# Analyzing and evaluating the prevalence and metabolic profile of lean NAFLD compared to obese NAFLD: a systemic review and meta-analysis

Hareer Fatima, Hussain Sohail Rangwala, Muhammad Saqlain Mustafa, Muhammad Ashir Shafique<sup>D</sup>, Syed Raza Abbas and Burhanuddin Sohail Rangwala

# Abstract

**Background:** Non-alcoholic fatty liver disease (NAFLD) is a common liver condition affecting 25%–40% of the worldwide population. NAFLD is traditionally related to obesity and metabolic disorders. NAFLD can also affect non-obese individuals, termed "lean NAFLD" (LN), who exhibit a paradoxical combination of physical leanness and metabolic obesity. Factors contributing to LN remain unclear, necessitating further research. This analysis aims to understand LN's prevalence and metabolic characteristics compared to obese NAFLD (ON) populations.

**Methods:** This meta-analysis searched various databases until August 1, 2023. Inclusion criteria involved observational studies comparing LN with overweight/obese NAFLD. Data extraction included baseline characteristics, disease occurrence, metabolic profile, and clinical parameters—statistical analysis employed calculating risk ratios (RR) and standard mean differences.

**Results:** Twenty-five studies were analyzed. LN is associated with lower prevalence in both NAFLD (RR 0.27, 95% confidence interval (CI) 0.14–0.52, p = <0.0001) and total (RR 0.27, 95% CI 0.15–0.51, p < 0.0001) population. LN had lower diabetes mellitus (RR 0.78, 95% CI 0.71–0.87, p < 0.00001), dyslipidemia (RR 0.87, 95% CI 0.79–0.95, p = 0.002), hypertension (RR 0.80, 95% CI 0.74–0.87, p < 0.00001), and metabolic syndrome (RR 0.45, 95% CI 0.31–0.64, p < 0.00001) compared to those with ON. The LN group's lipid profile, blood pressure, and other clinical parameters were favorable compared to ON.

**Conclusion:** The prevalence of NAFLD among lean and non-lean individuals varies by region. Our analysis revealed that LN is associated with lower metabolic diseases, fasting blood sugar, blood pressure, and a more favorable lipid profile compared to ON.

# Plain language summary

## NAFLD prevalence and its characteristics among obese vs lean population

Non-alcoholic fatty Liver Disease (NAFLD) is a prevalent liver condition affecting a substantial portion of the global population, commonly linked to obesity and metabolic disorders. However, a subset of individuals with NAFLD, termed "lean NAFLD" (LN), challenges the conventional association by presenting with physical leanness despite metabolic obesity. The factors contributing to this condition are not well understood, prompting this meta-analysis to explore the prevalence and metabolic characteristics of

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LN compared to obese NAFLD (ON) populations. The study, conducted through August 1st, 2023, analyzed 25 studies meeting inclusion criteria, which involved observational studies comparing LN with Overweight/Obese NAFLD. Data extraction included baseline characteristics, disease occurrence, metabolic profiles, and clinical parameters. Statistical analysis utilized risk ratios (RR) and standard mean differences. The results indicated that LN is associated with a significantly lower prevalence in both the NAFLD and general populations. LN demonstrated lower occurrences of diabetes (DM), dyslipidemia, hypertension, and metabolic syndrome compared to ON. Additionally, the LN group exhibited a more favorable lipid profile, blood pressure, and other clinical parameters in comparison to the ON group. In conclusion, the prevalence of NAFLD varies among lean and non-lean individuals across different regions. The meta-analysis revealed that LN is linked to a lower occurrence of metabolic diseases, lower fasting blood sugar levels, lower blood pressure, and a more favorable lipid profile compared to those with ON. These findings contribute valuable insights into the distinct metabolic characteristics of LN, shedding light on potential avenues for further research and clinical considerations in the understanding and management of NAFLD.

Keywords: lean NAFLD, metabolic profile, NAFLD, prevalence

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# Introduction

Non-alcoholic fatty liver disease (NAFLD) arises from fat accumulation in the liver. It is one of the most prevalent liver-related pathologies, impacting 25%–40% of the global population.<sup>1</sup> NAFLD encompasses a broad spectrum of liver-related conditions, including steatosis, which can progress to steatohepatitis and advanced fibrosis, potentially culminating in cirrhosis.<sup>2</sup> It is a prevalent condition affecting a significant portion of the general population, elevating the risk of individuals developing a range of systemic complications. These complications encompass diabetes mellitus (DM), chronic kidney disease, extra-hepatic and hepatic malignancies, and cardiovascular diseases.<sup>3,4</sup> NAFLD has been intricately associated with obesity, which is closely intertwined with many metabolic disorders. These disorders include abnormal lipid profiles, fatty acid cytotoxicity, and insulin resistance (IR).<sup>5</sup> NAFLD disturbs lipid and glucose homeostasis, primarily through IR. De novo lipogenesis and IR play a major role in fat accumulation in the liver.6 Approximately 70%-75% of NAFLD patients are diagnosed with type 2 DM, and around 60% also meet the criteria for metabolic syndrome (MS). Notably, 90% of obese individuals are affected by NAFLD.<sup>7</sup> Recently, there has been a significant revision in the definition of NAFLD, now called metabolic-associated fatty liver disease (MAFLD). This updated terminology underscores the importance of metabolic dysfunction in conjunction with the presence of fatty liver.<sup>8</sup>

NAFLD can manifest in individuals who are not classified as obese, typically with a body mass index (BMI) less than 30 kg/m<sup>2</sup> in non-Asians or less than 27.5 kg/m<sup>2</sup> in Asians, and even in those who fall within the normal-weight range, with a BMI less than  $25 \text{ kg/m}^2$  in non-Asians or less than 23 kg/m<sup>2</sup> in Asians.<sup>9</sup> It has been revealed that non-obese patients with NAFLD exhibit an abnormal metabolic profile compared to those without the condition, placing them at an increased risk of cardiovascular morbidity and mortality. Physicians often refer to this group as "physically lean but metabolically obese" due to this paradoxical combination of their physical appearance and metabolic health.9 This lean phenotype is observed in about 25% of the NAFLD population. While it was initially presumed that this lean variant might be less severe than its obese counterpart, emerging evidence indicates that individuals with lean NAFLD (LN) face a more challenging clinical course, including a higher risk of severe liver disease, reduced survival rates, advanced fibrosis, and an overall poorer prognosis.  $^{10}\,$ 

There is a notable lack of consensus regarding the factors associated with lean and obese NAFLD (ON) populations. Some factors that have been identified include differences in age, genetic predisposition, and the stage of fibrosis. However, it is important to underscore that more extensive research is required to fully understand the factors contributing to LN, particularly given that risk factors and prognosis can vary among racial or ethnic groups. Further investigations are essential to unravel the complexities of this condition and its diverse manifestations.<sup>7</sup> In this research, we performed an extensive meta-analysis of the available literature to assess the overall occurrence and metabolic attributes of LN in comparison to ON.

# Methods

## Data sources and search strategy

This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure a rigorous and standardized approach.<sup>11</sup> In pursuit of a comprehensive and unbiased search, PubMed and Cochrane Library databases were searched, spanning publications till August 1, 2023. The dual-database search was designed to mitigate the potential for publication bias. Our search strategy was meticulously crafted, employing a well-constructed search string to identify studies relevant to our research. This search string encompassed a myriad of MeSH terms, including but not limited to "Diabetes Mellitus," "Dyslipidemias," "Hypertension," "Metabolic Syndrome," "Nonalcoholic Fatty Liver Disease," and "Obesity." Subsequently, articles were manually retrieved and assessed for further evaluation.

# Inclusion criteria

The study selection criteria were as follows: (a) inclusion of only observational studies, (b) comparison of LN with overweight/obese NAFLD in the selected studies, (c) lean was defined within the parameters of the shortlisted article as individuals with a BMI of  $\leq 25 \text{ kg/m}^2$ , and for the Asian population, a BMI of  $\leq 23 \text{ kg/m}^2$ , (d) overweight/obese individuals were those with a BMI of  $\geq 25.0 \text{ kg/m}^2$ , and for the Asian population, a BMI of selection, a BMI  $\geq 23 \text{ kg/m}^2$ , and (e) inclusion of studies that

reported outcomes of interest. Articles in Languages apart from English and non-observational studies were excluded from the analysis. These criteria were applied to ensure the relevance and consistency.

# Data extraction and quality assessment

We meticulously reviewed relevant studies in the initial screening phase to filter out those failing to meet our predefined eligibility criteria. In order to prevent the inclusion of duplicate articles, we employed the EndNote Reference Library program. Subsequently, we obtained the full-text versions of shortlisted articles and subjected them to a thorough examination to determine their suitability for inclusion in our meta-analysis. Four authors collaborated to extract pertinent information from each included study to maintain consistency and accuracy in the data extraction process. These data encompassed baseline characteristics and all outcomes of interest. The primary outcomes were to explore the prevalence of LN compared to ON in both the entire NAFLD cohort and the general population.

Additionally, we sought to examine the occurrence of systemic diseases and the presence of MS in lean versus ON patients. Our secondary outcomes of interest encompassed a comparative analysis of critical clinical parameters, including high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol levels, triglycerides, systolic and diastolic blood pressures (BPs), waist circumference (WC), and fasting blood sugar (FBS) levels between lean and ON patients. Any discrepancies or uncertainties arising during the data extraction process were addressed through collaborative discussions among the authors to ensure the integrity of the data. One of our authors employed the Newcastle Ottawa Scale (NOS) for the quality assessment of the included studies.12

# Statistical analysis

For the statistical analysis in our study, we utilized Revman Version 5.4.1. To assess the significance of differences between LN and ON groups, we calculated the risk ratio (RR) and standard mean difference (SMD) outcomes, along with their respective 95% confidence intervals (CIs). In cases where studies exhibited substantial heterogeneity, we employed the  $I^2$  statistic,

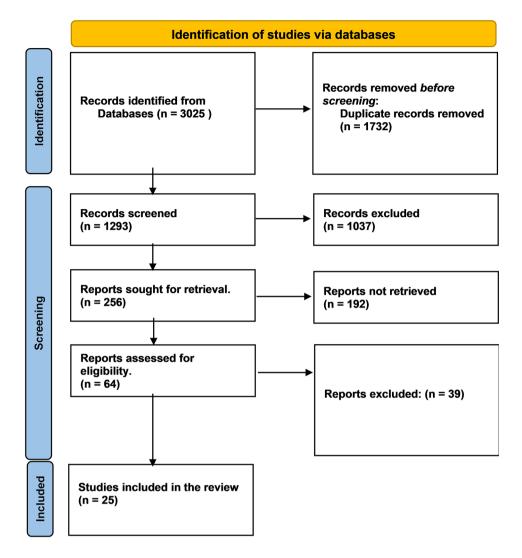


Figure 1. PRISMA flowchart.

considering values less than 50% indicative of mild heterogeneity. Sensitivity analysis using the leave-one-out method was performed for studies with high heterogeneity. We regarded a p value below 0.05 as having statistical significance, signifying the presence of a meaningful difference between the groups.

