Supplementary Figure 1 Risk of bias summary of the included studies.
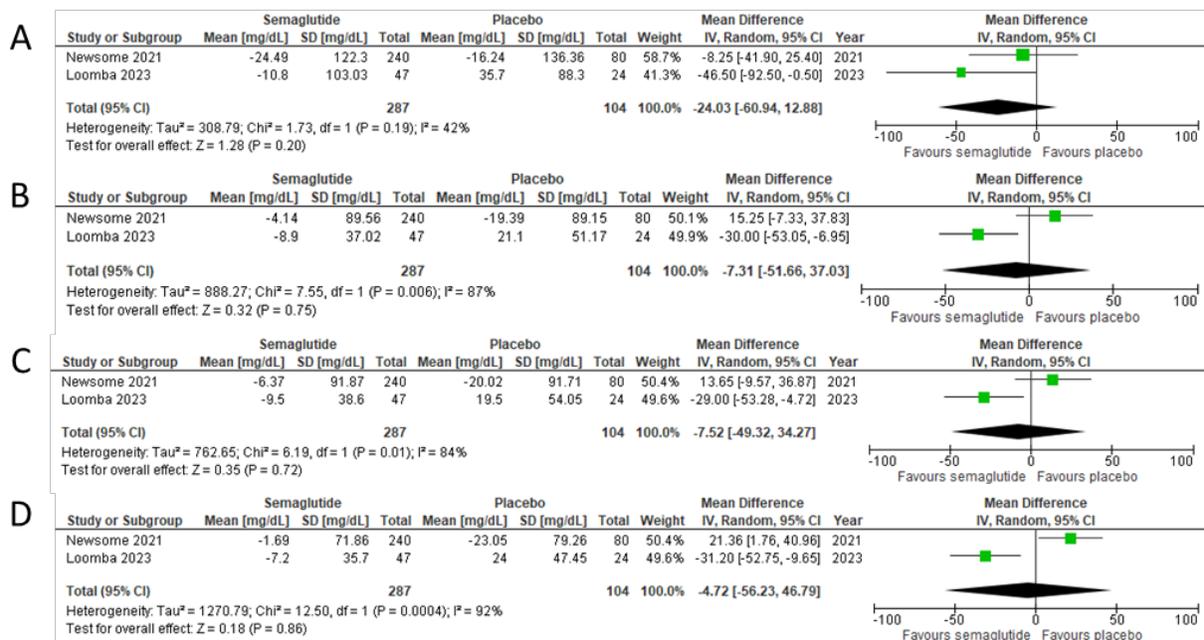
Supplementary Figure 2 Effect of semaglutide on cardiometabolic parameters. A: Triglycerides; B: total cholesterol; C: non-HDL cholesterol; D: LDL cholesterol. HDL=high-density lipoprotein. LDL=low-density lipoprotein.

Supplementary Table 1 Study selection inclusion and exclusion criteria

	Inclusion	Exclusion
Design	- Randomized controlled trial. - Non-randomized controlled trial. - Prospective controlled trial.	- All other study designs.
Population	- Age ≥ 18 years old. - NAFLD diagnosed by imaging (US, CT, MRI) or liver biopsy. Includes the spectrum of NAFLD (fatty liver, non-alcoholic steatohepatitis, cirrhosis) - May include if subset of NAFLD patients reported separately.	- Age <18 years old. o May include if adult and pediatric outcomes reported separately. - Significant alcohol use (>14 drinks/week). - Liver disease from other etiologies such as viral hepatitis, autoimmune hepatitis, Wilson's disease, hemochromatosis, acute fatty liver of pregnancy.
Intervention	- Semaglutide regardless of route or dose. - Semaglutide in addition to standard of care (eg. Patient	- New initiation of combination therapy including semaglutide (eg. New start metformin + semaglutide).

	previously already on other anti-diabetic medications for diabetes).	o May include if separate group with semaglutide only as comparison. - Intervention duration <12 weeks.
Comparison	- Placebo. - No intervention. - Standard of care (eg. Diet, exercise, pharmacologic therapies if underlying medical indication such as anti-diabetic medications for diabetes).	- No comparator group.
Outcome	- Any outcomes.	- None.

