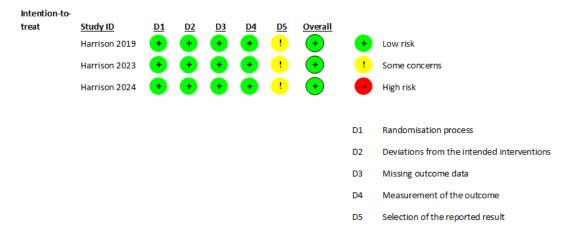
Supplementary Material

Efficacy and Safety of resmetirom for the Treatment of Nonalcoholic Steatohepatitis (NASH): A										
GRADE assessed Systematic Review and Meta-Analysis										
This supplemental material has been provided by the authors to give readers additional										
information about their work.										

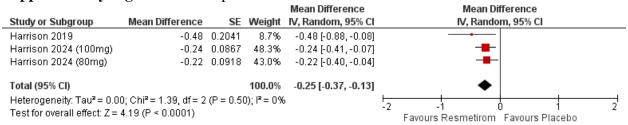
Supplementary Table S1: Detailed Database Search Strategy:

PubMed	("resmetirom"[Supplementary Concept] OR "resmetirom"[All Fields] OR "mgl 3196"[All Fields])) AND ("naflds"[All Fields] OR "non alcoholic fatty liver disease"[MeSH Terms] OR ("non alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR "nafld"[All Fields] OR "nash"[All Fields])	44
Google	((resmetirom) OR (MGL-3196)) AND ((((NASH) OR (NAFLD)) OR ("Non-alcoholic	1,490
scholar	Fatty Liver Disease")) OR ("non-alcoholic steatohepatitis"))	
Cochrane	((resmetirom) OR (MGL-3196)) AND ((((NASH) OR (NAFLD)) OR ("Non-alcoholic	56
	Fatty Liver Disease")) OR ("non-alcoholic steatohepatitis"))	
Scopus	(resmetirom) OR (mgl-3196) AND (nash) OR (nafld) OR ("Non-alcoholic Fatty	163
	Liver Disease") OR ("non-alcoholic steatohepatitis")	

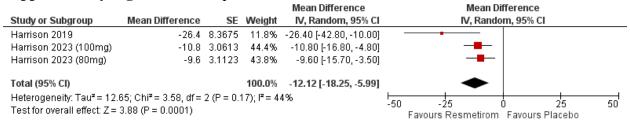
Supplementary Figure 1: QA of RCTs



Supplementary Figure 2: Forest plot of ELF score



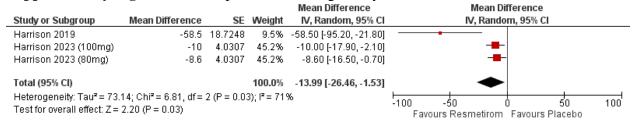
Supplementary Figure 3: Forest plot of Alanine aminotransferase



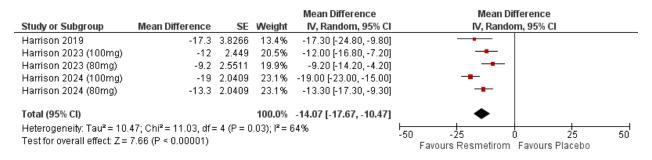
Supplementary Figure 4: Forest plot of Aspartate aminotransferase

				Mean Difference	Mean Difference	
Study or Subgroup	Mean Difference	SE	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Harrison 2019	-11.1	3.4184	22.0%	-11.10 [-17.80, -4.40]		
Harrison 2023 (100mg)	-4.3	2.2449	39.6%	-4.30 [-8.70, 0.10]	-	
Harrison 2023 (80mg)	-5	2.296	38.5%	-5.00 [-9.50, -0.50]	-	
Total (95% CI)			100.0%	-6.06 [-9.61, -2.51]	•	
Heterogeneity: Tau ² = 3.2		-50 -25 0 25	50			
Test for overall effect: Z=	3.35 (P = 0.0008)				Favours Resmetirom Favours Placebo	

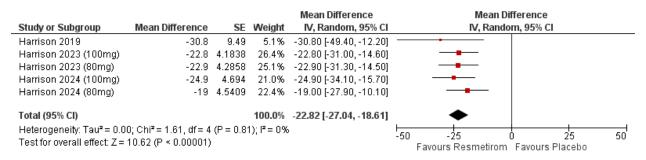
Supplementary Figure 5: Forest plot of Gamma-glutamyl transferase