## Results

## Studies selection

A comprehensive literature search in databases such as PubMed, Medline, and Cochrane identified an initial total of 3025 papers. After eliminating duplicates, 1293 unique records remained for further screening, and subsequent evaluation of titles and abstracts led to the selection of 64 articles for detailed examination. After a meticulous review, 25 articles were shortlisted<sup>13–33</sup> (Figure 1).

# Characteristics of the included studies

Twenty-five meticulously chosen observational studies, 14 cohorts, and 11 cross-sectional studies were analyzed. They were conducted across a diverse array of geographic regions, including the United States of America, India, China, Italy, Spain, South Korea, Japan, Singapore, Bangladesh, Austria, Thailand, and Saudi Arabia. These studies were designed to address a wide spectrum of population characteristics. The sample sizes in these studies were quite variable, with participant numbers ranging from as low as 113 to a substantial 194,787, totaling 263,756 individuals diagnosed with NAFLD. The follow-up durations in these studies spanned a broad range, from as short as 1 year to as long as 37 years, with the combined average follow-up period across all the studies amounting to 9.4 years. The average mean age of participants hovered around 57.119 (4.1203) years for lean individuals and 51.412 (9.0101) for obese (Table 1).

#### Quality assessment

We employed the NOS to evaluate the study quality, with a \* being awarded for each category, results in Supplemental Table S1. Majority of our studies were deemed to exhibit minimal risk of bias, affirming their high level of reliability.

## Prevalence

Prevalence data comparing LN to overweight or ON patients among the total NAFLD and general population indicate that LN is significantly less common. In the analysis of total NAFLD patients, the prevalence of LN was notably lower in Asia (RR 0.24, 95% CI 0.16–0.38, p<0.0001), Europe (RR 0.36, 95%) CI 0.23-0.56, *p*<0.00001), North America (RR 0.33, 95% CI 0.09–1.30, *p* < 0.11), and total (RR 0.27, 95% CI 0.14-0.52, p < 0.0001). Among the Asian population, 11.7% of NAFLD cases were found in the lean population, while 88.0% were among the non-lean, indicating a slightly higher prevalence in this group. In the European population, 20% were lean, and 79% were non-lean. Among the North American countries, 55.2% were non-lean, and 44.8% were lean. In total, 48.6% of the diagnosed NAFLD cases were in the lean population, and 51.4% were in the non-lean population, showing a nearly equal distribution (Figure 2).

Similar trends were observed in the prevalence of LN within the general population, with (RR 0.24, 95% CI 0.16–0.37, p < 0.00001) in Asia, (RR 0.34, 95% CI 0.23–0.51, p < 0.00001) in Europe (RR 0.33, 95% CI 0.08–1.31, p = 0.12) in North America, and (RR 0.27, 95% CI 0.15–0.51, p = <0.0001) in total. The prevalence of NAFLD was 2.8% among the lean Asian population, with 21.1% occurring in non-lean individuals. Among the European population, 8.1% of lean individuals had NAFLD, and 32.4% of non-lean individuals had the condition. In the North American population, the prevalence was 0.33% among the

lean population and 0.27% among the non-lean population. In the total population, the prevalence was 0.34% among lean individuals and 0.36% among those who were either obese or non-lean and had NAFLD (Figure 3).

These prevalence figures underscore the global distribution of lean and ON and provide context for interpreting the impact of body composition on the metabolic outcomes observed in the meta-analysis.

#### Systemic diseases

Regarding metabolic health outcomes, the metaanalysis revealed that individuals with LN have more favorable results than those with ON. LN individuals showed a 22% lower risk of developing DM (RR 0.78, 95% CI 0.71-0.87, p < 0.00001), a 13% lower risk of dyslipidemia (RR 0.87, 95% CI 0.79–0.95, p<0.002), a 20% lower risk of hypertension (HTN) (RR 0.80, 95% CI 0.74–0.87, p < 0.00001), and a remarkable 55% lower risk of MS (RR 0.45, 95% CI 0.31-0.64, p < 0.00001) compared to those with ON. Heterogeneity was high in all outcomes for which sensitivity analysis was performed. These findings indicate that individuals with LN are less prone to these metabolic disorders than those with ON (Figure 4).

#### Lipid profile

Regarding lipid profiles, LN individuals exhibited more favorable outcomes than their ON counterparts. Specifically, they had higher levels of HDL (SMD 0.29, 95% CI 0.17–0.41, p<0.00001) and lower levels of triglycerides (SMD –0.21, 95% CI –0.30 to –0.11, p<0.0001) and LDL (SMD –0.09, 95% CI –0.16 to –0.02, p=0.01). Heterogeneity was high in all outcomes for which sensitivity analysis was performed. These differences in lipid levels suggest that LN may have a lower cardiovascular risk than those with ON (Figure 5).

#### Blood pressure

When considering BP measurements, LN individuals showed slightly lower levels of both systolic (SMD -0.23, 95% CI -0.36 to -0.11, p < 0.0003) and diastolic (SMD -0.27, 95% CI -0.37 to -0.16, p < 0.00001) BP compared to individuals with ON. Heterogeneity was high in

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# Table 1. Baseline characteristics.

Study	Location	Study type	Sample size	Number of lean (L) and obese (O) NAFLD	Mean age of lean (L) and obese (O) NAFLD, <i>N</i> (SD)	Median follow- up period years (years)
Bhat et al. (2013) <sup>13</sup>	India	Cross-sectional	150	L-30 0-120	L-39.9 + 7.4 0-42.8 + 8.3	-
Kumar et al. (2013) <sup>14</sup>	India	Cross-sectional	205	L-27 0-178	L-38 (15.4) O-40.9 (12.59)	3
Feng et al. (2014) <sup>15</sup>	China	Cross-sectional	898	L-143 0-764	L-48.17 (10.5) O-46.92 (11.19)	1
Fracanzani et al. (2017) <sup>16</sup>	Italy	Cohort	669	L-143 0-526	L-46 (13) O-49 (12)	_
Gonzalez-Cantero et al. (2018) <sup>17</sup>	Spain	Cross-sectional	113	L-55 O-58	L-41.35 (10.29) O-46.25 (11.08)	_
Kim et al. (2018) <sup>18</sup>	South Korea	Cohort	924	L-420 O-504	L-48.1 (9.2) O-47.3 (8.8)	10
Sinha et al. (2020) <sup>19</sup>	India	Cross- sectional	120	L-37 0-83	L-58.5 (13.8) O-54.3 (10)	1
Zou et al. (2020) <sup>9</sup>	USA	Cohort	4711	L-1528 O-3183	_	17
Shah et al. (2020) <sup>6</sup>	India	Cross-sectional	250	L-69 O-181	-	1.5
Hirose et al. (2020) <sup>20</sup>	Japan	Cohort	223	L-102 0-121	L-40.7 (11.8) O-42.9 (14.3)	37
Rahman et al. (2020) <sup>21</sup>	Bangladesh	Cross-sectional	242	L-57 O-185	L-48.98 (13.78) O-45.22 (11.71)	2
Lum et al. (2020) <sup>22</sup>	Singapore	Cohort	263	L-57 0-206	L-54 (12.9) O-49.5 (12.5)	13
Semmler et al. (2021) <sup>23</sup>	Austria	Cohort	1986	L-374 0-1612	L-59.98 (9.5) O-60.48 (8.7)	10
Khayyat et al. (2021) <sup>24</sup>	Saudi Arabia	Cross-sectional	1261	L-159 O-1102	L-49.95 (15.34) O-52.67 (13.8)	4
Navarroza and Wong (2021) <sup>7</sup>	China	Cross-sectional	546	L-60 O-486	L-55 (14.3) O-51.5 (14.4)	10
Oladunjoye et al. (2021) <sup>25</sup>	USA	Cohort	194787	L-119048 O-75739	L-57.5 (0.1) O-51.5 (0.1)	5
Tan et al. (2022) <sup>26</sup>	India Singapore China	Cross-sectional	1812	L-392 0-1420	L-49.64 (12.47) O-47.34 (12.9)	13
Boonchai et al. (2022) <sup>27</sup>	Thailand	Cross-sectional	424	L-41 0-383	L-75 (10.7) O-66.8 (11.9)	10
Wang et al. (2022) <sup>28</sup>	China	Cohort	5533	L-1034 O-4499	L-50.66 (13.15) O-48.8 (13.28)	6
Qazi-Arisar et al. (2022) <sup>10</sup>	Canada	Cohort	176	L-54 0-122	L-61.6 (19.11) O-60.3 (29.12)	7

(Continued)

Study	Location	Study type	Sample size	Number of lean (L) and obese (O) NAFLD	Mean age of lean (L) and obese (O) NAFLD, <i>N</i> (SD)	Median follow- up period years (years)
Lan et al. (2022) <sup>30</sup>	China	Cohort	23197	L-1543 0-21654	L-53.6 (11.4) O-52.8 (11.5)	1
Ahmed et al. (2023) <sup>29</sup>	USA	Cohort	4834	L-414 0-4420	L-51.5 (18) O- 51.83 (14.6)	20
Wijarnpreecha et al. (2023) <sup>31</sup>	USA	Cohort	18594	L-2137 0-16457	L-51 (20) O-50.55 (15.9)	10
Li et al. (2023) <sup>32</sup>	China	Cohort	845	L-160 0-685	L-45 (10.37) O-41 (11.11)	2
Biswas et al. (2023) <sup>33</sup>	India	Cohort	1051	L-127 O-924	L-34 (14.81) O-40.43 (11.9)	23

#### Table 1. (Continued)

NAFLD, non-alcoholic fatty liver disease.

