Supplementary

Appendix 1

A full list of NOS-adapted questions

❖ **Representativeness of the sample.***
The sample is clearly or somewhat representative of the general population or the population of interest.

❖ **Sample size—Justified and satisfactory.***
The appropriate sample size for a study assessed using the NOS is not predetermined, **as the scale does not require a specific sample size**. The adequacy of sample size is evaluated based on the precision of the estimates, the confidence intervals, the effect sizes, and the statistical significance of the results.

❖ **Non-respondents.***
When comparability between respondents and non-respondents' characteristics is established, and the response rate is satisfactory.

❖ **Ascertainments of exposure**
When measurement tool is validated.**
When measurement tool is not validated but the tool is available or described.*

❖ **Comparability**
The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.
a) The study controls for the most important factor (e.g age, sex etc).*
b) The study control for any additional factor.*

❖ **Assessment of outcome**
Independent blind assessment.**
Record linkage.**
Self-report.*

❖ **Statistical test**
The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (P value).*

https://dx.doi.org/10.21037/tgh-23-31

Table S1 Literature search keywords

Journal databases keyword strategy
1) Outcome of interest: NAFLD • ("Non-alcoholic Fatty Liver Disease" [MeSH] OR "fatty liver" [Title/Abstract] OR "hepatic steatosis" [Title/Abstract] OR "NAFLD" [Title/Abstract])
2) Population of interest: lean individuals • ("lean" [Title/Abstract] OR "non-obese" [Title/Abstract] OR "normal weight" [Title/Abstract] OR "low BMI" [Title/Abstract]) AND ("Non-alcoholic Fatty Liver Disease" [MeSH] OR "fatty liver" [Title/Abstract] OR "hepatic steatosis" [Title/Abstract] OR "NAFLD" [Title/Abstract])
3) Determinants: genetics and epigenetics • ("genetics" [MeSH] OR "genetic factors" [Title/Abstract] OR "epigenetics" [MeSH] OR "epigenetic factors" [Title/Abstract] OR "epigenetic modifications" [Title/Abstract] OR "DNA methylation" [Title/Abstract] OR "histone modifications" [Title/Abstract] OR "microRNA" [Title/Abstract]) AND ("Non-alcoholic Fatty Liver Disease" [MeSH] OR "fatty liver" [Title/Abstract] OR "hepatic steatosis" [Title/Abstract] OR "NAFLD" [Title/Abstract]) AND ("lean" [Title/Abstract] OR "non-obese" [Title/Abstract] OR "normal weight" [Title/Abstract] OR "low BMI" [Title/Abstract])

Table S2 Eligibility criteria for studies upon screening the search results obtained

Inclusion criteria	Exclusion criteria
• Study conducted in English • Primary outcome reports genetic or epigenetic effects on NAFLD • Primary outcome reporting among lean individuals • Full-text paper available • Peer-reviewed prior to final publication	• Paper not peer-reviewed • Full-text paper not available • Written in non-English language • Study design being a review of the literature (e.g., scoping, systematic, narrative, or other reviews)

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Table S3 Results of Newcastle Ottawa Scale assessment for quality appraisal of cross-sectional studies

Study	Total score	Selection				Comparability	Outcome	
		Representativeness of the sample	Sample size	Non-respondents	Ascertainments of exposure	Based on design and analysis	Assessment of Outcome	Statistical Test
Adams *et al.*, 2012	7	*	*	*	*	*	*	*
Wei *et al.*, 2015	8	*	*	*	*	**	*	*
Chahal *et al.*, 2022	9	*	*	*	**	**	*	*
Shen *et al.*, 2014	6	*	*		*	*	*	*
Lin *et al.*, 2022	9	*	*	*	*	**	**	*
Honda *et al.*, 2016	9	*	*	*	**	**	*	*
Feldman *et al.*, 2017	7	*	*		*	*	**	*
Zeng *et al.*, 2021	5	*			*	**	*	*
Stasinou *et al.*, 2022	7	*	*		*	*	**	*
Li *et al.*, 2023	9	*	*	*	**	*	**	*
Petersen *et al.*, 2010	7	*			**	*	**	*
Chatterjee *et al.*, 2021	7	*	*		*	*	**	*

Table S4 Results of Newcastle Ottawa Scale assessment for quality appraisal of cohort studies

Study	Total score	Selection				Comparability	Outcome		
		Representativeness of the intervention cohort	Selection of non-intervention cohort	Ascertainments of exposure	Demonstration that outcome of interest was not present at start of study	Based on design and analysis	Assessment of Outcome	Was follow up long enough for outcomes to occur	Adequacy of follow up
Buzova *et al.*, 2020	7	*	*	*	*		*		*
Niriella *et al.*, 2019	10	*	*	*	*	**	*	*	**
Yoshida *et al.*, 2020	7	*	*	*	*	**	*		
Hagström *et al.*, 2017	10	*	*	*	*	**	**	*	*
Fracanzani *et al.*, 2017	6	*		*		**	**		
Stanislawski *et al.*, 2020	5			*	*	**	*		

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