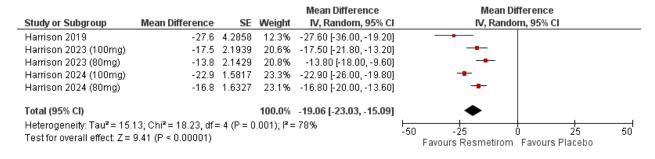
Supplementary Figure 6: Forest plot of LDL cholesterol



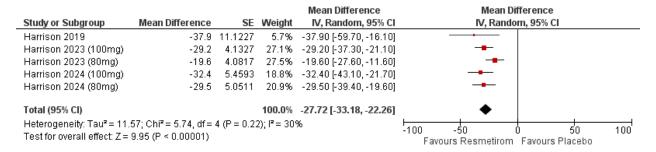
Supplementary Figure 7: Forest plot of Triglycerides



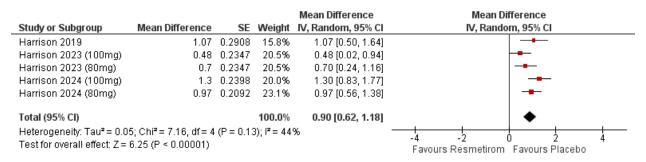
Supplementary Figure 8: Forest plot of Apolipoprotein b



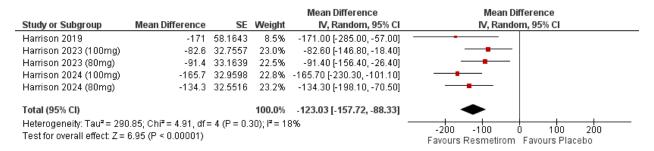
Supplementary Figure 9: Forest plot of Lpa



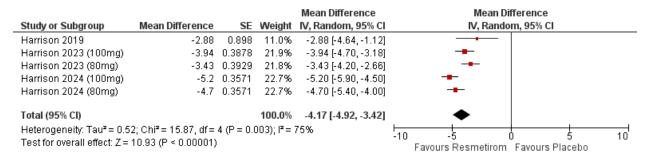
Supplementary Figure 10: Forest plot of Adiponectin



Supplementary Figure 11: Forest plot of CK18M30



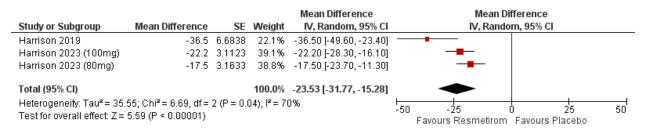
Supplementary Figure 12: Forest plot of Reverse T3



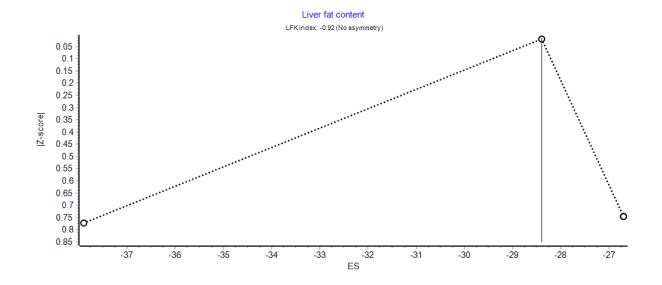
Supplementary Figure 13: Forest plot of FibroScan CAP

				Mean Difference	Mean Di	fference	
Study or Subgroup	Mean Difference	SE	Weight	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Harrison 2023 (100mg)	-24.4	4.796	24.9%	-24.40 [-33.80, -15.00]			
Harrison 2023 (80mg)	-18.3	4.847	24.3%	-18.30 [-27.80, -8.80]			
Harrison 2024 (100mg)	-26.9	4.745	25.4%	-26.90 [-36.20, -17.60]			
Harrison 2024 (80mg)	-25.2	4.745	25.4%	-25.20 [-34.50, -15.90]			
Total (95% CI)			100.0%	-23.75 [-28.44, -19.07]	•		
Heterogeneity: Tau² = 0.00 Test for overall effect: Z = 9		(P = 0.6	61); I² = 0'	%	-50 -25 Favours Resmetirom	l 25 D 25 Favours Placebo	50