	lean r	afld	obese	nafid		Risk Ratio		Risk Ratio
Study or Subgroup	Events		Events		Woight	M-H, Random, 95% Cl	Voar	M-H, Random, 95% Cl
3.1.1 Asia	Lvents	Total	Lvents	Total	weight	m-n, Random, 55% Ci	rear	M-H, Randolli, 95% Cl
Bhat 2013	20	150	100	150	4.00	0.05 (0.10, 0.05)	2012	
	30 27	150 205	120 178	150 205	4.0% 4.0%	0.25 [0.18, 0.35]		
Kumar 2013 Feng 2014	134	898	764	898	4.0%	0.15 [0.11, 0.22] 0.18 [0.15, 0.21]		
Kim 2017	420	924	504	924	4.0%	0.83 [0.76, 0.91]		+
Hirose 2020	102	223	121	223	4.0%	0.84 [0.70, 1.02]		
Lum 2020	57	263	108	223	4.0%	0.53 [0.40, 0.69]		
Rahman 2020	57	203	185	203	4.0%	0.31 [0.24, 0.39]		
Shah 2020	69	242	181	242	4.0%			
Sinha 2020	37	120	83	120	4.0%	0.38 [0.31, 0.47] 0.45 [0.33, 0.60]		
Khayyat 2021	159	1261	1102	1261	4.0%	0.14 [0.12, 0.17]		
Navarozza 2021	60	546	486	546	4.0%	0.12 [0.10, 0.16]		
Tan 2021	392	1812	1420	1812	4.0%	0.28 [0.25, 0.30]		+
Wang 2022	1034	5533	4499	5533	4.0%	0.23 [0.22, 0.24]		+
Boonchai 2022	41	424	383	424	4.0%	0.11 [0.08, 0.14]		<b>←</b> →−
Lan 2022	1543	23197	21654	23197	4.0%	0.07 [0.07, 0.07]		
Biswas 2023	127	1051	924	1051	4.0%	0.14 [0.12, 0.16]		
Li 2023	160	845	685	845	4.0%	0.23 [0.20, 0.27]		
Subtotal (95% CI)	100	37944	005	37944	68.0%	0.24 [0.16, 0.38]	2023	
Total events	4449		33397					
Heterogeneity: Tau <sup>2</sup> =		= 3544.04		(P < 0.00)	001)·IP=	100%		
Test for overall effect: 2				(, 0.00				
			.,					
3.1.2 Europe								
Fracanzani 2017	143	669	526	669	4.0%	0.27 [0.23, 0.32]	2017	
Cantero 2018	25	55	30	55	4.0%	0.83 [0.57, 1.21]	2018	
Semmler 2021	374	1986	1612	1986	4.0%	0.23 [0.21, 0.25]	2021	+
Subtotal (95% CI)		2710		2710	12.0%	0.36 [0.23, 0.56]		-
Total events	542		2168					
Heterogeneity: Tau <sup>2</sup> =	0.14; Chi2:	= 42.84, d	f= 2 (P =	0.00001)	;  = 95%	ò		
Test for overall effect: 2	Z = 4.53 (P	< 0.0000	1)					
3.1.3 North America								
Zou 2020	1528	4711	3183	4711	4.0%	0.48 [0.46, 0.50]		· · · · · · · · · · · · · · · · · · ·
Oladunjoye 2021		194787		194787	4.0%	1.57 [1.56, 1.58]		
Ahmed 2022	414	4834	4420	4834	4.0%	0.09 [0.09, 0.10]		+
Arisar 2022	54	176	122	176	4.0%	0.44 [0.35, 0.56]		
Wijarnpreecha 2023	2137	18594	16457	18594	4.0%	0.13 [0.12, 0.14]	2023	+
Subtotal (95% CI)		223102		223102	20.1%	0.33 [0.09, 1.30]		
Total events	123181		99921					
Heterogeneity: Tau <sup>2</sup> =			U, df = 4	(P < 0.00)	JU1); I*=	100%		
Test for overall effect: 2	2 = 1.59 (P	= 0.11)						
Total (95% CI)		263756		263756	100.0%	0.27 [0.14, 0.52]		
Total events	128172		135486					
Heterogeneity: Tau <sup>2</sup> =		= 53454.5		4 (P < 0.0)	0001); l² =	= 100%		
Test for overall effect: 2								0.1 0.2 0.5 1 2 5 10
Test for subgroup diffe				= 0.49).1	<sup>2</sup> =0%			Favours [Lean NAFLD] Favours [Obese NAFLD]

**Figure 2.** Forest plot for lean NAFLD versus obese NAFLD for prevalence in total NAFLD population: (3.1.1) Asia; (1.1.2) Europe; (3.1.3) North America. NAFLD, non-alcoholic fatty liver disease.

Ahmed 2022         414         7414         4420           Arisar 2022         54         265         122           Wijarnprecha 2023         2137         52556         16457           Subtotal (95% Cl)         37394386         37394386         99921           Heterogeneity: Tau <sup>2</sup> = 2.44; Chi <sup>2</sup> = 16932.21, df = 4 (P + Test for overall effect: Z = 1.57 (P = 0.12)         Total (95% Cl)         37559286	NAFLD	Risk Ratio	Risk Ratio
Kumar 2013         27         205         178           Shat 2013         30         280         120           ieng 2014         134         2000         764           im 2017         420         10141         504           um 2020         57         263         108           kahman 2020         57         1682         185           Shah 2020         69         750         181           Sinha 2020         37         240         83           Hrose 2020         102         6080         121           Vavarozza 2021         60         6995         486           ian 2021         1543         101510         21654           Wang 2022         1034         18395         4499           Sononchal 2022         127         1051         924           Subtotal (95% CI)         158211         166         16	Total Weight	M-H, Random, 95% Cl	Year M-H, Random, 95% Cl
Bhat 2013       30       280       120         ieng 2014       134       2000       764         (im 2017       420       10141       504         (im 2010       57       1682       185         Shaha 2020       67       1682       185         Shaha 2020       37       240       83         Hirose 2020       102       6080       121         Iavarozza 2021       60       6995       486         an 2021       392       1812       1420         (hayat 2021       1543       101510       21654         Vang 2022       1034       18395       4499         Salonchal 2022       1034       18395       4499         Sibowas 2023       127       1051       924         Vabtotal (95% CI)       158211       101       101         Total events       4449       33397       1612       113       30         Jantero 2018       25       113       30       30       1612			
eng 2014       134       2000       764         (im 2017       420       10141       504         (im 2017       420       1682       185         (inhan 2020       57       1682       181         (inha 2020       102       6080       121         (iavarozza 2021       60       6995       486         (in 2021       132       1812       1420         (iavarozza 2021       60       6995       486         (iar 2022       1543       101510       21654         Vang 2022       1034       18395       4499         (iaonchi 2022       1034       18395       4499         (ibotal 4055       685       18       1061       924         (ibotal (95% CI)       158211       924       1061       1612         (ibit events       449       33397       1612       1612       1612         (ibit events       2449       526       133       30       1612       1612       1612	205 4.0%		2013
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tahman 2020         57         1682         185           thah 2020         69         750         181           tinha 2020         37         240         83           tirose 2020         102         6080         121           tavarozza 2021         60         6995         486           an 2021         392         1812         1420           hayyat 2021         159         1753         1102           an 2022         1543         101510         21654           Vang 2022         1034         18395         4499           oonchal 2022         41         969         383           i 2023         160         4085         685           iswas 2023         127         1051         924           ubtotal (95% CI)         158211         odal events         4449           otal events         4449         33397         est for overall effect: Z = 6.73 (P < 0.00001)	10141 4.0%	0.83 [0.73, 0.95]	2017 -
hah 2020         69         750         181           inha 2020         37         240         83           iirose 2020         102         6080         121           hayarozza 2021         60         6995         486           an 2021         392         1812         1420           hayarozza 2021         60         6995         448           an 2021         159         1753         1102           an 2022         1543         101510         21654           van 2022         1034         18395         4499           oonchai 2022         41         969         383           i 2023         160         4085         685           iswas 2023         127         1051         924           ubtotal (95% CI)         158211         04         04085           otal events         4449         33397         1812           leterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P          689         526           racanzani 2017         143         669         526           racanzani 2017         143         669         526           racanzani 2017         143         669         526	263 4.0%	0.53 [0.40, 0.69]	2020
inha 2020         37         240         83           irose 2020         102         6080         121           avarozza 2021         60         6995         486           an 2021         392         1812         1420           hayyat 2021         159         1753         1102           an 2022         1543         101510         21654           yang 2022         1034         18395         4499           oonchai 2022         41         969         383           i2023         160         4085         685           iswas 2023         127         1051         924           ubtotal (95% CI)         158211         otal events         4449         33397           eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P          est for overall effect: Z = 6.73 (P < 0.00001)	1682 4.0%	0.31 [0.23, 0.41]	2020
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avarozza 2021         60         6995         486           an 2021         392         1812         1420           hayyal 2021         159         1753         1102           hayyal 2021         1543         101510         21654           an 2022         1543         101510         21654           ang 2022         1034         18395         4499           oonchai 2022         41         969         383           2023         160         4085         685           iswas 2023         127         1051         924           ubtotal (95% CI)         158211         014         eterogeneity: Tau <sup>a</sup> = 0.74; Chi <sup>a</sup> = 2411.77, df = 16 (P -           est for overall effect: Z = 6.73 (P < 0.00001)	240 4.0%	0.45 [0.32, 0.63]	2020
an 2021       392       1812       1420         hayyat 2021       159       1753       1102         an 2022       1543       101510       21654         ang 2022       1034       18395       4499         oonchai 2022       41       969       383         2023       160       4085       685         swas 2023       127       1051       924         ubtotal (95% CI)       158211       924         ubtotal (95% CI)       158211       924         otal events       4449       33397         eterogeneity: Tau <sup>a</sup> = 0.74; Chi <sup>a</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>a</sup> = 0.73 (P etorogeneity)       526         antero 2018       25       113       30         ermmler 2021       374       5907       1612         ubtotal (95% CI)       6689       526       6689         otal events       542       2168       21627       3183         otal events       542       2168       21627       3183         otal outpoye       119048       37312324       75739         otal events       12318       99921       144       7414       4420         risar 2022       54	6080 4.0%	0.84 [0.65, 1.09]	2020
hayyal 2021       159       1753       1102         an 2022       1543       101510       21654         /ang 2022       1034       18395       4499         oonchai 2022       1034       18395       4499         oonchai 2022       100       4085       685         iswas 2023       127       1051       924         ubtotal (95% CI)       158211	6995 4.0%	0.12 [0.09, 0.16]	2021
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fang 2022       1034       18395       4499         conchai 2022       41       969       383         2023       160       4085       685         iswas 2023       127       1051       924         ubtotal (95% CI)       158211       33397         eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P set for overall effect: Z = 6.73 (P < 0.00001)	1753 4.0%	0.14 [0.12, 0.17]	2021
bonchai 2022         41         969         383           2023         160         4085         685           swas 2023         127         1051         924           ubtotal (95% CI)         158211         924           otal events         4449         33397           eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 29.13, df = 2 (P < 0.00001)	101510 4.0%	0.07 [0.07, 0.07]	2022 4
2023       160       4085       685         iswas 2023       127       1051       924         ubtotal (95% CI)       158211       924         otal events       4449       33397         eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77; df = 16 (P        685         sat for overall effect: Z = 6.73 (P < 0.00001)	18395 4.0%	0.23 [0.22, 0.25]	2022 +
iswas 2023         127         1051         924           ubtotal (95% CI)         158211         93337           otal events         4449         33397           eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P          685           est for overall effect: Z = 6.73 (P < 0.00001)	969 4.0%	0.11 [0.08, 0.15]	2022
ubtotal (95% CI)         158211           total events         4449         33397           eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.73; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.73; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.73; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.73; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.73; Chi <sup>2</sup> = 2411.77, df = 16 (P eterogeneity: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 29.13, df = 2 (P < 0.00001)	4085 4.0%	0.23 [0.20, 0.28]	2023
otal events         4449         33397           eterogeneity: Tau <sup>2</sup> = 0.74; Chi <sup>2</sup> = 2411.77, df = 16 (P          est for overall effect: Z = 6.73 (P < 0.00001)	1051 4.0%	0.14 [0.12, 0.16]	2023
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est for overall effect: Z = 6.73 (P < 0.00001) 5.2 Europe acanzani 2017 143 669 526 antero 2018 25 113 30 emmiler 2021 374 5907 1612 bitotal (95% CI) 6689 otal events 542 2168 eterogeneity: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 29.13, df = 2 (P < 0.0 est for overall effect: Z = 5.28 (P < 0.00001) 5.3 North America pu 2020 1528 21827 3183 ladunjoye 2021 119048 37312324 75739 mmed 2022 414 7414 4420 isar 2022 54 265 1222 ijampreecha 2023 2137 52556 16457 bitotal (95% CI) 37394386 vial events 123181 99921 eterogeneity: Tau <sup>2</sup> = 2.44; Chi <sup>2</sup> = 16932.21, df = 4 (P < est for overall effect: Z = 1.57 (P = 0.12) vial (95% CI) 37559286			
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ubtotal (95% CI)         6689           otal events         542         2168           eterogeneity: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 29.13, df = 2 (P < 0.0	113 3.9%	0.83 [0.52, 1.32]	2018
otal events         542         2168           eterogeneity: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 29.13, df = 2 (P < 0.0	5907 4.0%	0.23 [0.21, 0.26]	2021 -
eterogeneity: Tau <sup>2</sup> = 0.11; Chi <sup>2</sup> = 29.13, df = 2 (P < 0.6	6689 12.0%	0.34 [0.23, 0.51]	◆
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nmed 2022         414         7414         4420           isar 2022         54         265         122           ijjampreecha 2023         2137         52556         16457           ibtotati (95% Cl)         37394386         99921           eterogeneity: Tau² = 2.44; Chi² = 16932.21, df = 4 (P +         9951 (P = 0.12)         9951 (P = 0.12)           stal (95% Cl)         37559286         37559286         37559286	21827 4.0%	0.48 [0.45, 0.51]	
isar 2022 54 265 122 jampreecha 2023 2137 52556 18457 jbtotal (95% CI) 37394386 123181 99921 aterogeneity: Tau <sup>2</sup> = 2.44; Chi <sup>2</sup> = 16932.21, df = 4 (P + st for overall effect: Z = 1.57 (P = 0.12) tral (95% CI) 37559286		1.57 [1.56, 1.59]	
ijarnpreecha 2023 2137 52556 16457 ibtotal (95% Cl) 37394386 vtal events 123181 99921 eterogeneity: Tau <sup>2</sup> = 2.44; Chi <sup>2</sup> = 16932.21, df = 4 (P + est for overall effect: Z = 1.57 (P = 0.12) vtal (95% Cl) 37559286	7414 4.0%	0.09 [0.09, 0.10]	
btotal (95% Cl)         37394386           tal events         123181         99921           sterogeneity: Tau <sup>2</sup> = 2.44; Chi <sup>2</sup> = 16932.21, df = 4 (P          st for overall effect: Z = 1.57 (P = 0.12)         st for overall effect: Z = 1.57 (P = 0.22)           tal (95% Cl)         37559286         37559286	265 4.0%	0.44 [0.34, 0.58]	
btal events         123181         99921           eterogeneity: Tau <sup>2</sup> = 2.44; Chi <sup>2</sup> = 16932.21, df = 4 (P + 254; Chi <sup>2</sup> = 16932.21, df = 4 (P + 254; Chi <sup>2</sup> = 1.57 (P = 0.12)         99921           staf (95% Cl)         37559286	52556 4.0%	0.13 [0.12, 0.14]	2023 •
eterogeneity: Tau <sup>2</sup> = 2.44; Chi <sup>2</sup> = 16932.21, df = 4 (P + st for overall effect: Z = 1.57 (P = 0.12) tal (95% Cl) 37559286	37394386 20.1%	0.33 [0.08, 1.31]	
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	< 0.00001); I <sup>z</sup> = 100%		
400470 405400	37559286 100.0%	0.27 [0.15, 0.51]	
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leterogeneity: Tau <sup>2</sup> = 2.56; Chi <sup>2</sup> = 38675.00, df = 24 (P	<pre>/ &lt; 0.00001); I<sup>2</sup> = 100<sup>4</sup></pre>	%	
est for overall effect: Z = 4.06 (P < 0.0001)			0.1 0.2 0.5 1 2 5 10 Favours [Lean NAFLD] Favours [Obese NAFLD]