Supplementary Table 2 Predefined Ovid MEDLINE® systematic review search strategy

#	Searches	Results
1	exp Fatty Liver/	45417
2	(Non-alcoholic Fatty Liver Diseas* or Non alcoholic Fatty Liver Diseas* or Nonalcoholic Fatty Liver Diseas* or NAFLD or NAFL).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	36698
3	(Non-alcoholic Steatohepatitis or Non alcoholic Steatohepatitis or Nonalcoholic Steatohepatitis or NASH).mp.	17603
4	exp Glucagon-Like Peptide 1/	10890
5	exp Incretins/	17326
6	(ozempic or semaglutide or rybelsus or wegovy).mp.	1119
7	1 or 2 or 3	60615
8	4 or 5 or 6	18147
9	7 and 8	474

Supplementary Table 3 Sensitivity analysis with individual study exclusion

Outcome	Study exclusion	Heterogeneity	Overall effect
	None	Chi² = 0.95, I² = 0%, P = 0.33	OR = 3.18, 95% CI 1.70 to 5.95, P = 0.0003
Resolution of NASH	**Newsome 2021**	**N/A**	**OR = 1.96, 95% CI 0.62 to 6.24, P = 0.25**
	Loomba 2023	N/A	OR = 3.89, 95% CI 1.85 to 8.19, P = 0.0003
	None	Chi² = 4.90, I² = 80%, P = 0.03	OR = 0.71, 95% CI 0.15 to 3.41, P = 0.67
Improvement in fibrosis stage	Newsome 2021	N/A	OR = 0.29, 95% CI 0.08 to 1.04, P = 0.06
	Loomba 2023	N/A	OR = 1.44, 95% CI 0.77 to 2.70, P = 0.25
	None	Chi² = 5.59, I² = 82%, P = 0.02	OR = 2.4, 95% CI 0.64 to 9.32, P = 0.19
Improvement in total NAS	Newsome 2021	N/A	OR = 1.15, 95% CI 0.42 to 3.14, P = 0.78
	Loomba 2023	**N/A**	**OR = 4.54, 95% CI 2.65 to 7.76, P < 0.00001**
	None	Chi² = 2.32, I² 57= %, P = 0.13	OR = 2.83, 95% CI 1.19 to 6.71, P = 0.02
Improvement in steatosis	**Newsome 2021**	**N/A**	**OR = 1.62, 95% CI 0.58 to 4.50, P = 0.36**
	Loomba 2023	N/A	OR = 4.00, 95% CI 2.28 to 7.01, P < 0.00001
	None	Chi² = 0.73, I² = 0%, P = 0.39	OR = 1.81, 95% CI 1.11 to 2.96, P = 0.02
Improvement in lobular inflammation	**Newsome 2021**	**N/A**	**OR = 1.23, 95% CI 0.45 to 3.38, P = 0.68**
	Loomba 2023	N/A	OR = 2.04, 95% CI 1.17 to 3.57, P = 0.01
Improvement in hepatocellular ballooning	None	Chi² = 0.12, I² = 0%, P = 0.72	OR = 2.92, 95% CI 1.83 to 4.65, P < 0.00001
	Newsome 2021	**N/A**	**OR = 2.48, 95% CI 0.89 to 6.90, P = 0.08**
	Loomba 2023	N/A	OR = 3.05, 95% CI 1.81 to 5.14, P < 0.00001

