Supplementary File

Table S1. PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	See Title
ABSTRACT			
Structured	2	Provide a structured summary including, as applicable:	See
summary		background; objectives; data sources; study eligibility criteria,	Abstract, 2
		participants, and interventions; study appraisal and synthesis	
		methods; results; limitations; conclusions and implications of key	
		findings; systematic review registration number.	
INTRODUCTI	ION		
Rationale	3	Describe the rationale for the review in the context of what is	3-4
		already known.	
Objectives 4		Provide an explicit statement of questions being addressed with	4
		reference to participants, interventions, comparisons, outcomes,	
		and study design (PICOS).	
METHODS	<u>'</u>		
Protocol and	5	Indicate if a review protocol exists, if and where it can be accessed	No
registration		(e.g. Web address), and, if available, provide registration	registration
		information including registration number.	
Eligibility	6	Specify study characteristics (e.g., PICOS, length of follow-up) and	5
criteria		report characteristics (e.g. years considered, language, publication	
		status) used as criteria for eligibility, giving rationale.	
Information	7	Describe all information sources (e.g. databases with dates of	5
sources		coverage, contact with study authors to identify additional studies)	
		in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database,	Table S2
		including any limits used, such that it could be repeated.	

Study selection	9	State the process for selecting studies (i.e. screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g. piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made.	Table 1
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	NA
Summary measures	13	State the principal summary measures (e.g. risk ratio, difference in means).	5-6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. I ²) for each meta-analysis.	5-6

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g. publication bias, selective reporting	NA
		within studies).	
Additional	16	Describe methods of additional analyses (e.g. sensitivity or	5-6
analyses		subgroup analyses, meta-regression), if done, indicating which	
		were pre-specified.	
RESULTS			
Study	17	Give numbers of studies screened, assessed for eligibility, and	Figure S1
selection		included in the review, with reasons for exclusions at each	
		stage, ideally with a flow diagram.	
Study	18	For each study, present characteristics for which data were	Table 1
characteristics		extracted (e.g. study size, PICOS, follow-up period) and	

		provide the citations.							
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).							
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 1						
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.							
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA						
Additional analysis	23	Give results of additional analyses, if done (e.g. sensitivity or subgroup analyses, meta-regression [see Item 16]).	7						
DISCUSSION	•								
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g. healthcare providers, users, and policy makers).	7-8						
Limitations	25	Discuss limitations at study and outcome level (e.g. risk of bias), and at review-level (e.g. incomplete retrieval of identified research, reporting bias).							
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.							
FUNDING									
Funding	27	Describe sources of funding for the systematic review and other support (e.g. supply of data); role of funders for the systematic review.	Indicated						

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097.

doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Table S2. Search strategy

Search strategy in PubMed

- #1 ((FNDC 5[Text Word]) OR (irisin[Text Word])) OR (FNDC-5[Text Word])
- #2 ((((((nonalcoholic fatty liver disease[Text Word]) OR (non-alcoholic steatohepatitis[Text Word])) OR (steatosis[Text Word])) OR (NASH[Text Word])) OR (fatty liver[Text Word])

 Word])
- #3 #1 and #2

Search strategy in Scopus

- #1 (TITLE-ABS-KEY (fndc 5) OR TITLE-ABS-KEY (irisin) OR TITLE-ABS-KEY (fndc-5))
- #2 (TITLE-ABS-KEY (nonalcoholic AND fatty AND liver AND disease) OR TITLE-ABS-KEY (nonalcoholic AND steatohepatitis) OR TITLE-ABS-KEY (steatosis) OR TITLE-ABS-KEY (nafld) OR TITLE-ABS-KEY (nash) OR TITLE-ABS-KEY (fatty AND liver))
- #3 #1 and #2

Search strategy in Cochrane Library

- #1 (FNDC 5):ti,ab,kw OR (Irisin):ti,ab,kw OR (FNDC-5):ti,ab,kw
- #2 (nonalcoholic fatty liver disease):ti,ab,kw OR (nonalcoholic steatohepatitis):ti,ab,kw OR (steatosis):ti,ab,kw OR (NAFLD):ti,ab,kw OR (NASH):ti,ab,kw OR (fatty liver):ti,ab,kw
- #3 #1 and #2

Figure S1. Circulating irisin in nonalcoholic fatty liver disease ascertained by magnetic resonance or liver biopsy vs. controls. NAFLD — nonalcoholic fatty liver disease; SMD — standardized mean difference; CI — confidence interval; SD — standard deviation

		NAFLD		Any controls				_
Author (year)	N	Mean	SD	N	Mean	SD	SMD (95% CI)	_
Canivet (2020)	22	5.48	23.13	10	3.25	8.16	0.11 (-0.64 to 0.86)	
Monserrat-Mesquida (2020)	70	99.9	82.88	30	60.7	55.9	0.51 (0.08 to 0.95)	-
Moreno-Perez (2018)	48	413.5	86	24	496.7	140	-0.77 (-1.28 to -0.26)	
Polyzos (2014)	31	33.2	7.2	52	41.1	14.7	-0.63 (-1.08 to -0.17)	
Waluga (2019)	25	4.98	2.02	25	29.67	19.9	-1.72 (-2.38 to -1.06)	
Zhang (2013)	222	6.8	9.37	74	9.01	11.3	-0.22 (-0.49 to 0.04)	-
Total $(I^2 = 87\%)$							-0.44 (-0.96 to 0.09)	•
								-2.0 0.0

Figure S2. Serum irisin in nonalcoholic fatty liver disease ascertained by magnetic resonance or liver biopsy vs. controls. NAFLD — nonalcoholic fatty liver disease; SMD — standardized mean difference; CI — confidence interval; SD — standard deviation

		NAFLD)	Any controls				_
Author (year)	N	Mean	SD	N	Mean	SD	— SMD (95% CI)	_
Canivet (2020)	22	5.48	23.13	10	3.25	8.16	0.11 (-0.64 to 0.86)	_
Moreno-Perez (2018)	48	413.5	86	24	496.7	140	-0.77 (-1.28 to -0.26)	
Polyzos (2014)	31	33.2	7.2	52	41.1	14.7	-0.63 (-1.08 to -0.17)	
Waluga (2019)	25	4.98	2.02	25	29.67	19.9	-1.72 (-2.38 to -1.06)	
Zhang (2013)	222	6.8	9.37	74	9.01	11.3	-0.22 (-0.49 to 0.04)	
Total (I ² = 81%)							-0.63 (-1.14 to -0.13)	•
								-2.0 0.0 2.0