Figure 3. Forest plot for lean NAFLD versus obese NAFLD for prevalence in total population: (2.5.1) Asia; (2.5.2) Europe: (2.5.3) North America. NAFLD, non-alcoholic fatty liver disease.

all outcomes for which sensitivity analysis was performed. These findings imply that individuals with LN may have better cardiovascular health regarding BP regulation than those with ON (Figure 6).

# Anthropometric measures

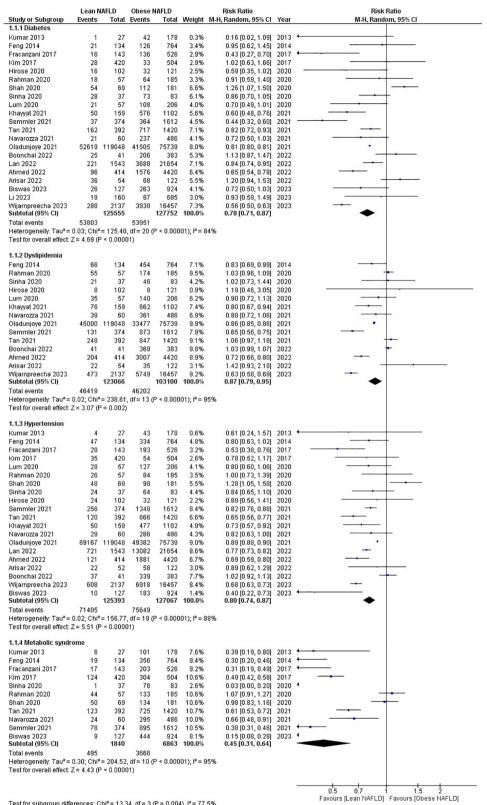
Anthropometric measures were significantly different between the two groups. LN individuals had substantially lower WCs (SMD -1.39, 95% CI -1.49 to -1.28, p < 0.00001) than those with ON. Heterogeneity was high in all outcomes for which sensitivity analysis was performed. This suggests that individuals with LN may have less abdominal adiposity than individuals with ON (Figure 7).

## Fasting blood sugar

FBS levels were slightly lower in individuals with LN than those with ON, although this difference was not statistically significant (SMD -0.05, 95% CI -0.12-0.02, p = 0.18) (Figure 8).

#### Sensitivity analysis

Sensitivity analysis further strengthened the initial findings by reducing heterogeneity in all outcomes. The results remained consistent and robust, confirming the lower risk of DM (RR 0.80, 95% CI 0.74-0.86, p<0.00001), dyslipidemia (RR 0.86, 95% CI 0.82–0.91, *p* < 0.00001), HTN (RR 0.86, 95% CI 0.81–0.92, p < 0.00001), and MS (RR 0.36, 95% CI 0.30-0.42, p < 0.00001) in LN individuals compared to ON



Test for subgroup differences: Chi<sup>2</sup> = 13.34, df = 3 (P = 0.004), l<sup>2</sup> = 77.5%

Figure 4. Forest plot for lean NAFLD versus obese NAFLD for systemic diseases: (1.1.1) Diabetes; (1.1.2) Dyslipidemia; (1.1.3) Hypertension; (1.1.4) Metabolic Syndrome. NAFLD, non-alcoholic fatty liver disease.

