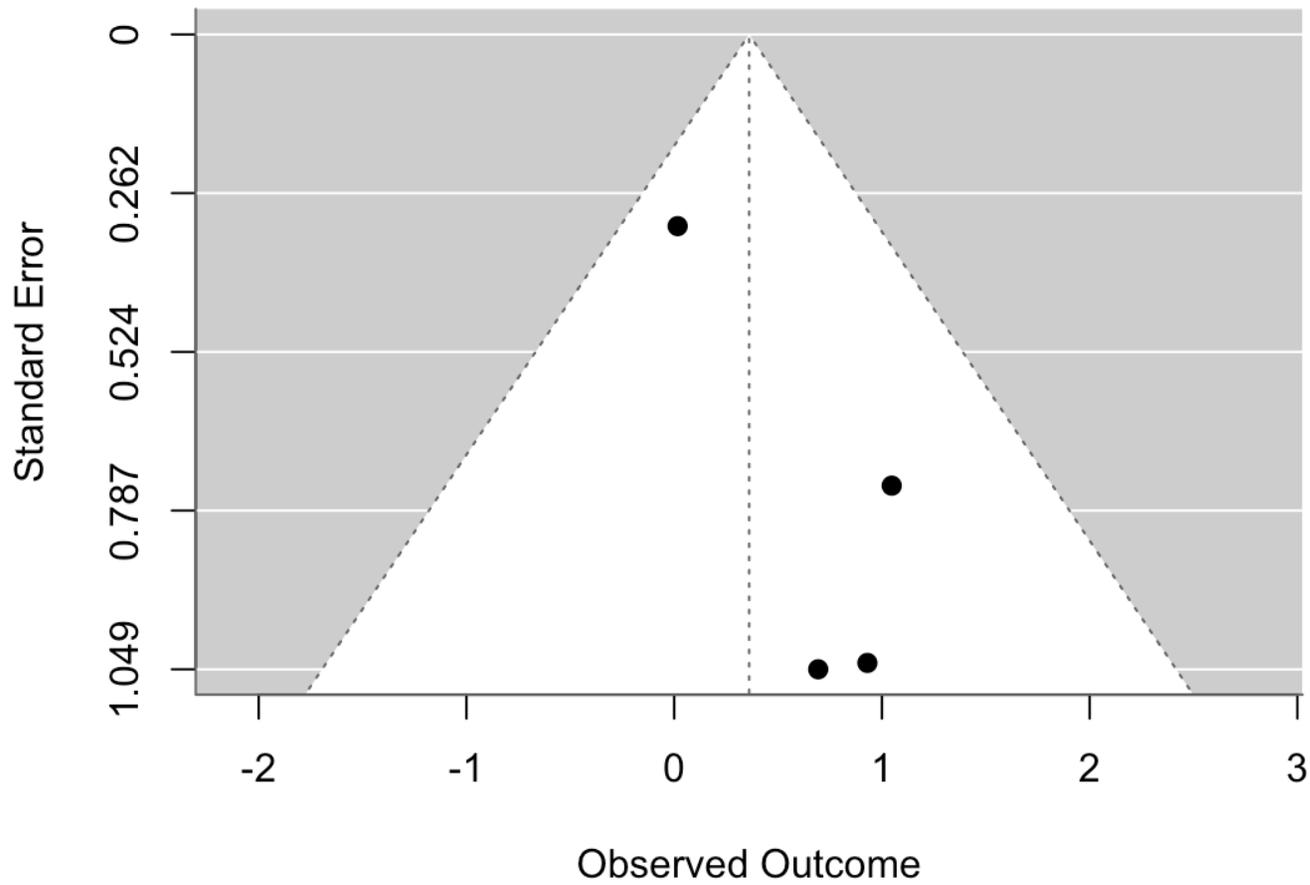
Supplementary Figure 34 Funnel plot of ELF score.



