

SUPPLEMENTARY

Section 1: Search strategy

A PubMed and Medline = 210

Intervention	Searches	Results
Sodium glucose Cotransporter-2 inhibitor	("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 ("non"[All Fields] AND "alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR ("hepatic"[All Fields] AND "steatosis"[All Fields]) OR "hepatic steatosis"[All Fields]) OR (("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields])) OR (("liver"[MeSH Terms] OR "liver"[All Fields] OR "livers"[All Fields] OR "liver s"[All Fields]) AND ("enzyme s"[All Fields] OR "enzymes"[MeSH Terms] OR "enzymes"[All Fields] OR "enzyme"[All Fields] OR "enzymic"[All Fields] OR "enzymically"[All Fields] OR "enzymology"[MeSH Subheading] OR "enzymology"[All Fields])) OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR "steatohepatitis"[All Fields])) AND (("sodium glucose transport proteins"[MeSH Terms] OR ("sodium glucose"[All Fields] AND "transport"[All Fields] AND "proteins"[All Fields]) OR "sodium glucose transport proteins"[All Fields] OR ("sodium"[All Fields] AND "glucose"[All Fields] AND "cotransporter"[All Fields]) OR "sodium glucose cotransporter"[All Fields]) AND "2"[All Fields] AND ("antagonists and inhibitors"[MeSH Subheading] OR ("antagonists"[All Fields] AND "inhibitors"[All Fields]) OR "antagonists and inhibitors"[All Fields] OR "inhibitors"[All Fields] OR "inhibitor"[All Fields] OR "inhibitor s"[All Fields]))	174
Empagliflozin	("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 ("non"[All Fields] AND "alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR ("hepatic"[All Fields] AND "steatosis"[All Fields]) OR "hepatic steatosis"[All Fields]) OR (("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields])) OR (("liver"[MeSH Terms] OR "liver"[All Fields] OR "livers"[All Fields] OR "liver s"[All Fields]) AND ("enzyme s"[All Fields] OR "enzymes"[MeSH Terms] OR "enzymes"[All Fields] OR "enzyme"[All Fields] OR "enzymic"[All Fields] OR "enzymically"[All Fields] OR "enzymology"[MeSH Subheading] OR "enzymology"[All Fields])) OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR "steatohepatitis"[All Fields])) AND ("empagliflozin"[Supplementary Concept] OR "empagliflozin"[All Fields])	36
Canagliflozin	("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 ("non"[All Fields] AND "alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR ("hepatic"[All Fields] AND "steatosis"[All Fields]) OR "hepatic steatosis"[All Fields]) OR (("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields])) OR (("liver"[MeSH Terms] OR "liver"[All Fields] OR "livers"[All Fields] OR "liver s"[All Fields]) AND ("enzyme s"[All Fields] OR "enzymes"[MeSH Terms] OR "enzymes"[All Fields] OR "enzyme"[All Fields] OR "enzymic"[All Fields] OR "enzymically"[All Fields] OR "enzymology"[MeSH Subheading] OR "enzymology"[All Fields])) OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR "steatohepatitis"[All Fields])) AND ("canagliflozin"[MeSH Terms] OR "canagliflozin"[All Fields])	40

A PubMed and Medline Cd.