Outcome	Study excluded	Heterogeneity	Effect estimate
	None	Chi² = 4.61, I² = 57%, P = 0.10	SMD = -0.48, 95% CI -0.86 to -0.11, P = 0.01
	Newsome 2021	**Chi² = 0.03, I² = 0%, P = 0.87**	**SMD = -0.27, 95% CI -0.62 to 0.07, P = 0.12**
	Flint 2021	Chi² = 2.61, I² = 62%, P = 0.11	SMD = -0.58, 95% CI -1.05 to -0.11, P = 0.02
Liver stiffness	Loomba 2023	Chi² = 3.37, I² = 70%, P = 0.07	SMD = -0.55, 95% CI -1.07 to -0.02, P = 0.04
	None	Chi² = 2.81, I² = 64%, P = 0.09	MD = -4.96, 95% CI -9.92 to 0.01, P = 0.05
	Flint 2021	N/A	MD = -2.93, 95% CI -5.58 to -0.28, P = 0.03
Liver steatosis	Loomba 2023	N/A	MD = -8.13, 95% CI -13.61 to -2.65, P = 0.004
	None	Chi² = 1.61, I² = 0%, P = 0.45	MD = -14.06, 95% CI -22.06 to -6.07, P = 0.0006
	Newsome 2021	Chi² = 1.56, I² = 36%, P = 0.21	MD = -14.93, 95% CI -28.80 to -1.05, P = 0.03
	Flint 2021	Chi² = 0.79, I² = 0%, P = 0.37	MD = -16.27, 95% CI -25.59 to -6.95, P = 0.0006
ALT	Loomba 2023	Chi² = 0.28, I² = 0%, P = 0.59	MD = -11.33, 95% CI -20.58 to -2.07, P = 0.02
	None	Chi² = 1.62, I² = 0%, P = 0.45	MD = -11.44, 95% CI -17.23 to -5.65, P = 0.0001
	Newsome 2021	Chi² = 1.62, I² = 38%, P = 0.20	MD = -11.80, 95% CI -22.36 to -1.23, P = 0.03
	Flint 2021	Chi² = 0.69, I² = 0%, P = 0.41	MD = -13.16, 95% CI -19.92 to -6.40, P = 0.0001
AST	Loomba 2023	Chi² = 0.42, I² = 0%, P = 0.52	MD = -9.71, 95% CI -16.28 to -3.15, P = 0.004

Outcome	Study	Heterogeneity	Effect
	None	Chi² = 1.25, I² = 0%, P = 0.54	MD = -6.53, 95% CI -11.21 to -1.85, P = 0.006
	Newsome 2021	Chi² = 0.06, I² = 0%, P = 0.81	MD = -9.47, 95% CI -16.52 to -2.41, P = 0.009
	Flint 2021	**Chi² = 0.41, I² = 0%, P = 0.52**	**MD = -5.23, 95% CI -10.67 to 0.21, P = 0.06**
Body weight	Loomba 2023	Chi² = 1.83, I² = 10%, P = 0.29	MD = -6.24, 95% CI -11.76 to -0.71, P = 0.03
	None	Chi² = 2.83, I² = 29%, P = 0.24	MD = -1.10, 95% CI -1.48 to -0.72, P < 0.00001
	Newsome 2021	Chi² = 1.46, I² = 31%, P = 0.23	MD = -1.27, 95% CI -1.82 to -0.72, P < 0.00001
	Flint 2021	Chi² = 2.76, I² = 64%, P = 0.10	MD = -1.18, 95% CI -1.82 to -0.54, P = 0.0003
HgA1c with T2DM	Loomba 2023	Chi² = 0.07, I² = 0%, P = 0.80	MD = -0.93, 95% CI -1.28 to -0.58, P < 0.00001
	None	Chi² = 2.55, I² = 61%, P = 0.11	MD = -0.37, 95% CI -0.79 to 0.06, P = 0.09
HgA1c without T2DM	Newsome 2021	N/A	MD = -0.10, 95% CI -0.57 to 0.37, P = 0.68
	Flint 2021	**N/A**	**MD = -0.54, 95% CI -0.80 to -0.28, P < 0.0001**
	None	Chi² = 1.73, I² = 42%, P = 0.19	MD = -24.03, 95% CI -60.94 to 12.88, P = 0.20
	Newsome 2021	**N/A**	**MD = -46.50, 95% CI -92.50 to -0.50, P = 0.05**
Triglycerides	Loomba 2023	N/A	MD = -8.25, 95% CI -41.90 to 25.40, P = 0.63
Total cholesterol	None	Chi² = 7.55, I² = 87%, P = 0.006	MD = -7.31, 95% CI -51.66 to 37.03, P = 0.75