reakmanna 2017 53 20 143 48 13 526 53% 0.34 [0.15, 0.52 2017 min 2017 47, 4 10, 4 20 45.7 8, 504 505 476, 0.17 [0.04, 0.30 2017 min 2020 44, 3 7.02 69 42, 38 10.7 181 4.6% 0.20 +0.7, 0.04 2020 min 2020 44, 3 7.02 69 42, 38 10.7 181 4.6% 0.20 +0.7, 0.04 2020 min 2020 44, 3 7.02 69 42, 38 10.7 181 4.6% 0.20 +0.7, 0.04 2020 min 2020 46, 9 159, 252 45, 12, 28 9, 316 6.1% 0.11 [0.56, 0.71 2020 min 2020 46, 9 159, 252 45, 12, 28 9, 316 6.1% 0.11 [0.56, 0.71 2020 min 2020 54, 16, 15, 15, 15, 15, 16 0 47, 26 54 48 47, 0.14 [0.56, 0.71 2020 min 2021 52, 66 15, 27 159 48, 116, 86 1102 55% 0.27 [0.10, 0.43 2021 min 2022 54 16.1 41 51, 51, 24 393 42% 0.19 [0.14, 0.51 2022 min 2022 23, 4 5.76 1034 21, 5 5.04 4499 5.0% 0.07 [0.50, 0.57 2022 min 2022 23, 4 5.76 1034 21, 5 5.04 4499 5.0% 0.07 [0.50, 0.57 2022 min 2022 23, 4 5.76 1034 21, 5 5.04 4499 5.0% 0.07 [0.50, 0.50, 2022 min 2022 23, 4 5.76 1034 21, 5 5.04 4499 5.0% 0.07 [0.50, 0.50, 2022 min 2022 23, 4 5.76 1034 21, 5 5.04 4499 5.0% 0.07 [0.50, 0.50, 2022 min 2022 34 5.76 1034 21, 5 5.04 4499 5.0% 0.07 [0.50, 0.50, 2022 min 2022 12, 12, 4 5, 76 1034 21, 5 5.04 4499 5.0% 0.07 [0.50, 0.50, 2022 min 2022 12, 12, 4 5, 76 1034 21, 5 5.04 4499 5.0% 0.08 [0.50, 0.52] 2023 min 2020 11, 21, 22, 25, 10 10, 11, 15 16457 6.1% 0.08 [0.50, 0.52] 2023 min 2020 11, 21, 3 22, 4 5, 70 10 124 2, 23 120 2.3% 0.11 [0.50, 0.51, 2022 min 2020 11, 22, 22 11, 38 37.08 30 1.5% 0.01 [0.50, 0.23] 2021 min 2020 11, 22, 4 2, 21 11, 24 2, 23 120 2.3% 0.01 [0.50, 0.23] 2021 min 2020 11, 3 2, 24 2, 14 24 2, 3 120 2.3% 0.01 [0.50, 0.23] 2021 min 2020 11, 3 2, 24 2, 4 2, 14 24 2, 3 120 2.3% 0.01 [0.50, 0.23] 2021 min 2020 11, 3 2, 24 2, 14 24 3, 17, 22 14, 24 3, 37, 04 30 1.5% 0.01 [0.50, 0.23] 2021 min 2020 11, 3 2, 34 41 9, 45 31 9, 36 3, 178 3.0% 0.00 [0.50, 0.23] 2021 min 2020 11, 35, 57 152 11, 65 31 136 32, 65 44 65, 0.03 [0.01, 0, 00] 2021 min 2020 11, 35, 57 14, 31 12, 71 143 14, 31, 51 12, 24 30, 12, 40 0, 13, 2020 min 2020 11, 13, 24 14, 14 3, 175 11, 14 3, 14 3, 14	n Difference
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an 2022       28.8       2.7       18.42       2164       6.1%       0.10       0.05       0.15       2022         Biswas 2023       22       23.4       6.76       103.4       11.6       16.46       6.0%       0.35       0.23       2022         Biswas 2023       21.2       20.7       21.7       11.7       11.6       16.46       7.8%       0.00       0.55       0.23 <t< td=""><td></td></t<>	
Wang 2022       23.4       6.76       1034       21.6       5.04       4499       6.0%       0.35       0.28       0.22       222         Wijamprecha 2023       51       20.7       21.7       43.7       11.56       16.457       6.1%       0.060       10.56,0.65       2023         Jubitol 1(5%)       C)       21.42       56       160       18.4       18.66       5.4%       0.060       10.56,0.65       2023         Subtol 1(5%)       C)       0.68       4.97       5.4396       100.0%       0.29       10.7       0.41         Velarogeneity: Tau* = 0.06       Chr = 3.55.45, df = 19 (P < 0.00001); P = 95%	
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shat 2013       118.2       62.7       30       124.2       42.3       120       2.3%       -0.13 [0.53, 0.27]       2013         cumar 2013       120.8       44.3       27       15.08       35.43       176       2.2%       0.016 [0.20, 0.56]       2013         cmg 2014       56.16       14.04       134       56.34       14.04       764       55.%       -0.01 [0.20, 0.17]       2014         cmater 2018       10       82.2       25       118.3       32.6       56.4       6.3%       0.03 [0.26, 0.33]       2014         sumar 2020       12.3       32.6       77.9       128.6       2.28       118.3       3.3%       0.03 [0.30, 0.09]       2020         semmler 2021       148.26       33.2       37.1       116.12       7.2%       -0.02 [0.47, 0.01]       2021         semmler 2021       148.24       33.2       37.4       148.91       36.1       112.2       120.2       -0.02 [0.14, 0.08]       2021         semmler 2021       158.4       17.8       3.34       1612       7.2%       -0.02 [0.14, 0.08]       2021       -0.39 [0.14, 0.08]       2021       -0.39 [0.14, 0.08]       2021       -0.39 [0.14, 0.08]       2021       -0.39 [0.14, 0.08]	
Bhat 2013       118.2       62.7       30       124.2       42.3       120       2.3%       -0.13 [0.53, 0.27]       2013         Cumar 2013       120.8       44.3       27       115.08       35.43       178       2.2%       0.16 [0.25, 0.56]       2013         Geng 2014       56.16       11.04       134       56.34       1.04       764       5.5%       -0.01 [0.20, 0.17]       2014         Gentero 2016       100       22.2       51.14.36       3.26       56.4       6.8%       -0.03 [0.67, 0.11]       2020         Janha 2020       112.33       21.18       56       112.36       22.6       113.13       3.8%       -0.03 [0.67, 0.01]       2020         Sammele 2021       118.2       47.5       60       125.5       39.8       486       3.9%       -0.01 [0.45, 0.03]       2021         Sammele 2021       148.26       33.2       37.14       149.81       3.61.1       112       7.2%       -0.02 [0.14, 0.08]       2021         Sammele 2021       148.26       33.2       37.44       49.81       3.61.1       112       7.2%       -0.02 [0.14, 0.08]       2021         Sammele 2022       39.6       13.34       154.3       3.14.2 </td <td></td>	
Aumar 2013       120.8       44.3       27       115.06       36.43       178       2.2%       0.16       10.25       0.56       2013         Fing 2014       66.16       14.04       134       66.34       14.04       764       65.84       -0.01       10.020       0.17       2014         Cantero 2018       109       28.22       25       114.83       37.09       30       1.5%       -0.016       10.020       0.07       2014	
Feng 2014       56.16       14.04       124       66.34       14.04       764       5.5%       -0.01       0.20       0.71       2014         Cantero 2018       109       28.22       25       114.36       37.09       30       1.5%       -0.01       6.005       0.211       2017         Cantero 2018       109       28.22       25       114.36       37.09       30       1.5%       -0.01       6.005       0.211       2010         Sinha 2020       112.33       21.86       62.26       16.2       206       3.6%       0.03       6.007       0.011       2020       -         Navaroza 2021       118.2       47.76       60       12.55       39.8       466       3.9%       -0.01       6.043       0.001       2020       -       -         Tan 2021       53.64       17.82       1420       7.2%       -0.02       10.01       0.01       2021       -       -       -       -       -       -       1102       5.9%       -0.03       10.01       2021       -       -       -       -       -       -       0.02       10.01       0.01       -       -       -       0.03       10.01	
dim_2017       121.3       32.5       420       118.6       32.6       50.4       6.8%       0.08 [0.05, 0.21]       2017         canlero 2018       109       28.22       25       114.36       37.09       30       15%       -0.16 [0.68, 0.37]       2018         mum 2020       57.24       33.66       57       65.2       16.2       206       3.5%       -0.03 [0.67, 0.11]       2020         Shah 2020       118.6       57.7       136       51.1       83       8.3%       -0.03 [0.67, 0.10]       2020         Zou 2020       118.6       47.5       60.125.5       39.8       486.3       39.8%       -0.01 [0.45, 0.09]       2021         wararozza 2021       118.24       47.5       60.115.9       115.9       41.35       1102       5.5%       -0.02 [0.13, 0.10]       2021         Shayat2021       118.84       412.1       159       15.19       41.35       1102       5.5%       -0.03 [0.14, 0.08]       2021       -0.02 [0.13, 0.10]       2021       -0.02 [0.13, 0.10]       2021       -0.02 [0.13, 0.10]       2021       -0.03 [0.16, 0.50, 0.61]       2021       -0.03 [0.16, 0.50, 0.61]       2021       -0.03 [0.16, 0.50, 0.61]       2021       -0.03 [0.10, 0.60, 0.60]       2021 </td <td></td>	
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Jum 2020       57 24       38 66       57       56 52       16.2       206       3.5%       0.03 [-0.26, 0.03]       20.0         Shah 2020       113.33       21.18       69       123.66       28.2       181       3.7%       -0.39 [-0.67, -0.11]       2020         Sinha 2020       12.2.3       39.5       37       186       51.1       83       2.4%       -0.28 [-0.67, -0.11]       2020         Source 2021       118.2       47.5       60       125.5       39.8       40.8       3.9%       -0.14 [-0.45, 0.09]       2021         Sammer 2021       118.84       17.82       140.77.28       -0.03 [-0.14, 0.08]       2021	
Shah 2020       113.33       21.18       60       128.68       28.2       181       3.7%       -0.38 [+0.67, 0.11]       2020         Sinha 2020       12.3       39.5       37       136       51.1       83       2.4%       -0.28 [+0.67, 0.11]       2020         Navarozza 2021       118.2       47.5       60       125.5       39.8       486       3.9%       -0.18 [+0.45, 0.01]       2020         Semmler 2021       148.26       39.2       54.18       17.82       1420       7.2%       -0.03 [+0.10, 0.01]       2021         Anayat 2021       118.84       42.12       159       115.19       41.35       1102       5.9%       -0.03 [+0.4, 0.08]       2021         Anayat 2022       39.6       13.34       154.3       43.2       13.34       2155.4       6.9%       -0.28 [+0.46, 0.08]       2022         Anayat 2022       57.3       14.4       149.4       5.38       -0.32 [+0.51, -0.02]       2022	
Binha 2020       122.3       39.5       37       136       51.1       83       2.4%       -0.28 [0.67, 0.10]       2020         Zou 2020       118       57.79       1528       118.5       56.11       318.8       8.3%       0.03 [-0.03, 0.09]       2020         Semmiler 2021       118.2       47.5       60       125.5       38.8       486       3.9%       -0.02 [-0.13, 0.10]       2021         Semmiler 2021       118.4       47.22       25.34       118.72       142.0       7.2%       -0.02 [-0.14, 0.08]       2021         Anayat 2021       118.44       42.12       159       115.19       41.35       1102       5.9%       0.09 [-0.08, 0.26]       2022         Lan 2022       39.6       13.34       154.3       43.2       13.34       164.55%       -0.27 [-0.32, -0.22]       2022         Vang 2022       52.2       12.78       103.4       55.48       164.57       8.5%       -0.20 [-0.24, -0.15]       2023         Subtotal (95% C)       8354       54.67       18.67       8.68       -0.02 [-0.24, -0.15]       2023         Liotal (95% C)       8354       14.47       100.0%       -0.09 [-0.16, -0.02]       2023       -0.01       -0.01 [-0.24, -	•
Zou 2020       118       57.79       15.28       116.5       66.11       318.3       8.3%       0.03       0.03       0.03       0.09       2020         Navarozza 2021       118.2       47.5       60       125.5       39.8       486       3.9%       -0.18       0.45       0.09       2021         Fan 2021       148.26       39.32       37.4       148.1       36.71       1612       7.2%       -0.03       6.01.40.08       2021         Semmier 2021       118.84       41.2       15.91       115.19       41.35       110.2       5.9%       0.03       6.03.0.61       2022         Sonchai 2022       90.2       31.4       41       94.6       31.9       383       31.%       -0.14       6.04       0.18       2022         Lan 2022       39.6       13.34       15.4       43.2       13.34       21654       8.5%       -0.27       1.032.0.21       2022       2022         Silewas 2023       102       37.76       127       17.14.3       31.61       92.4       5.5%       -0.32       0.51.0.14       203       2023       2023       2024       -0.01       2024       -0.01       2024       -0.01       -0.08 <td></td>	
Navarozza 2021 118.2 47.5 60 125.5 39.8 486 3.9% -0.18 [0.45,0.09] 2021	
Semmler 2021       148.26       39.32       374       148.91       36.71       1612       7.2%       -0.02[-0.13, 0.10]       2021         Tan 2021       53.64       17.82       392       64.18       17.82       1420       7.2%       -0.03[-0.14, 0.08]       2021         Sonchai 2022       90.2       31.4       41       94.6       31.9       383       31%       -0.14[-0.46, 0.18]       2022         Lan 2022       39.6       13.34       1543       43.2       13.34       21654       8.5%       -0.27[-0.32, -0.22]       2022         Nang 2022       52.2       12.78       1034       55.4       1647       8.6%       -0.27[-0.32, -0.22]       2022         Jiamprechaz 2023       19       37.78       127       17.98       35.54       1647       8.6%       -0.20[-0.24, -0.15]       2023         Li2023       57.33       14.4       160       58.5       14.67       685       5.8%       -0.20[-0.24, -0.16]       2013         Subtotal (195% CI)       8354       1647       685       -0.08[-0.35, 0.46]       2013         Fest for overall effect Z = 2.59 (P = 0.010)       8354       164.5       5.8%       -0.010[-0.28, 0.08]       2014 <tr< td=""><td></td></tr<>	
Berminer 2021 148.26 39.32 374 148.91 36.71 1612 7.2% -0.03[-0.13,0.10] 2021 Tan 2021 53.64 17.82 392 54.18 17.82 1420 7.2% -0.03[-0.14,0.08] 2021 Anayat 2021 118.84 42.12 159 115.19 41.35 1102 5.9% -0.09[-0.16,0.2] 2022 30.06 13.34 14 14 94.6 31.9 383 3.1% -0.14[-0.46,0.18] 2022 Anay 2022 39.6 13.34 1454 34.2 13.4 2166 4.65% -0.27[-0.32,0.22] 2022 Anay 2022 32.6 13.34 1543 45.2 81.26 4499 8.2% -0.09[-0.15,0.02] 2022 Anay 2022 31.02 37.78 127 112.43 31.61 924 5.5% -0.32[-0.51,-0.14] 2023 Anay 2023 102 37.78 127 112.43 31.61 924 5.5% -0.32[-0.51,-0.14] 2023 Anay 2023 57.33 14.4 160 58.5 14.67 885 5.8% -0.09[-0.26,0.09] 2023 J2023 57.33 14.4 160 58.5 14.67 685 5.8% -0.09[-0.26,0.09] 2023 J2023 57.33 14.4 160 58.5 14.67 685 5.8% -0.09[-0.26,0.09] 2023 Heterogeneik: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 100.11, df = 18 (P < 0.00001); P = 82% Test for overall effect Z = 2.58 (P = 0.010) 2.1.4 Triglycerides Aumar 2013 190.4 97.2 27 184.53 107.56 178 3.0% 0.06[-0.35,0.46] 2013 	