Intervention	Searches	Results
Dapagliflozin	("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 ("non"[All Fields] AND "alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR ("hepatic"[All Fields] AND "steatosis"[All Fields]) OR "hepatic steatosis"[All Fields]) OR (("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields])) OR ("liver"[MeSH Terms] OR "liver"[All Fields] OR "livers"[All Fields] OR "liver s"[All Fields]) AND ("enzyme s"[All Fields] OR "enzymes"[MeSH Terms] OR "enzymes"[All Fields] OR "enzyme"[All Fields] OR "enzymic"[All Fields] OR "enzymically"[All Fields] OR "enzymology"[MeSH Subheading] OR "enzymology"[All Fields])) OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR "steatohepatitis"[All Fields])) AND ("2 3 4 ethoxybenzyl 4 chlorophenyl 6 hydroxymethyltetrahydro 2h pyran 3 4 5 triol"[Supplementary Concept] OR "2 3 4 ethoxybenzyl 4 chlorophenyl 6 hydroxymethyltetrahydro 2h pyran 3 4 5 triol"[All Fields] OR "dapagliflozin"[All Fields])	39
Ipragliflozin	("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 ("non"[All Fields] AND "alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR ("hepatic"[All Fields] AND "steatosis"[All Fields]) OR "hepatic steatosis"[All Fields]) OR (("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields])) OR ("liver"[MeSH Terms] OR "liver"[All Fields] OR "livers"[All Fields] OR "liver s"[All Fields]) AND ("enzyme s"[All Fields] OR "enzymes"[MeSH Terms] OR "enzymes"[All Fields] OR "enzyme"[All Fields] OR "enzymic"[All Fields] OR "enzymically"[All Fields] OR "enzymology"[MeSH Subheading] OR "enzymology"[All Fields])) OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR "steatohepatitis"[All Fields])) AND ("ipragliflozin"[Supplementary Concept] OR "ipragliflozin"[All Fields])	22
Luseogliflozin	("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 ("non"[All Fields] AND "alcoholic"[All Fields] AND "fatty"[All Fields] AND "liver"[All Fields] AND "disease"[All Fields]) OR "non alcoholic fatty liver disease"[All Fields] OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR ("hepatic"[All Fields] AND "steatosis"[All Fields]) OR "hepatic steatosis"[All Fields]) OR (("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields]) AND ("disease"[MeSH Terms] OR "disease"[All Fields] OR "diseases"[All Fields] OR "disease s"[All Fields] OR "diseased"[All Fields])) OR ("liver"[MeSH Terms] OR "liver"[All Fields] OR "livers"[All Fields] OR "liver s"[All Fields]) AND ("enzyme s"[All Fields] OR "enzymes"[MeSH Terms] OR "enzymes"[All Fields] OR "enzyme"[All Fields] OR "enzymic"[All Fields] OR "enzymically"[All Fields] OR "enzymology"[MeSH Subheading] OR "enzymology"[All Fields])) OR ("non-alcoholic"[All Fields] AND ("fatty liver"[MeSH Terms] OR ("fatty"[All Fields] AND "liver"[All Fields]) OR "fatty liver"[All Fields] OR "steatohepatitis"[All Fields])) AND ("1 5 anhydro 1 5 4 ethoxybenzyl 2 methoxy 4 methylphenyl 1 thioglucitol"[Supplementary Concept] OR "1 5 anhydro 1 5 4 ethoxybenzyl 2 methoxy 4 methylphenyl 1 thioglucitol"[All Fields] OR "luseogliflozin"[All Fields])	10
7	1 or 2 or 3 or 4 or 5 or 6	210

B Cochrane library = 16

#	Searches	Results
1	("Non-alcoholic Fatty Liver Disease" [MeSH terms] AND "Sodium-Glucose Transporter 2 Inhibitors" [MESH terms])	3
2	("Non-alcoholic Fatty Liver Disease" [MeSH terms] AND "Empagliflozin" [keywords])	7
3	("Non-alcoholic Fatty Liver Disease" [MeSH terms] AND "Canagliflozin" [keywords])	0
4	("Non-alcoholic Fatty Liver Disease" [MeSH terms] AND "Dapagliflozin" [keywords])	0

#	Searches	Results
5	("Non-alcoholic Fatty Liver Disease" [MeSH terms] AND "Ipragliflozin" [keywords])	1
6	("Non-alcoholic Fatty Liver Disease" [MeSH terms] AND "Luseogliflozin" [keywords])	1
7	1 or 2 or 3 or 4 or 5 or 6	12