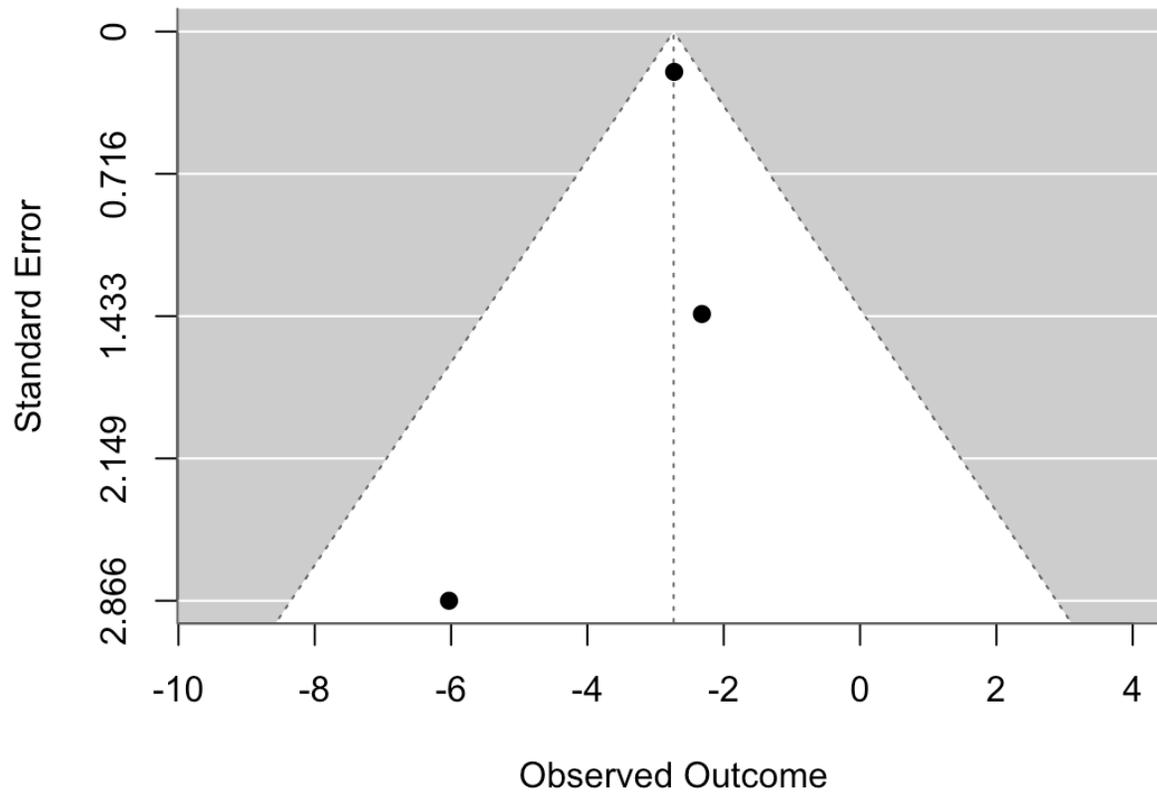
Supplementary Figure 35 Funnel plot of HDL cholesterol.