Tan 2021       53.64       17.82       392       54.18       17.82       1420       7.2%       -0.03[-0.14] 0.08       2021         Chayyal 2021       118.84       42.12       159       15.19       41.35       1102       5.9%       0.09[-0.14] 0.08       0.25       2021         Lan 2022       39.6       13.34       154.3       43.2       13.34       216.4       8.9%       -0.07[-0.32,-0.22]       2022         Jan 2022       32.6       13.34       154.3       43.2       13.44       216.6       8.6%       -0.32[-0.51,-0.01]       2022         Jan 2023       57.33       14.4       160       58.5       -0.08[-0.24,-0.15]       2023         J2023       57.33       14.4       160       58.5       -0.08[-0.25,0.09]       2023         J2023       57.33       14.4       160       58.5       -0.08[-0.25,0.46]       2013         J12023       57.33       14.4       160       18.8       100.001); P= 82%       -0.08[-0.35,0.46]       2013         Est for overall effect Z = 2.59 (P = 0.010)       21.42       76.4       54.%       -0.01[-0.28,0.08]       2017         Zantario 13       190.4       97.2       27       184.53       1	•
Khayyat 2021       118.84       42.12       159       115.19       41.35       1102       5.9%       0.008 [0.08 [0.25]       2021         Boonchai 2022       90.2       31.4       41       94.8       31.9       383       -0.014 [0.46, 0.18]       2022         Wang 2022       52.2       12.78       1034       53.28       12.6       4499       8.2%       -0.09 [-0.15, -0.02]       2022         Wang 2022       52.2       12.78       1034       53.28       12.6       4499       8.2%       -0.08 [-0.5, -0.02]       2022         Wigampreecha 2023       91       37.04       217       17.93       35.54       16457       8.6%       -0.20 [-0.24, -0.15]       2023         Wigampreecha 2023       57.33       14.4       160       58.5       14.67       8.6%       -0.08 [-0.25, 0.09]       2023         Li 2023       57.33       14.4       160       58.5       14.67       8.6%       -0.09 [-0.4, -0.15]       2013         Heterogeneity: Tau"= 0.01; ChiP= 100.11, df = 18 (P < 0.00001); P = 82%	
Boonchai 2022 90.2 31.4 41 94.6 31.9 383 31% -0.14 [-0.46,0.18] 2022 an 2022 32.6 13.34 1543 43.2 13.34 21654 8.5% -0.27 [-0.32, -0.22] 2022 Wang 2022 52.2 12.78 1034 53.28 12.6 44.98 8.2% -0.09 [-0.15, -0.14] 2023 Biswas 2023 102 37.78 127 112.43 31.61 924 5.5% -0.32 [-0.51, -0.14] 2023 Wijanpreecha 2023 91 37.04 2137 97.98 35.54 16457 8.6% -0.08 [-0.56, 0.09] 2023 Jul 2023 57.3 14.4 160 58.5 14.67 665 5.8% -0.08 [-0.26, 0.09] 2023 Subtotal (95% Cl) 8354 54.471 100.0% -0.09 [-0.16, -0.02] Peterogeneity. Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 100.11, df = 18 (P < 0.00001); P = 82% Fest for overall effect Z = 2.59 (P = 0.010) 2.1.4 Triglycerides Kumar 2013 190.4 97.2 27 184.53 107.56 178 3.0% 0.06 [-0.35, 0.46] 2013 Bhat 2013 185.6 114.4 30 175.6 118.8 120 3.1% 0.08 [-0.32, 0.48] 2013 Feng 2014 30.78 22.14 134 32.94 21.42 764 5.4% -0.05 [-0.23, 0.48] 2014 (m 2017 1735 97.3 420 197.1 122.5 504 6.0% -0.21 [-0.34, -0.08] 2014 (m 2017 1735 97.3 420 197.1 122.5 502 6.54% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 54.9% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 131 278 143 144 275 526 56.4% -0.05 [-0.23, 0.14] 2017 Fraenzani 2017 16.58 23.77 69 206.64 56.23 181 4.2% -0.83 [-1.11, -0.54] 2020 Jona 2020 186.58 190.32 1528 185.2 215.81 3183 6.6% 0.00 [-0.06, 0.06] 2020 Jana 2020 170.5 34.2 37 186.4 43.8 83 31% -0.28 [-0.17, [-0.34, -0.00] 2021 Jana 2022 27 16 154.3 12.4 198 21654 6.7% -0.27 [-0.33, 0.22] 2021 Jana 2022 176 154.3 12.4 198 21654 6.7% -0.27 [-0.33, 0.22] 2022 Jana 2022 115 51.11 41 131 56.3 333 3.8% -0.29 [-0.61, 0.04] 2022 Jana 2022 125 74.81 2137 160.55 90.26 16457 6	
Lan 2022 39.6 13.34 1643 43.2 13.34 21654 8.5% -0.27 [0.32, 0.22] 2022 Vang 2022 52.2 12.78 1034 53.28 12.6 4499 8.2% -0.08 [0.15, 0.02] 2022 Migrapprecha 2023 91 37.04 2137 97.98 35.54 16457 8.6% -0.20 [0.24, -0.15] 2023 J 2023 57.33 14.4 180 58.5 14.67 685 5.8% -0.20 [0.24, -0.15] 2023 L 2023 57.33 14.4 180 58.5 14.67 685 5.8% -0.20 [0.24, -0.15] 2023 L 2023 57.33 14.4 180 58.5 14.67 685 5.8% -0.20 [0.26, 0.09] 2023 L 2023 57.33 14.4 180 58.5 14.67 685 5.8% -0.20 [0.26, 0.09] 2023 L 2023 57.33 14.4 180 58.5 14.67 685 5.8% -0.09 [-0.16, -0.02] Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 100.11, df = 18 (P < 0.00001); P = 82% Test for overall effect: Z = 2.59 (P = 0.010) 2.1.4 Triglycerides Kumar 2013 190.4 97.2 27 184.53 107.56 178 3.0% 0.06 [-0.35, 0.46] 2013 Ter 30, 78 22.14 134 32.94 21.42 764 5.4% -0.010 [-0.28, 0.08] 2014 (m 2017 173.5 97.3 420 197.1 122.5 504 6.0% -0.21 [-0.34, -0.08] 2017 Fracanzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fracanzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fracanzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fracanzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fracanzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.23, 0.14] 2017 Fracanzani 2017 131 278 143 144 275 526 5.4% -0.05 [-0.34, 0.08] 2014 (	
Wang 2022       52.2       12.78       1034       53.28       12.6       4499       8.2%       -0.09       -0.15       -0.02       2022         Biswas 2023       102       37.78       127       112.43       31.61       924       5.5%       -0.32       10.15       -0.02       2022         Li 2023       57.33       14.4       160       58.5       14.67       685       5.8%       -0.08       -0.09       2023         Subtotal (95% CI)       8354       54471       100.0%       -0.09       2023       -0.09       2023         Fetorgeneity: Tau <sup>2</sup> = 0.01; Ch <sup>2</sup> = 100.11       df = 8       (P < 0.00001); P = 82%	
Biswas 2023 102 37.78 127 112.43 31.61 924 5.5% -0.32 [0.51, -0.14] 2023 Wijampreecha 2023 91 37.04 2137 97.98 35.54 16457 8.6% -0.20 [-0.24, -0.15] 2023 Subtotal (95% CI) 8354 54471 100.0% -0.09 [-0.16, -0.02] Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 100.11, df = 18 (P < 0.00001); P = 82% Test for overall effect: Z = 2.59 (P = 0.010) 2.1.4 Triglycerides Kumar 2013 190.4 97.2 27 184.53 107.56 178 3.0% 0.06 [-0.35, 0.46] 2013 Feng 2014 30.78 22.14 134 32.94 21.42 764 5.4% -0.10 [-0.28, 0.08] 2014 Kim 2017 173.5 97.3 420 197.1 122.5 504 6.0% -0.21 [-0.34, -0.08] 2017 Fracanzani 2017 131 278 143 144 275 526 5.4% -0.02 [-0.32, 0.14] 2027 Cantero 2018 80.2 41.57 25 135.75 70.7 30 2.0% -0.92 [-1.48, -0.36] 2018 Shah 2020 165.58 23.77 69 206.64 56.23 181 4.2% -0.83 [-1.1, -0.54] 2020 Fan 2020 185.35 190.32 1528 185.2 215.81 3183 6.6% 0.00 [-0.05, 0.06] 2020 Ta 2021 36.72 27.9 392 35.1 24.48 1420 6.2% 0.06 [-0.35, 0.46] 2021 Kawarozza 2021 163.1 98.5 60 167.8 100.5 486 4.4% -0.05 [-0.32, 0.22] 2021 Mayarozza 2021 163.1 98.5 60 167.8 100.5 486 4.4% -0.05 [-0.32, 0.22] 2021 Wayarozza 2021 163.1 98.5 60 167.8 100.5 486 4.4% -0.05 [-0.32, 0.22] 2021 Mayarozza 2021 163.1 98.5 60 167.8 100.5 486 4.4% -0.05 [-0.32, 0.22] 2021 Mayarozza 2021 163.1 98.5 60 167.8 100.5 486 4.4% -0.05 [-0.32, 0.22] 2021 Mayarozza 32.94 15.5 11.1 41 131 56.3 383 3.8% -0.27 [-0.61, 0.04] 2022 Mang 2022 33.3 22.86 1034 34.56 21.96 4499 6.6% -0.06 [-0.17, 0.03] 2020 Mayarozza 2021 155 11.1 41 131 56.3 383 3.8% -0.29 [-0.61, 0.04] 2022 Mang 2022 33.3 22.86 1034 34.56 21.96 4499 6.6% -0.02 [-0.61, 0.04] 2022 Mang 2022 32 125 74.81 2137 160.55 90.26 16457 6.7% -0.40 [-0.45, 0.03] 2023 Mijampreecha 2023 125 74.81 2137 160.55 90.26 16457 6.7% -0.40 [-0.45, 0.03] 2023 Mijampreecha 2023 125 74.81 2137 160.55 90.26 16457 6.7% -0.27 [-0.33, 0.22] 2023 Mijampreecha 2023 125 74.81 2137 160.55 90.26 16457 6.7% -0.27 [-0.36, 0.02] 2023 Mijampreecha 2023 125 74.81 2137 160.55 90.26 16457 6.7% -0.27 [-0.36, 0.02] 2023 Mijampreecha 2023 125	_
Wijampreecha 2023       91       37.04       2137       97.98       35.54       16457       8.6%       -0.20 [-0.24, -0.15]       2023         Li 2023       57.33       14.4       160       58.5       1.4.67       685       5.8%       -0.08 [-0.25, 0.09]       2023         Subtotal (95% CI)       8354       54471       100.0%       -0.09 [-0.16, -0.02]       -0.09 [-0.16, -0.02]         Heterogeneity: Tau <sup>2</sup> = 0.01; Ch <sup>2</sup> = 100.11, df = 18 (P < 0.00001); P = 82%	
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Subtotal (95% CI)         8354         54471         100.0%         -0.09 [-0.16, -0.02]           Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 100.11, df = 18 (P < 0.00001); P = 82%	
Heterogeneity: Tau <sup>2</sup> = 0.01; Ch <sup>2</sup> = 100.11, df = 18 (P < 0.00001); P = 82%	
Test for overall effect: Z = 2.59 (P = 0.010)         2.1.4 Triglycerides         Kumar 2013       190.4       97.2       27       184.53       107.56       178       3.0%       0.06 [-0.35, 0.46]       2013         Bhat 2013       185.6       114.4       30       175.6       118.8       120       3.1%       0.08 [-0.32, 0.48]       2013         Feng 2014       30.78       22.14       134       32.94       21.4       764       5.4%       -0.10 [-0.28, 0.08]       2014         Kim 2017       173.5       97.3       420       197.1       122.5       504       6.0%       -0.21 [-0.34, -0.08]       2017         Fracanzani 2017       131       278       143       144       275       526       5.4%       -0.05 [-0.23, 0.14]       2017         Cantero 2018       80.2       41.57       57       70.7       30       20.0%       -0.92 [-1.48, -0.36]       2014         Lum 2020       28.08       18.72       57       30.6       13.86       206       4.1%       -0.03 [-1.11, -0.64]       2020         Zou 2020       185.35       190.32       1528       185.2       215.81       3183       6.6%       0.006 [-0.05, 0.06]       2020	
Kumar 2013       190.4       97.2       27       184.53       107.56       178       3.0%       0.06 [-0.35, 0.46]       2013         Bhat 2013       185.6       114.4       30       175.6       118.8       120       3.1%       0.08 [-0.32, 0.48]       2013         Feng 2014       30.78       22.14       134       32.94       21.42       764       5.4%       -0.10 [-0.28, 0.68]       2014         Kim 2017       173.5       97.3       420       197.1       122.5       504       6.0%       -0.21 [-0.34, -0.08]       2017         Fracanzani 2017       131       278       143       144       275       526       5.4%       -0.05 [-0.23, 0.14]       2017         Cantero 2018       80.2       41.57       25       15.55       7.7       30       200%       -0.92 [-1.48, -0.36]       2018       -         Lum 2020       28.08       18.72       57       30.6       13.86       206       4.1%       -0.03 [-1.14, -0.64]       2020       -       -       -       -       30.7       0.06 [-0.05, 0.18]       2020       -       -       -       -       -       30.7       0.01 [-0.34, -0.01]       2020       -       -       -<	
Kumar 2013       190.4       97.2       27       184.53       107.56       178       3.0%       0.06 [-0.35, 0.46]       2013         Bhat 2013       185.6       114.4       30       175.6       118.8       120       3.1%       0.08 [-0.32, 0.48]       2013         Sinat 2013       185.6       114.4       30       175.6       118.8       120       3.1%       0.08 [-0.32, 0.48]       2013         Sinat 2017       173.5       97.3       420       197.1       122.5       504       6.0%       -0.21 [-0.34, -0.08]       2017         Tracanzani 2017       131       278       143       144       275       526       5.4%       -0.05 [-0.23, 0.14]       2017         Cantero 2018       80.2       41.57       257       30.6       13.86       206       4.1%       -0.17 [-0.46, 0.13]       2020         Sinha 2020       186.55       190.32       1528       185.2       215.81       3183       6.6%       0.00 [-0.06, 0.06]       2020       100.4         Zou 2020       185.35       190.32       1528       185.2       215.81       3183       6.6%       0.00 [-0.06, 0.06]       2020       166       6.7%       0.27, [-0.34, -0.01]       2021<	
Bhat 2013       185.6       114.4       30       175.6       118.8       120       3.1%       0.08 [-0.32, 0.48]       2013         Feng 2014       30.78       22.14       134       32.94       21.42       764       5.4%       -0.01 [-0.28, 0.08]       2014         Kim 2017       173.5       97.3       420       197.1       122.5       504       6.0%       -0.21 [-0.34, -0.08]       2017         Fracanzani 2017       131       278       143       144       275       526       5.4%       -0.05 [-0.23, 0.14]       2017         Cantero 2018       80.2       41.57       25       135.75       70.7       30       2.0%       -0.92 [-1.48, -0.36]       2014         Jum 2020       28.08       18.72       57       30.6       13.86       206       4.1%       -0.17 [-0.46, 0.13]       2020       4         Shah 2020       170.5       34.2       37       186.4       43.8       83       3.1%       -0.38 [-0.77, 0.01]       2020       4         Cau 2020       185.35       190.32       1528       185.2       215.81       3183       6.6%       -0.06 [-0.65, 0.18]       2021       4         Navarozza 2021       186.3	
Feng 2014       30.78       22.14       134       32.94       21.42       764       5.4%       -0.01[-0.28,0.08]       2014         Kim 2017       173.5       97.3       420       197.1       122.5       504       6.0%       -0.21[-0.34,-0.08]       2017         Cantero 2018       80.2       41.57       25       135.75       70.7       30       2.0%       -0.92[-1.48,-0.36]       2018         Cantero 2018       80.2       41.57       25       135.75       70.7       30       2.0%       -0.92[-1.48,-0.36]       2018         Shah 2020       185.58       23.77       69       20.64       562.3       181       4.2%       -0.83[-0.71,0.01]       2020         Shah 2020       185.35       190.32       152.8       185.2       215.81       3183       6.6%       0.006[-0.06,0.06]       2020         Cau 2020       185.35       190.32       152.8       185.2       215.81       3183       6.6%       0.006[-0.05,0.18]       2021	