C CINAHL

#	Searches	Results
1	"Sodium glucose cotransporter 2 inhibitor" [All text] AND "non-alcoholic fatty liver disease" [All text] OR "Sodium glucose cotransporter 2 inhibitor" [All text] AND "nonalcoholic steatohepatitis" [All text] OR "Sodium glucose cotransporter 2 inhibitor" [All text] AND "non-alcoholic hepatic steatosis" [All text] OR "Sodium glucose cotransporter 2 inhibitor" [All text] AND "liver enzymes" [All text]	11
2	"Empagliflozin" [All text] AND "non-alcoholic fatty liver disease" [All text] OR "Empagliflozin" [All text] AND "nonalcoholic steatohepatitis" [All text] OR "Empagliflozin" [All text] AND "non-alcoholic hepatic steatosis" [All text] OR "Empagliflozin" [All text] AND "liver enzymes" [All text]	7
3	"Canagliflozin" [All text] AND "non-alcoholic fatty liver disease" [All text] OR "Canagliflozin" [All text] AND "nonalcoholic steatohepatitis" [All text] OR "Canagliflozin" [All text] AND "non-alcoholic hepatic steatosis" [All text] OR "Canagliflozin" [All text] AND "liver enzymes" [All text]	2
4	"Dapagliflozin" [All text] AND "non-alcoholic fatty liver disease" [All text] OR "Dapagliflozin" [All text] AND "nonalcoholic steatohepatitis" [All text] OR "Dapagliflozin" [All text] AND "non-alcoholic hepatic steatosis" [All text] OR "Dapagliflozin" [All text] AND "liver enzymes" [All text]	4
5	"Ipragliflozin" [All text] AND "non-alcoholic fatty liver disease" [All text] OR "Ipragliflozin" [All text] AND "nonalcoholic steatohepatitis" [All text] OR "Ipragliflozin" [All text] AND "non-alcoholic hepatic steatosis" [All text] OR "Ipragliflozin" [All text] AND "liver enzymes" [All text]	2
6	"Luseogliflozin" [All text] AND "non-alcoholic fatty liver disease" [All text] OR "Luseogliflozin" [All text] AND "nonalcoholic steatohepatitis" [All text] OR "Luseogliflozin" [All text] AND "non-alcoholic hepatic steatosis" [All text] OR "Luseogliflozin" [All text] AND "liver enzymes" [All text]	0
7	1 or 2 or 3 or 4 or 5 or 6'	17

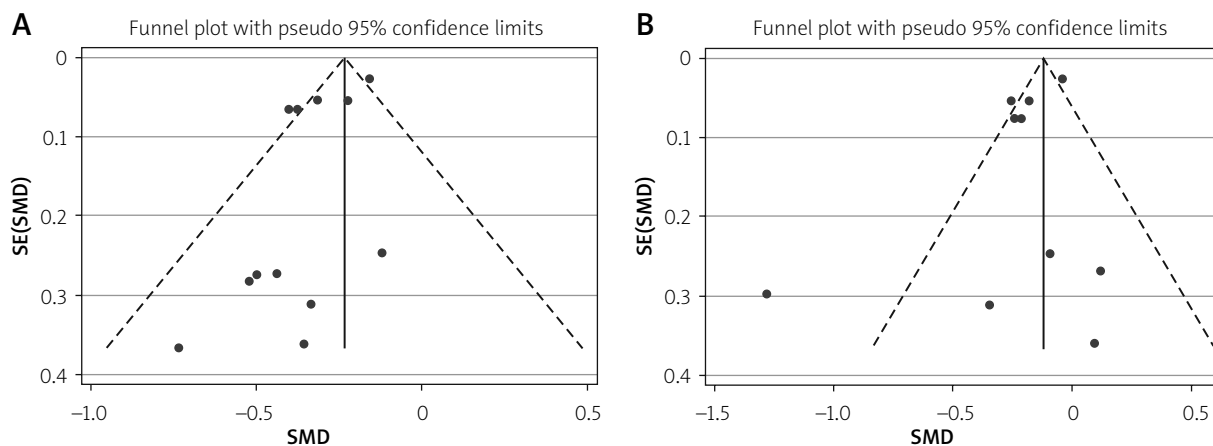
D ClinicalTrials.gov (Completed trials N = 7)