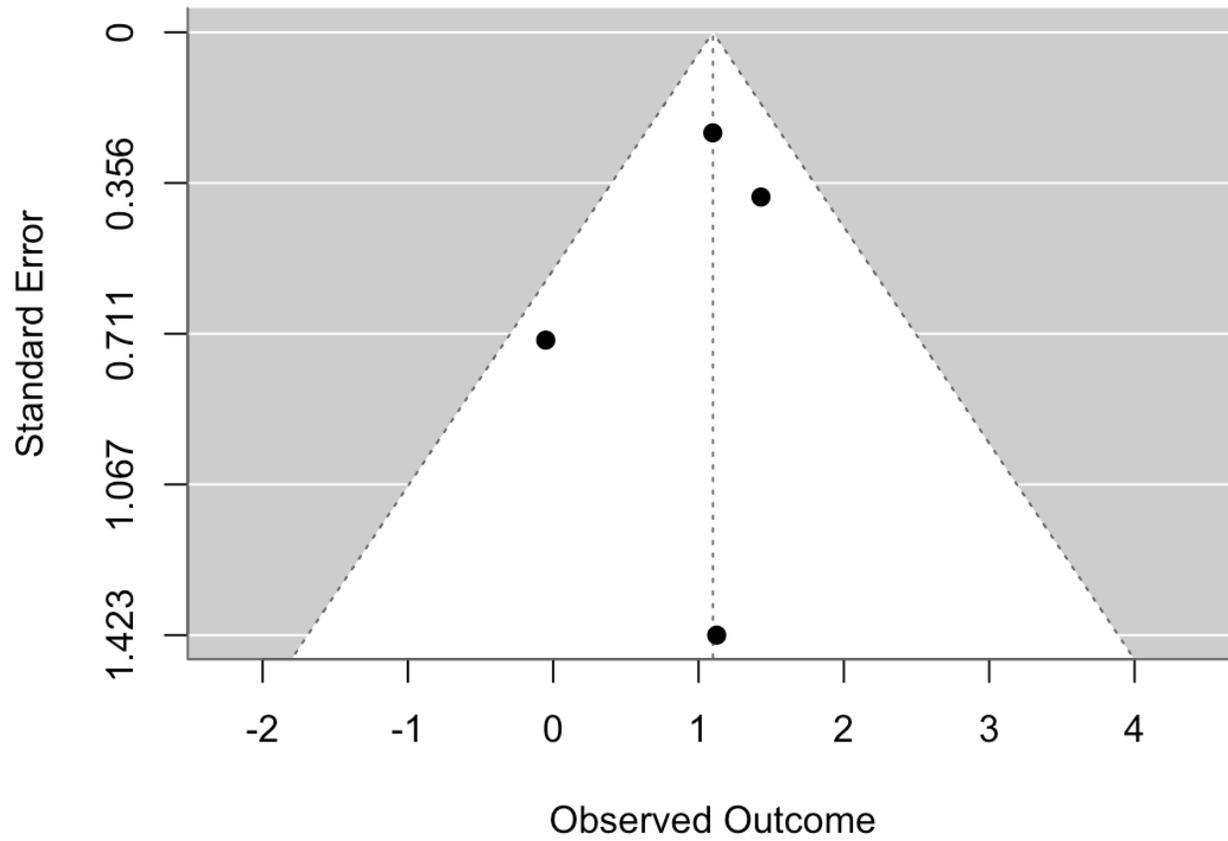
Supplementary Figure 36 Funnel plot of HOMA-IR.



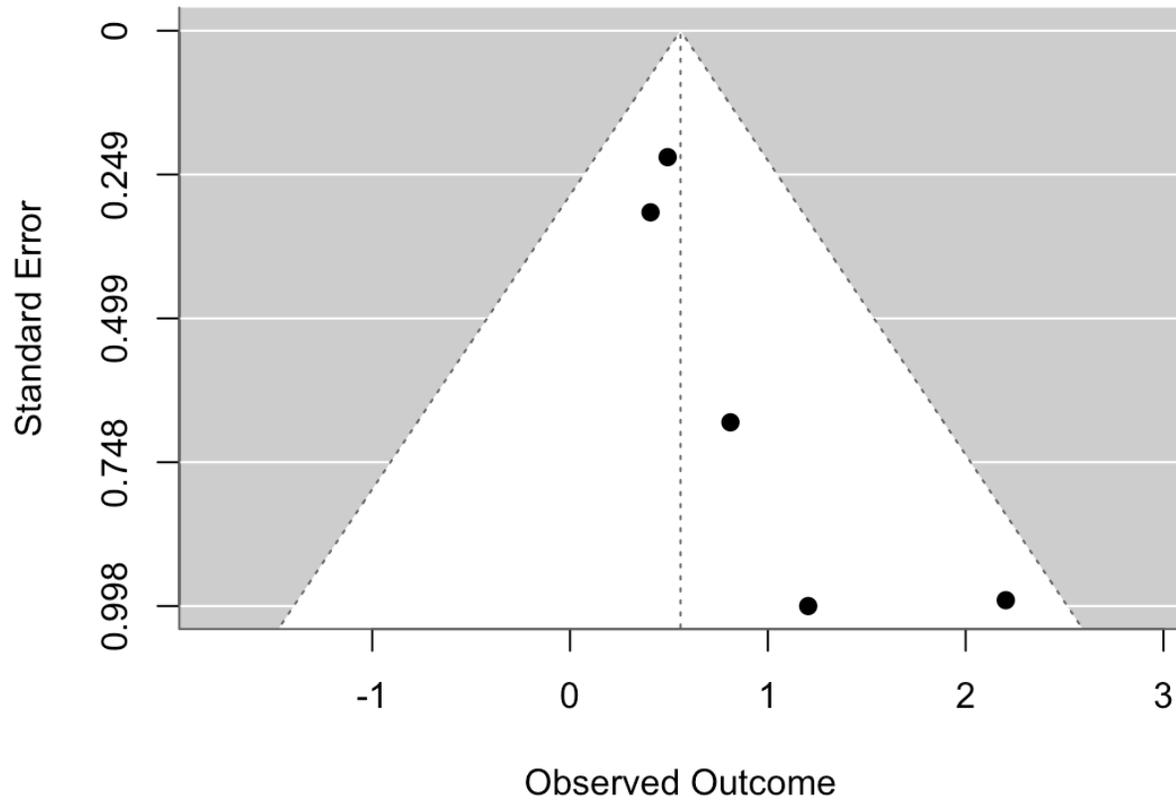