Outcome	Study	Heterogeneity	Effect estimate
	Newsome 2021	**N/A**	**MD = -30.00, 95% CI -53.05 to -6.95, P = 0.01**
	Loomba 2023	N/A	MD = 15.25, 95% CI -7.33 to 37.83, P = 0.19
	None	Chi² = 6.19, I² = 84%, P = 0.01	MD = -7.52, 95% CI -49.32 to 34.27, P = 0.72
Non-HDL cholesterol	**Newsome 2021**	**N/A**	**MD = -29.00, 95% CI -53.28 to -4.72, P = 0.02**
	Loomba 2023	N/A	MD = 13.65, 95% CI -9.57 to 36.87, P = 0.25
	None	Chi² = 12.50, I² = 92%, P = 0.0004	MD = -4.72, 95% CI -56.23 to 46.79, P = 0.86
LDL cholesterol	**Newsome 2021**	**N/A**	**MD = -31.20, 95% CI -52.75 to -9.65, P = 0.005**
	Loomba 2023	**N/A**	**MD = 21.36, 95% CI 1.76 to 40.96, P = 0.03**
	None	Chi² = 1.95, I² = 49%, P = 0.16	OR = 3.72, 95% CI 1.68 to 8.23, P = 0.001
GI related side effects	**Newsome 2021**	N/A	OR = 6.55, 95% CI 2.21 to 19.36, P = 0.0007
	Loomba 2023	N/A	OR = 2.78, 95% CI 1.65 to 4.67, P = 0.0001
	None	Chi² = 0.03, I² = 0%, P = 0.98	OR = 1.40, 95% CI 0.75 to 2.62, P = 0.29
Serious adverse events	**Newsome 2021**	Chi² = 0.02, I² = 0%, P = 0.90	OR = 1.48, 95% CI 0.47 to 4.69, P = 0.50
	Flint 2021	Chi² = 0.03, I² = 0%, P = 0.86	OR = 1.40, 95% CI 0.71 to 2.77, P = 0.33
	Loomba 2023	Chi² = 0.00, I² = 0%, P = 0.99	OR = 1.37, 95% CI 0.70 to 2.69, P = 0.36

Supplementary Table 4 Sensitivity analysis of fixed effect analysis model

Outcome	Heterogeneity	Overall effect
Resolution of NASH	Chi² = 0.95, I² = 0%, P = 0.33	SMD = 3.18, 95% CI 1.70 to 5.95, P = 0.0003
Improvement in fibrosis stage	Chi² = 4.90, I² = 80%, P = 0.03	OR = 1.06, 95% CI 0.60 to 1.86, P = 0.85
Improvement in total NAS	Chi² = 5.59, I² = 82%, P = 0.02	OR = 3.34, 95% CI 2.08 to 5.36, P < 0.00001
Improvement in steatosis	Chi² = 2.32, I² = 57%, P = 0.13	OR = 3.25, 95% CI 1.99 to 5.31, P < 0.00001
Improvement in lobular inflammation	Chi² = 0.73, I² = 0%, P = 0.39	OR = 1.81, 95% CI 1.11 to 2.96, P = 0.02
Improvement in hepatocellular ballooning	Chi² = 0.12, I² = 0%, P = 0.72	OR = 2.92, 95% CI 1.83 to 4.65, P < 0.00001
Liver stiffness	Chi² = 4.61, I² = 57%, P = 0.10	MD = -0.55, 95% CI -0.78 to -0.31, P < 0.00001
Liver steatosis	Chi² = 2.81, I² = 64%, P = 0.09	MD = -3.92, 95% CI -6.30 to -1.53, P = 0.001
ALT	Chi² = 1.61, I² = 0%, P = 0.45	MD = -14.06, 95% CI -22.06 to -6.07, P = 0.0006
AST	Chi² = 1.62, I² = 0%, P = 0.45	MD = -11.44, 95% CI -17.23 to -5.65, P = 0.0001
Body weight	Chi² = 1.25, I² = 0%, P = 0.54	MD = -6.53, 95% CI -11.21 to -1.85, P = 0.006
HgA1c with T2DM	Chi² = 2.83, I² = 29%, P = 0.24	MD = -1.07, 95% CI -1.38 to -0.76, P < 0.00001
Triglycerides	Chi² = 1.73, I² = 42%, P = 0.19	MD = -21.58, 95% CI -48.74 to 5.57, P = 0.12
Total cholesterol	Chi² = 7.55, I² = 87%, P = 0.006	MD = -6.92, 95% CI -23.05 to 9.21, P = 0.40

Non-HDL cholesterol	Chi² = 6.19, I² = 84%, P = 0.01	MD = -6.72, 95% CI -23.50 to 10.06, P = 0.43
LDL cholesterol	Chi² = 12.50, I² = 92%, P = 0.0004	MD = -2.44, 95% CI -16.94 to 12.07, P = 0.74
GI related side effects	Chi² = 1.95, I² = 49%, P = 0.16	OR = 3.26, 95% CI 2.04 to 5.21, P < 0.00001
Serious adverse events	Chi² = 0.03, I² = 0%, P = 0.98	OR = 1.40, 95% CI 0.75 to 2.62, P = 0.29