Intervention	Title [NCT number]	Date completed
Tofogliflozin	SGLT2 Inhibitor Versus Sulfonylurea on Type 2 Diabetes With NAFLD [02649465]	No result posted
Dapagliflozin	SGLT2 Inhibitors and Metformin on Metabolism and Non-Alcoholic SteatoHepatitis (SMASH) [02696941]	No result posted
Empagliflozin	SGLT2 Inhibitors as a Novel Treatment for Pediatric Non-Alcoholic Fatty Liver Disease [02696941]	Suspended
Empagliflozin	Effect of Empagliflozin on Liver Fat in Non-diabetic Patients [04642261]	No results posted
Ipragliflozin	Effects of Ipragliflozin on Excessive Fat in Type 2 Diabetes Patients With Non-alcoholic Fatty Liver Disease Treated With Metformin and Pioglitazone [02875821]	06/23/2017
Empagliflozin	Effect of Empagliflozin on Liver Fat Content in Patients With Type 2 Diabetes (E-LIFT) [02686476]	08/15/2019
Dapagliflozin	Dapagliflozin Efficacy and Action in NASH (DEAN) [03723252]	Recruiting
Empagliflozin	Effects of Empagliflozin on Liver Fat Content, Energy Metabolism and Body Composition in Patients With Type 2 Diabetes (EmLiFa) [02637973]	01/14/2019
Empagliflozin	The Effect of Empagliflozin on NAFLD in Asian Patients With Type 2 Diabetes [02964715]	Unknown
Dapagliflozin	Effects of Dapagliflozin 10 mg on Insulin Resistance in Patients With Type 2 Diabetes Mellitus	02/05/2018
Canagliflozin	CANagliflozin Treatment And Trial Analysis-Sulfonylurea (CANTATA-SU) SGLT2 Add-on to Metformin Versus Glimepiride [00968812]	06/02/2013
Dapagliflozin	A Study to Investigate Effects of Omega-3 Carboxylic Acids and Dapagliflozin on Liver Fat Content in Diabetic Patients [02279407]	01/27/2017
Empagliflozin	(Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients [01131676]	05/16/2016

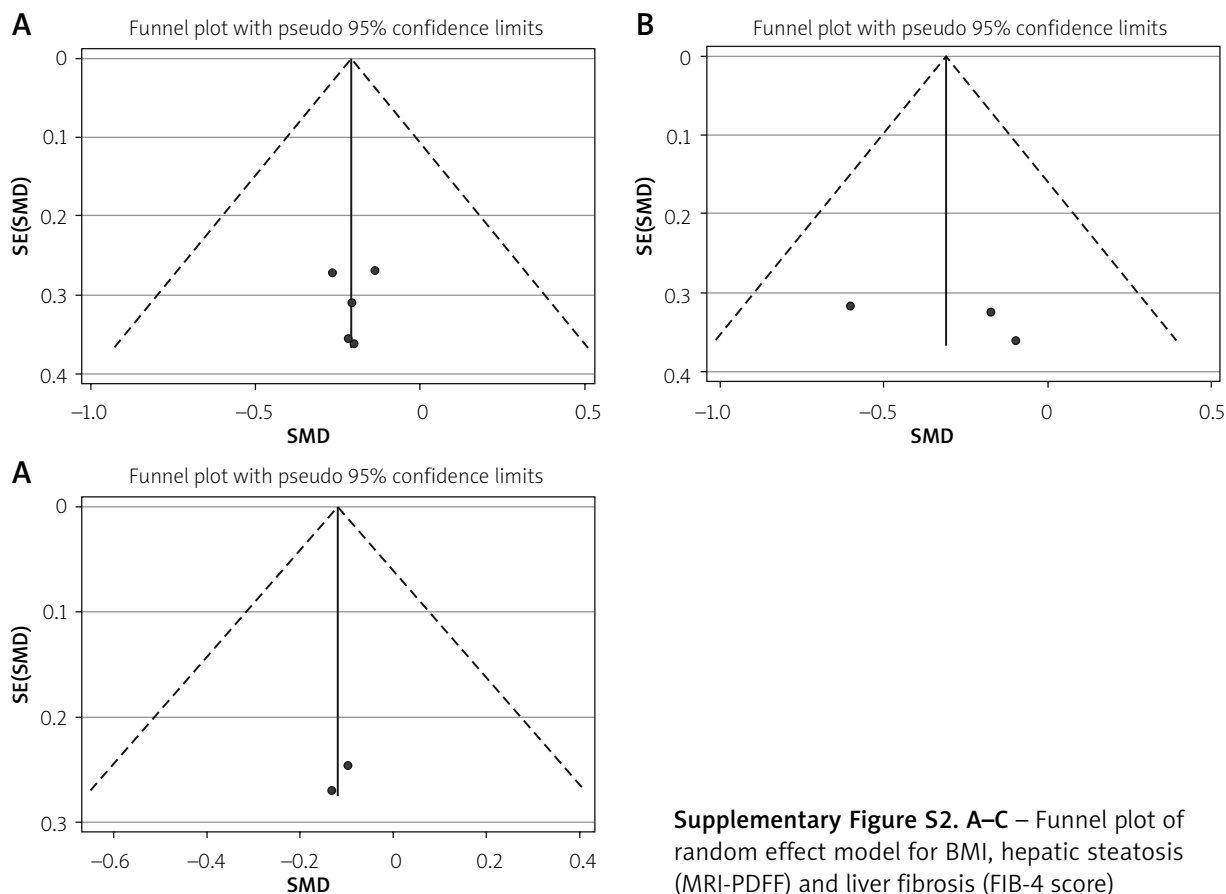
Duplicates = 34, Records screened = 212, Clinical trials = 49, Clinical trials excluded = 38, Clinical trials analysed = 11