Supplementary Figure 37 Funnel plot of injection site reaction.



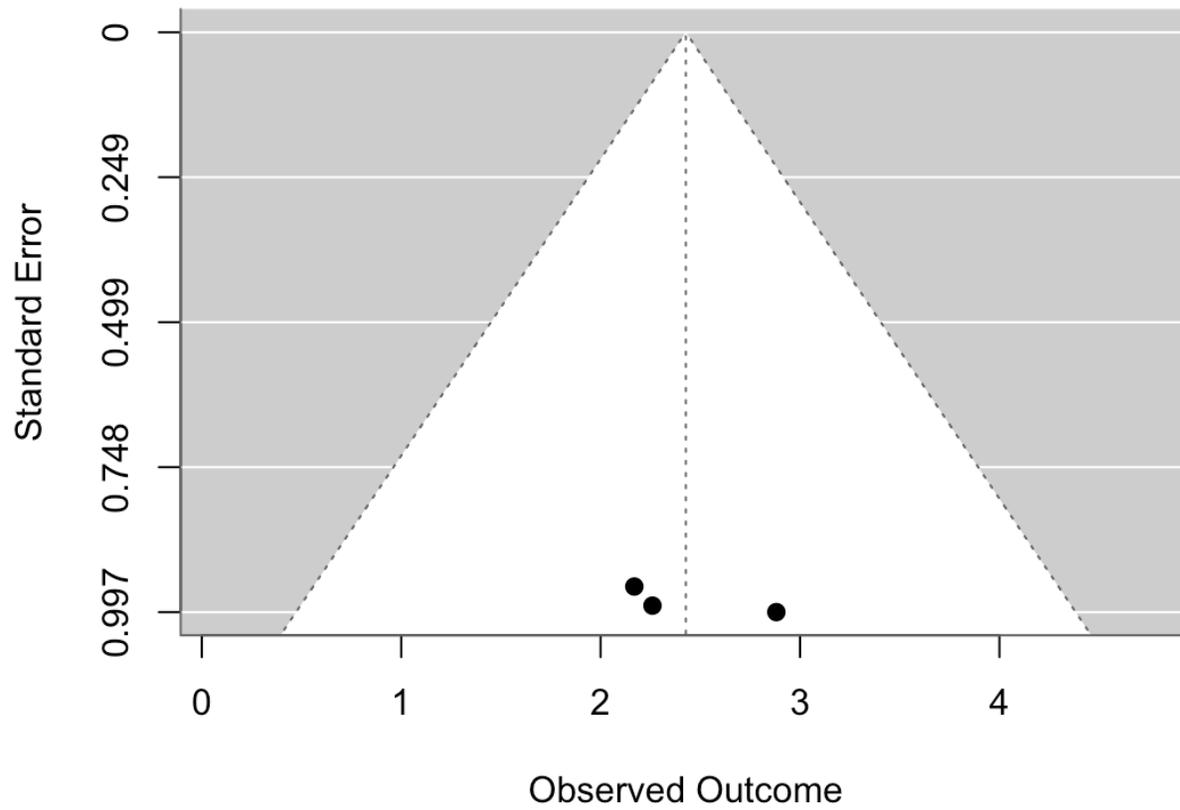
Supplementary Figure 38 Funnel plot of liver stiffness score.