Kim 2017       173.5       97.3       420       197.1       122.5       504       6.0%       -0.21 [-0.34, -0.09]       2017         rracanzani 2017       131       278       143       144       275       526       5.4%       -0.05 [-0.23, 0.14]       2017         cantero 2018       80.2       41.57       25       15.57       70.7       30       2.0%       -0.92 [-1.48, -0.36]       2018         Lum 2020       28.08       18.72       57       30.6       13.86       206       4.1%       -0.17 [-0.46, 0.13]       2020         Shah 2020       170.5       34.2       37       1864       43.8       83       31%       -0.38 [-1.11, -0.54]       2020         Zou 2020       185.35       190.32       1528       185.2       215.81       3183       6.6%       0.00 [-0.06, 0.06]       2020         Tan 2021       36.72       27.9       392       35.1       24.48       1420       6.2%       -0.016 [-0.05, 0.18]       2021	
Fracanzani 2017       131       278       143       144       275       526       5.4%       -0.05 [-0.23, 0.14]       2017         Cantero 2018       80.2       41.57       25       135.75       70.7       30       2.0%       -0.02 [-1.48, -0.36]       2018         Jum 2020       28.08       18.72       57       30.6       13.86       206       4.1%       -0.17 [-0.46, 0.13]       2020         Shah 2020       185.58       23.77       69       206.64       56.23       181       4.2%       -0.83 [-0.77, 0.01]       2020         Sinha 2020       185.35       190.32       152       185.12       215.81       3183       6.6%       0.00 [-0.06, 0.06]       2020         Cau 2020       185.35       190.32       152       185.1       24.48       1420       6.2%       0.00 [-0.06, 0.06]       2020         Cau 2020       185.35       190.32       152       133.67       86.56       1102       5.6%       -0.17 [-0.34, -0.00]       2021         Cau 2020       185.35       190.32       37.4       128.49       57.39       1612       6.2%       -0.05 [-0.32, 0.22]       2021	
Cantero 2018       80.2       41.57       25       135.75       70.7       30       2.0%       -0.92 [-1.48, -0.36]       2018	
Lum 2020       28.08       18.72       57       30.6       13.86       206       4.1%       -0.17 [-0.46, 0.13]       2020         Shah 2020       165.58       23.77       69       206.64       56.23       181       4.2%       -0.083 [-1.11, -0.54]       2020         Sinha 2020       170.5       34.2       37       186.4       43.8       83       31%       -0.38 [-0.77, 0.01]       2020         Zou 2020       185.35       190.32       1528       185.2       215.81       3183       6.6%       0.00 [-0.06, 0.06]       2020         Fan 2021       36.72       27.9       392       35.1       24.48       1420       6.2%       0.05 [-0.05, 0.18]       2021	
Shah 2020       165.58       23.77       69       206.64       56.23       181       4.2%       -0.83 [-1.11, -0.54]       2020       4         Sinha 2020       170.5       34.2       37       186.4       43.8       83       3.1%       -0.38 [-0.77, 0.01]       2020       4         Zou 2020       185.35       190.32       1528       185.2       215.81       3183       6.6%       0.00 [-0.66, 0.06]       2020         Anayat 2021       186.72       27.9       392       35.1       24.48       1420       6.2%       0.06 [-0.05, 0.18]       2021         Anayat 2021       186.31       98.56       110.5       486       4.4%       -0.05 [-0.32, 0.22]       2021         Semmler 2021       103.39       45.93       374       128.49       57.39       1812       6.2%       -0.05 [-0.32, 0.22]       2021         Lan 2022       27       16       1543       32.4       19.98       21654       6.7%       -0.027 [-0.33, -0.22]       2022       -         Vang 2022       33.3       22.86       134       34.56       21.96       4499       6.6%       -0.027 [-0.33, -0.22]       2022       -       -         Li 2023       32.94 <td></td>	
Sinha 2020       170.5       34.2       37       186.4       43.8       83       3.1%       -0.38 [-0.77, 0.01]       2020         Sou 2020       185.35       190.32       1528       185.2       215.81       318.3       6.6%       0.00 [-0.06, 0.06]       2020         Fan 2021       36.72       27.9       392       35.1       24.48       1420       6.2%       0.06 [-0.05, 0.18]       2021         Awayat 2021       118.69       79.73       159       133.67       88.56       1102       5.6%       -0.17 [-0.34, -0.00]       2021         Awayat 2021       103.39       45.93       374       128.49       57.39       1612       6.2%       -0.05 [-0.32, 0.22]       2021         Semmler 2021       103.39       45.93       374       128.49       57.39       1612       6.2%       -0.05 [-0.32, 0.22]       2021         Anar 2022       27       16       1643       32.4       19.98       21654       6.7%       -0.27 [-0.33, -0.22]       2022       -         Anag 2022       33.3       22.86       1034       34.56       21.96       4499       6.6%       -0.027 [-0.43, -0.01]       2022       -       -         J2023	
Zou 2020         185.35         190.32         1528         185.2         215.81         3183         6.6%         0.00 [-0.06, 0.06]         2020           ran 2021         36.72         27.9         392         35.1         24.48         1420         6.2%         0.06 [-0.05, 0.16]         2020	
Tan 2021       36.72       27.9       392       35.1       24.48       1420       6.2%       0.06 [-0.05, 0.18]       2021         Khayat 2021       118.69       79.73       159       133.67       88.56       1102       5.6%       -0.07 [-0.34, -0.00]       2021         Navarozza 2021       163.1       98.5       60       167.8       100.5       486       4.4%       -0.05 [-0.32, 0.22]       2021         Lan 2022       27       16       154.3       32.4       19.98       21654       6.7%       -0.27 [-0.33, -0.22]       2022         Wang 2022       33.3       22.86       1034       34.66       21.96       4499       6.6%       -0.06 [-0.12, 0.01]       2022         Soonchai 2022       115       51.11       41       131       56.3       383       3.8%       -0.29 [-0.61, 0.04]       2022         J2023       32.94       15.2       160       38.16       20       685       5.5%       -0.27 [-0.44, -0.10]       2023         Jigmpreecha 2023       125       74.81       2137       160.55       90.26       16457       6.7%       -0.04 [-0.45, -0.36]       2023         Jigmpreecha 2023       125       74.81       2137	+
Khayyat 2021       118.69       79.73       159       133.67       88.56       1102       5.6%       -0.17 [-0.34, -0.00]       2021         Navarozza 2021       163.1       98.5       60       167.8       100.5       486       4.4%       -0.05 [-0.32, 0.22]       2021         Semmler 2021       103.39       45.93       374       128.49       57.39       1612       6.2%       -0.45 [-0.32, 0.22]       2021         Jan 2022       27       16       1543       32.4       19.98       21654       6.7%       -0.027 [-0.33, -0.22]       2022         Wang 2022       33.3       22.86       1034       34.56       21.96       4499       6.6%       -0.027 [-0.33, -0.22]       2022         Soonchai 2022       115       51.11       41       131       56.3       383       3.8%       -0.29 [-0.61, 0.04]       2022         J2023       32.94       15.2       160       88.16       20       685       5.5%       -0.27 [-0.44, -0.10]       2023         J2023       129.2       1237       160.55       90.26       16457       6.7%       -0.047 [-0.44, -0.10]       2023         Subtotal (95% CI)       8497       54997       100.0%       -0.	+
Khayyat 2021       118.69       79.73       159       133.67       88.56       1102       5.6%       -0.17 [-0.34, -0.00]       2021         Navarozza 2021       163.1       98.5       60       167.8       100.5       486       4.4%       -0.05 [-0.32, 0.22]       2021         Semmler 2021       103.39       45.93       374       128.49       57.39       1612       6.2%       -0.45 [-0.32, 0.22]       2021         Jan 2022       27       16       1543       32.4       19.98       21654       6.7%       -0.027 [-0.33, -0.22]       2022         Wang 2022       33.3       22.86       1034       34.56       21.96       4499       6.6%       -0.027 [-0.33, -0.22]       2022         Soonchai 2022       115       51.11       41       131       56.3       383       3.8%       -0.29 [-0.61, 0.04]       2022         J2023       32.94       15.2       160       88.16       20       685       5.5%       -0.27 [-0.44, -0.10]       2023         J2023       129.7       74.81       2137       160.55       90.26       16457       6.7%       -0.047 [-0.44, -0.10]       2023         Subtotal (95% CI)       8497       54997       100.	
Navarozza 2021       163.1       98.5       60       167.8       100.5       486       4.4%       -0.05 [-0.32, 0.22]       2021         Bermier 2021       103.39       45.93       374       128.49       67.39       1612       6.2%       -0.045 [-0.57, -0.34]       2021         Lan 2022       27       16       163.3       32.4       19.98       21654       6.7%       -0.27 [-0.51, 0.04]       2022         Wang 2022       33.3       22.86       1034       34.56       21.96       4499       6.6%       -0.02 [-0.61, 0.04]       2022         Joan Alago       115       51.11       41       131       56.3       383       3.8%       -0.29 [-0.61, 0.04]       2022         Joan Science       12023       32.94       15.2       160       816       20       685       5.5%       -0.27 [-0.44, -0.10]       2023         Aligampreecha 2023       125       74.81       2137       160.55       90.26       16457       6.7%       -0.040 [-0.45, -0.36]       2023         Silswas 2023       133       72.22       127       144.9       69.38       924       5.4%       -0.17 [-0.36, 0.02]       2023         Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 215.07, df	-
Semmler 2021         103.39         45.93         374         128.49         57.39         1612         6.2%         -0.45 [-0.57, -0.34]         2021           .an 2022         27         16         1543         32.4         19.98         21654         6.7%         -0.27 [-0.33, -0.27]         2021           Wang 2022         33.3         22.86         1034         34.56         21.96         4499         6.6%         -0.027 [-0.31, -0.27]         2022           Jaconchal 2022         115         51.11         41         131         56.3         383         3.8%         -0.29 [-0.61, 0.04]         2022           Jaconchal 2023         125         74.81         2137         160.55         90.26         16457         6.7%         -0.04 [-0.45, -0.36]         2023           Vijampreecha 2023         125         74.81         2137         160.55         90.26         16457         6.7%         -0.40 [-0.45, -0.36]         2023           Vijampreecha 2023         133         72.22         127         144.9         69.38         924         5.4%         -0.17 [-0.36, 0.02]         2023           Subtotal (95% Cl)         8497         54997         100.0%         -0.21 [-0.30, -0.11]         -0.21 [-0.30, -0.11] <td>+</td>	+
Lan 2022 27 16 1543 32.4 19.98 21654 6.7% -0.27 [-0.33], -0.22] 2022 Wang 2022 33.3 22.86 1034 34.56 21.96 4499 6.6% -0.06 [-0.12, 0.01] 2022 Soonchai 2022 115 51.11 41 131 56.3 383 3.8% -0.29 [-0.61, 0.04] 2022 J2023 32.94 15.2 160 38.16 20 685 5.5% -0.27 [-0.44, -0.10] 2023 Wijampreecha 2023 125 74.81 2137 160.55 90.26 16457 6.7% -0.40 [-0.45, -0.36] 2023 Subtotal (95% (1) 8497 54997 100.0% -0.21 [-0.30, -0.11] Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 215.07, df = 19 (P < 0.0001); I <sup>2</sup> = 91%	
Wang 2022       33.3       22.86       1034       34.56       21.96       4499       6.6%       -0.06 [-0.12, 0.01]       2022         30onchai 2022       115       51.11       41       131       56.3       383       3.8%       -0.29 [-0.61, 0.04]       2022         J2023       32.94       15.2       160       88.16       20       685       5.5%       -0.27 [-0.44, -0.10]       2023         Mijampreecha 2023       125       74.81       2137       160.55       90.26       16457       6.7%       -0.40 [-0.45, -0.36]       2023         Siswas 2023       133       72.22       127       144.9       69.38       924       5.4%       -0.17 [-0.36, 0.02]       2023         Vibtotal (95% (L))       8497       54997       100.0%       -0.21 [-0.30, -0.11]       -0.21 [-0.30, -0.11]         reterogeneity: Tau <sup>#</sup> = 0.03; Chi <sup>#</sup> = 215.07, df = 19 (P < 0.00001); I <sup>#</sup> = 91%       91%       -0.21 [-0.30, -0.11]       -0.21 [-0.30, -0.11]	
Boonchai 2022         115         51.11         41         131         56.3         383         3.8%         -0.29 [-0.61, 0.04]         2022           Li 2023         32.94         15.2         160         38.16         20         685         5.5%         -0.27 [-0.44, -0.10]         2023           Alijampreecha 2023         125         74.81         2137         160.55         90.26         16457         6.7%         -0.40 [-0.45, -0.36]         2023           Biswas 2023         133         72.22         127         144.9         69.38         924         5.4%         -0.17 [-0.36, 0.02]         2023           Subtotal (95% CI)         8497         54997         100.0%         -0.21 [-0.30, -0.11]         -0.21 [-0.30, -0.11]           Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 215.07, df = 19 (P < 0.00001); P = 91%	+
Li 2023 32.94 15.2 160 38.16 20 685 5.5% -0.27 [-0.44, -0.10] 2023 ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓	
Mijampreecha 2023       125       74.81       2137       160.55       90.26       16457       6.7%       -0.40 [-0.45, -0.36]       2023         Biswas 2023       133       72.22       127       144.9       69.38       924       5.4%       -0.17 [-0.36, 0.02]       2023         Subtotal (95% CI)       8497       54997       100.0%       -0.21 [-0.30, -0.11]         Heterogeneity: Tau <sup>a</sup> = 0.03; Chi <sup>a</sup> = 215.07, df = 19 (P < 0.00001); I <sup>a</sup> = 91%       -0.21 [-0.30, -0.11]	
Biswas 2023 133 72.22 127 144.9 69.38 924 5.4% -0.17 [-0.36, 0.02] 2023 Subtotal (95% CI) 8497 54997 100.0% -0.21 [-0.30, -0.11] Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 215.07, df = 19 (P < 0.00001); I <sup>2</sup> = 91%	
Subtotal (95% CI) 8497 54997 100.0% -0.21 [-0.30, -0.11] Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 215.07, df = 19 (P < 0.00001); I <sup>2</sup> = 91%	
Heterogeneity: Tau <sup>2</sup> = 0.03; Chi <sup>2</sup> = 215.07, df = 19 (P < 0.00001); I <sup>2</sup> = 91%	T
-0.2 -0.1 0	0 0.1 0.2
	) Favours [Obese NAFLD]