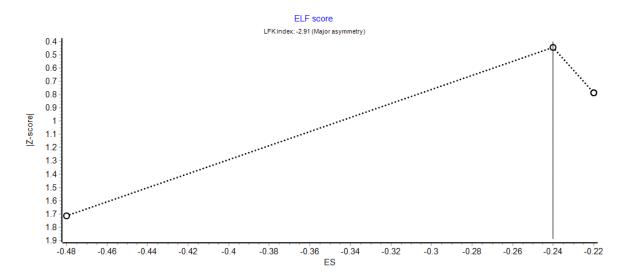
Supplementary Figure 14: Forest plot of Apolipoprotein CIII



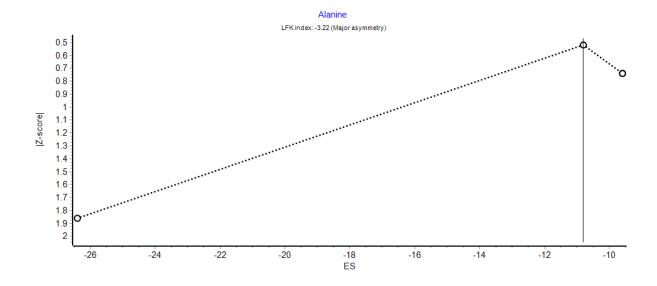
Supplementary Figure 15: Doi plot of Liver fat content



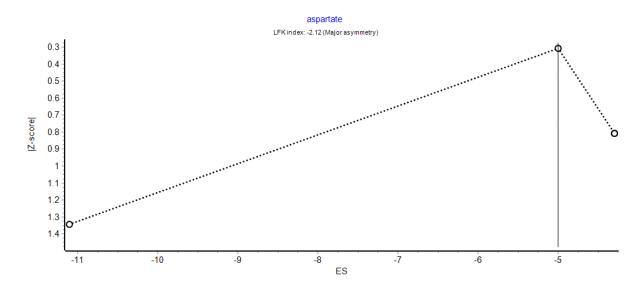
Supplementary Figure 16: Doi plot of ELF score



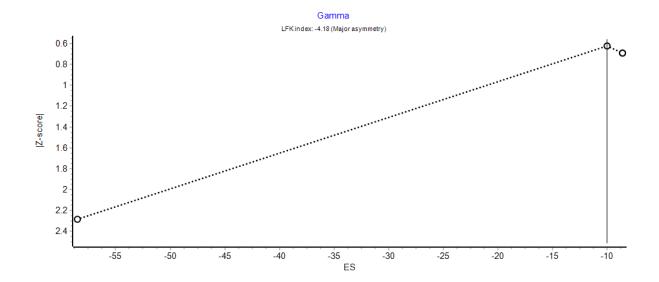
Supplementary Figure 17: Doi plot of Alanine aminotransferase



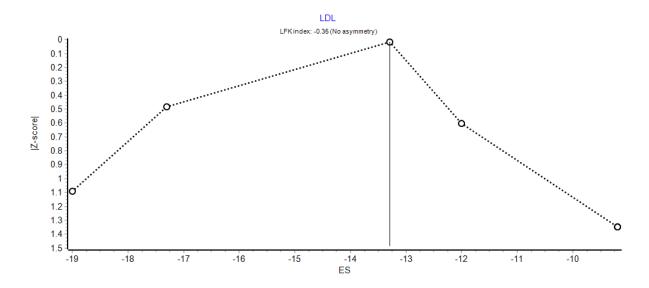
Supplementary Figure 18: Doi plot of Aspartate aminotransferase



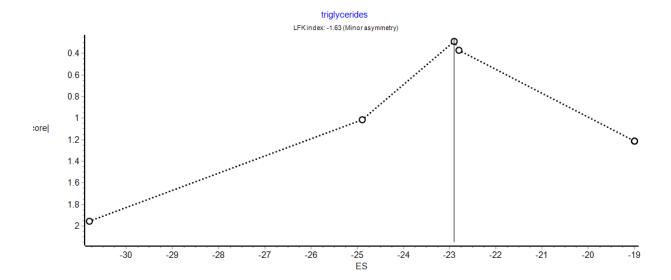
Supplementary Figure 19: Doi plot of Gamma glutamyl transferase