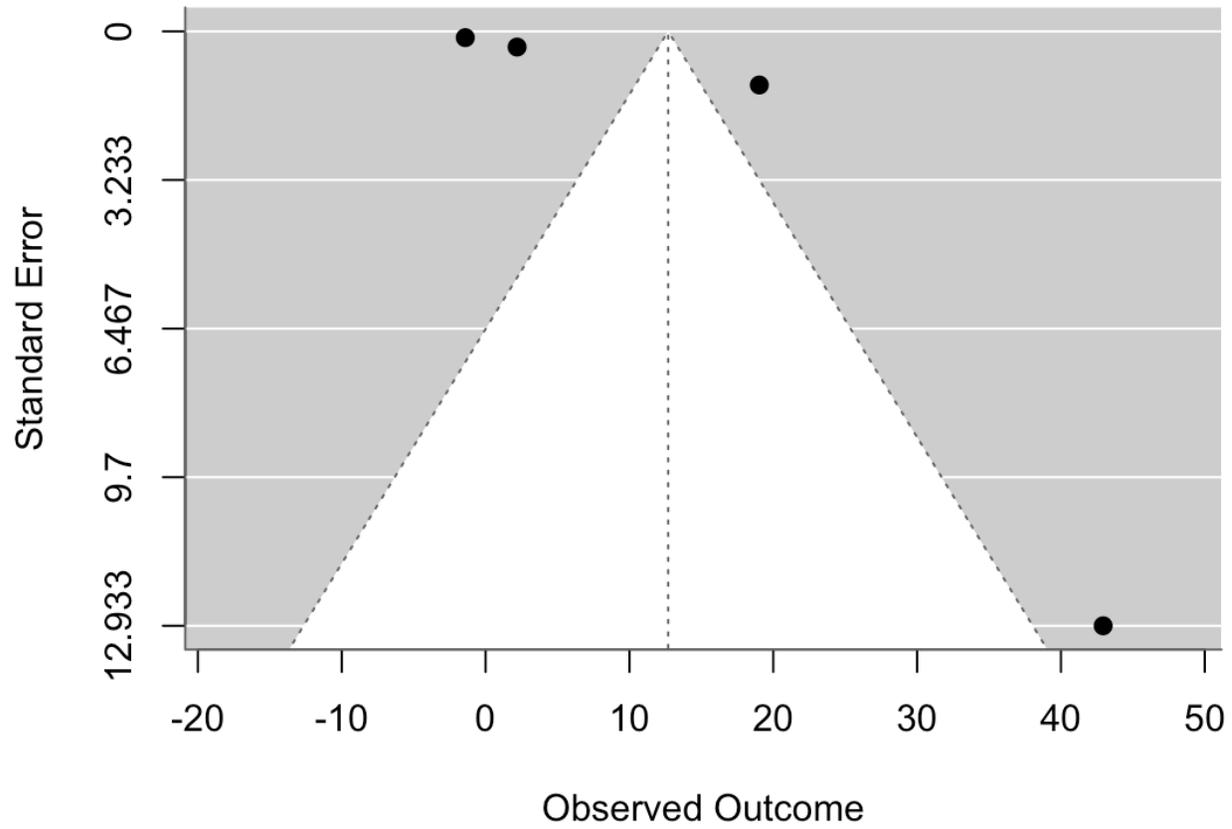
Supplementary Figure 39 Funnel plot of MASH resolution without worsening of fibrosis.