Section 2. Definitions

Variable	Common definition
Non-alcoholic fatty liver disease (NAFLD)	Hepatic steatosis in the absence of alcohol use and other causes of fatty liver.
Non-alcoholic steatohepatitis (NASH)	Presence of $\geq 5\%$ HS with inflammation and hepatocyte injury with or without fibrosis. This can progress to cirrhosis, liver failure, and rarely liver cancer

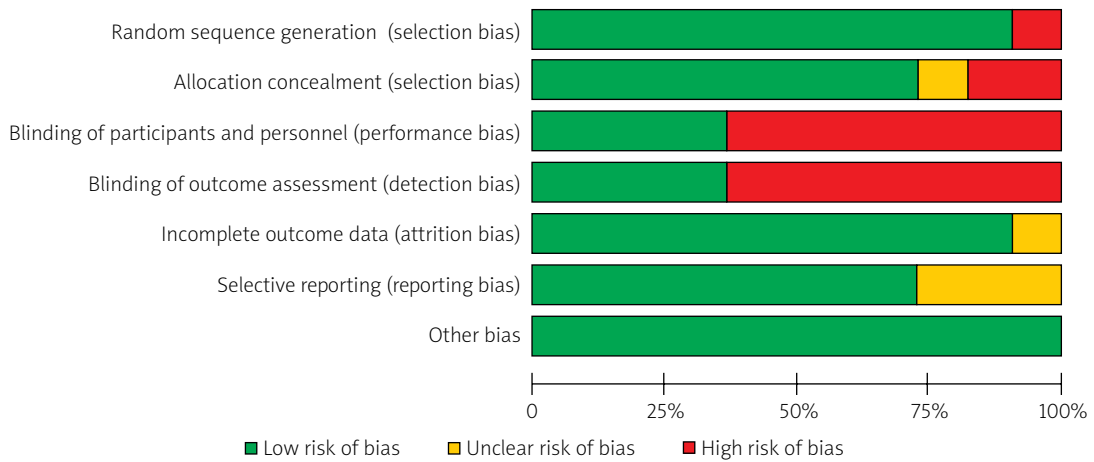


Supplementary Figure S1. A, B – Funnel plot of random effect model for Alanine transaminase (ALT) and aspartate transaminase (AST) measurement. The vertical axis of the plot used standard error to estimate the sample size of the study, plotting large population studies at the top and smaller at the bottom. The horizontal spread reflected the power and effect size of the included studies



Supplementary Figure S2. A–C – Funnel plot of random effect model for BMI, hepatic steatosis (MRI-PDFF) and liver fibrosis (FIB-4 score)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aso 2019	+	+	-	-	+	?	+
Bando 2017	+	+	-	-	+	+	+
Cefalu 2013	+	+	+	+	+	+	+
Eriksson 2018	+	+	+	+	+	+	+
Ito 2017	+	?	-	-	+	+	+
Kuchay 2018	+	-	-	-	+	+	+
Kurinami 2018	-	-	-	-	?	?	+
Latva-Rasku 2019	+	+	+	+	+	+	+
Leiter 2016	+	+	-	-	+	+	+
Shibuya 2018	+	+	-	-	+	?	+
Zinman 2016	+	+	+	+	+	+	+



Supplementary Figure S3. Raveman Bias assessment and summary