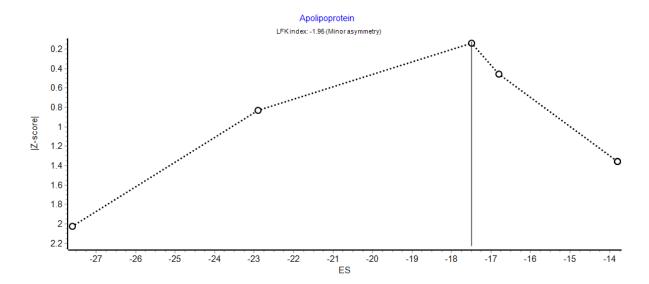
Supplementary Figure 20: Doi plot of LDL cholesterol



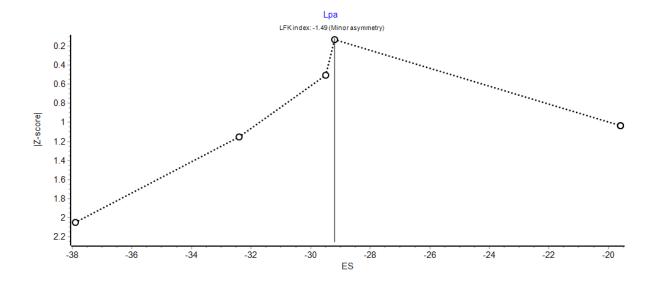
Supplementary Figure 21: Doi plot of Triglycerides



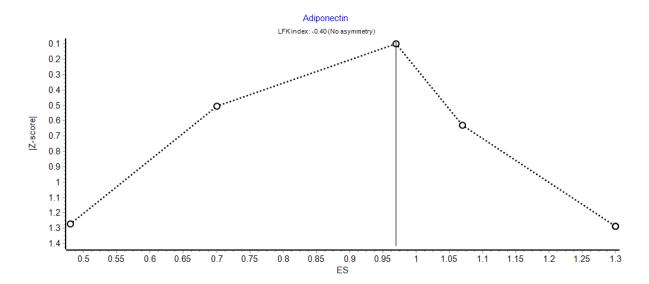
Supplementary Figure 22: Doi plot of Apolipoprotein b



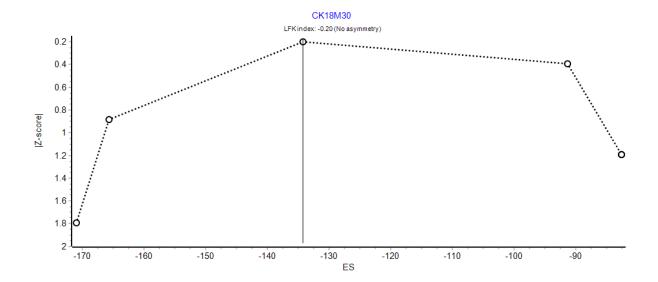
Supplementary Figure 23: Doi plot of Lpa



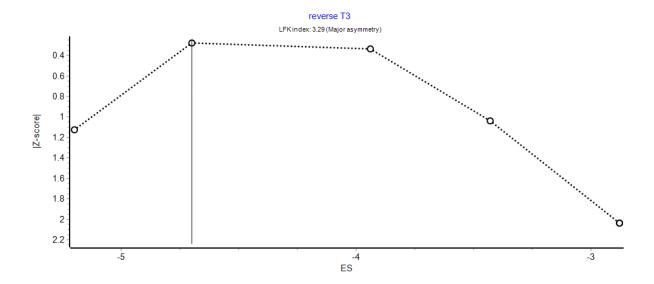
Supplementary Figure 24: Doi plot of Adiponectin



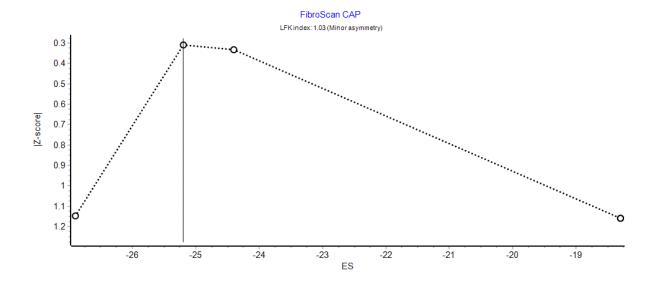
Supplementary Figure 25: Doi plot of CK18M30