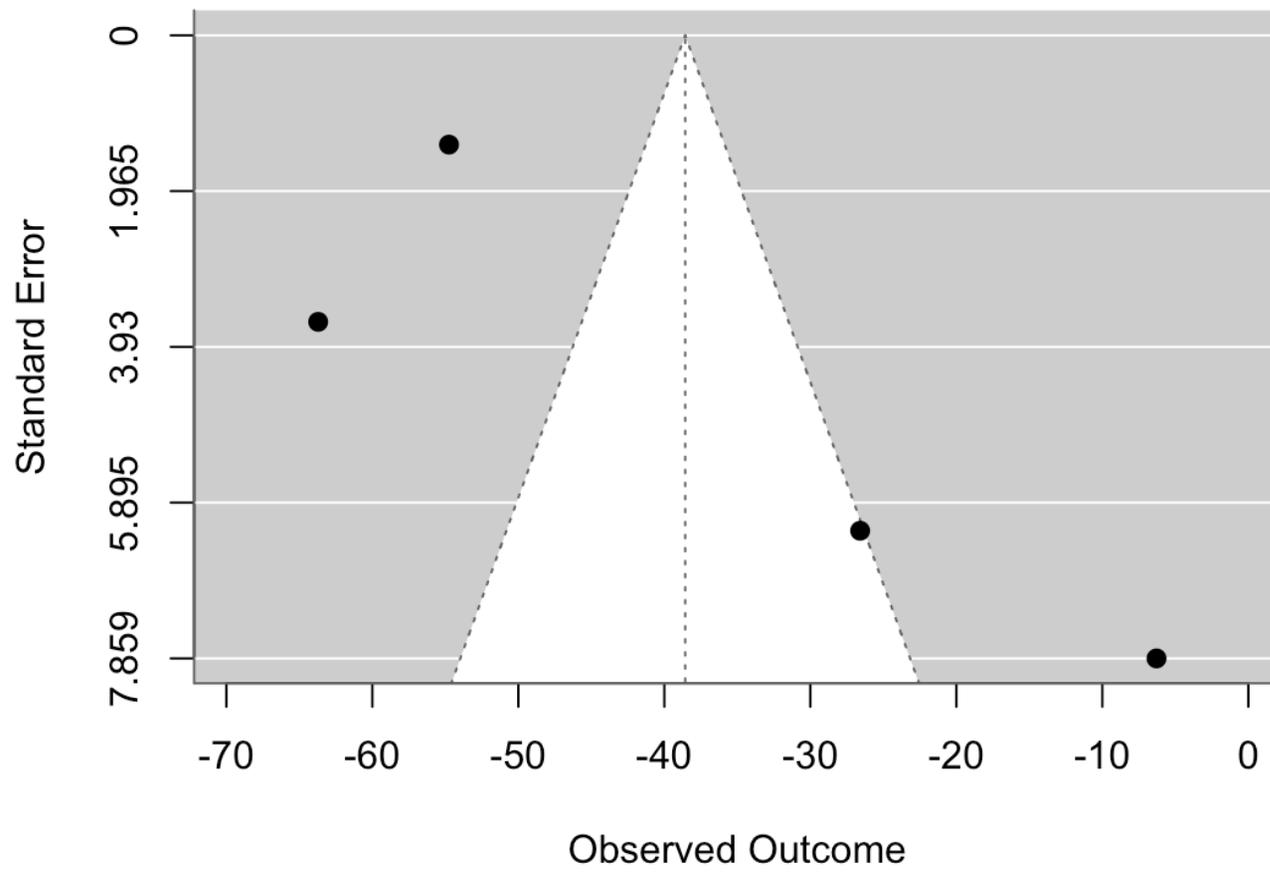
Supplementary Figure 40 Funnel plot of nausea.



Supplementary Figure 41 Funnel plot of normalized liver fat.



Supplementary Figure 42 Funnel plot of percentage change in adiponectin.



Supplementary Figure 43 Funnel plot of triglyceride change.