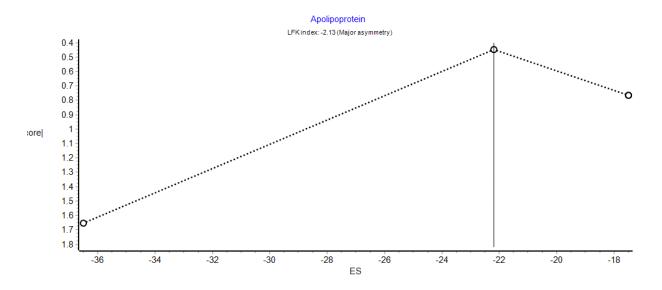
Supplementary Figure 26: Doi plot of Reverse T3



Supplementary Figure 27: Doi plot of FibroScan CAP



Supplementary Figure 28: Doi plot of Apolipoprotein CIII



Supplementary Figure 29: Forest plot of Diarrhea

	Rosmeti	irom	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Harrison 2019	28	84	3	41	3.3%	4.56 [1.47, 14.11]	
Harrison 2023	229	822	44	318	46.0%	2.01 [1.50, 2.71]	-
Harrison 2024	195	645	50	321	50.7%	1.94 [1.47, 2.57]	-
Total (95% CI)		1551		680	100.0%	2.03 [1.65, 2.50]	•
Total events	452		97				
Heterogeneity: Tau² = Test for overall effect:			0.1 0.2 0.5 1 2 5 10 Favours Resmetirom Favours Placebo				

Supplementary Figure 30: Forest plot of Nausea

	Resmet	irom	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Harrison 2019	12	84	2	41	3.0%	2.93 [0.69, 12.48]	-
Harrison 2023	122	822	25	318	37.7%	1.89 [1.25, 2.85]	
Harrison 2024	132	645	40	321	59.3%	1.64 [1.18, 2.28]	-
Total (95% CI)		1551		680	100.0%	1.76 [1.37, 2.27]	•
Total events	266		67				
Heterogeneity: Tau ² =	: 0.00; Chi	2 = 0.76	df = 2 (P	01 02 05 1 2 5 10			
Test for overall effect:	Z = 4.40 (P < 0.00	001)				0.1 0.2 0.5 1 2 5 10 Favours Resmetirom Favours Placebo

Supplementary Figure 31: Forest plot of Fatigue

	Resmet	irom	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Harrison 2019	4	84	4	41	6.9%	0.49 [0.13, 1.85]	
Harrison 2023	47	822	13	318	32.5%	1.40 [0.77, 2.55]	
Harrison 2024	59	645	28	321	60.6%	1.05 [0.68, 1.61]	-
Total (95% CI)		1551		680	100.0%	1.09 [0.77, 1.55]	•
Total events	110		45				
Heterogeneity: Tau² =	= 0.01; Chi	= 2.09	df = 2 (F	9 = 0.35); I ² = 4%		
Test for overall effect				0.1 0.2 0.5 1 2 5 10 Favours Resmetirom Favours Placebo			

Supplementary Figure 32: Forest plot of Headache

	Resmet	irom	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Harrison 2019	11	84	6	41	19.5%	0.89 [0.36, 2.25]	
Harrison 2023	62	822	24	318	80.5%	1.00 [0.64, 1.57]	
Total (95% CI)		906		359	100.0%	0.98 [0.65, 1.47]	•
Total events	73		30				
Heterogeneity: Tau² = Test for overall effect:	•			0.1 0.2 0.5 1 2 5 10 Favours Resmetirom Favours Placebo			

Supplementary Figure 33: Forest plot of Covid

	Resmet	irom	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Harrison 2023	75	822	27	318	28.8%	1.07 [0.71, 1.64]	—
Harrison 2024	123	645	66	321	71.2%	0.93 [0.71, 1.21]	-
Total (95% CI)		1467		639	100.0%	0.97 [0.77, 1.21]	*
Total events	198		93				
Heterogeneity: Tau² =	0.00; Chi	$^{2} = 0.34$	df = 1 (P	01 02 05 1 2 5 10			
Test for overall effect:	Z = 0.29 (I	P = 0.78	3)				Favours Resmetirom Favours Placebo

Supplementary Figure 34: Forest plot of UTI

	Resmetirom Placebo		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Harrison 2019	9	84	4	41	7.6%	1.10 [0.36, 3.36]	-
Harrison 2023	50	822	23	318	41.9%	0.84 [0.52, 1.35]	
Harrison 2024	60	645	27	321	50.5%	1.11 [0.72, 1.71]	-
Total (95% CI)		1551		680	100.0%	0.99 [0.72, 1.34]	*
Total events	119		54				
Heterogeneity: Tau² = Test for overall effect:	•			0.1 0.2 0.5 1 2 5 10 Favours Resmetirom Favours Placebo			

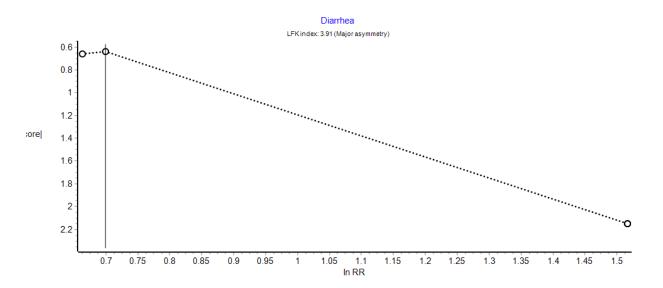
Supplementary Figure 35: Forest plot of Back pain

	Resmetirom Placebo				Risk Ratio	Risk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI		
Harrison 2023	42	822	14	318	29.4%	1.16 [0.64, 2.10]			
Harrison 2024	62	645	38	321	70.6%	0.81 [0.55, 1.19]			
Total (95% CI)		1467		639	100.0%	0.90 [0.65, 1.24]	•		
Total events	104		52						
Heterogeneity: Tau² = Test for overall effect:					0.1 0.2 0.5 1 2 5 10 Favours Resmetirom Favours Placebo				

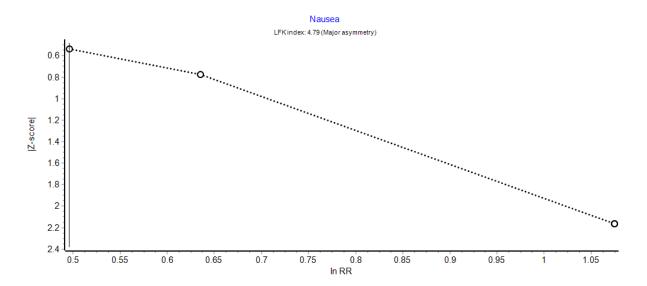
Supplementary Figure 36: Forest plot of Arthalgia

	Resmet	irom	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Harrison 2023	67	822	21	318	35.8%	1.23 [0.77, 1.98]	
Harrison 2024	83	645	40	321	64.2%	1.03 [0.73, 1.47]	-
Total (95% CI)		1467		639	100.0%	1.10 [0.83, 1.46]	*
Total events	150		61				
Heterogeneity: Tau² =	0.00; Chi	$^2 = 0.35$	df = 1 (F	01 02 05 1 2 5 10			
Test for overall effect:	Z = 0.66 (P = 0.51)				Favours Resmetirom Favours Placebo

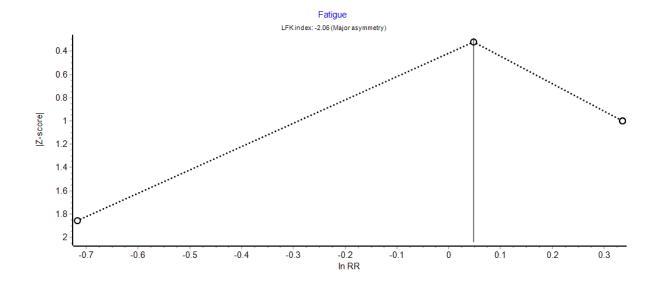
Supplementary Figure 37: Doi plot of Diarrhea



Supplementary Figure 38: Doi plot of Nausea



Supplementary Figure 39: Doi plot of Fatigue



Supplementary Figure 40: Doi plot of UTI