Figure 5. Forest plot for lean NAFLD versus obese NAFLD for lipid profile: (2.1.2) HDL; (2.1.3) LDL; (2.1.4) Triglycerides.

HDL, high-density lipoprotein; LDL, low-density lipoprotein; NAFLD, non-alcoholic fatty liver disease.

		n NAFLE			se NAFL	-		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean		Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% Cl
2.3.1 Systolic blood	pressure									
eng 2014	126.46	16.24	134	132.2	17.29	764	11.4%	-0.33 [-0.52, -0.15]	2014	
<im 2017<="" td=""><td>122.4</td><td>15.6</td><td>420</td><td>129.5</td><td>16.2</td><td>504</td><td>13.0%</td><td>-0.45 [-0.58, -0.31]</td><td>2017</td><td></td></im>	122.4	15.6	420	129.5	16.2	504	13.0%	-0.45 [-0.58, -0.31]	2017	
Zou 2020	127	24.91	1528	126.1	25.897	3183	14.7%	0.04 [-0.03, 0.10]	2020	+
Sinha 2020	138.3	17.6	37	137.9	15.3	83	6.2%	0.02 [-0.36, 0.41]	2020	
Semmler 2021	132.16	18.33	374	136.42	17.51	1612	13.5%	-0.24 [-0.35, -0.13]	2021	
_an 2022	132.4	20.5	1543	137.8	21.1	21654	14.8%	-0.26 [-0.31, -0.20]	2022	±
Nang 2022	123.8	15.71	1034	128.64	14.97	4499	14.5%	-0.32 [-0.39, -0.25]	2022	
_i 2023	128.5	15.56	160	132	16.67	685	11.8%	-0.21 [-0.38, -0.04]	2023	
Subtotal (95% CI)			5230			32984	100.0%	-0.23 [-0.36, -0.11]		◆
Heterogeneity: Tau <sup>2</sup> :	= 0.03; Ch	i <sup>2</sup> = 90.9	99, df =	7 (P < 0.0	)00001); P	= 92%				
Fest for overall effect	Z = 3.63	(P = 0.0)	003)							
2.3.2 Diastolic blood										A11
Feng 2014		11.74	134	82.84	10.57	764	12.1%	-0.26 [-0.44, -0.08]	2014	
<im 2017<="" td=""><td>76.3</td><td>10.5</td><td>420</td><td>80.3</td><td>10.7</td><td>504</td><td>14.9%</td><td>-0.38 [-0.51, -0.25]</td><td>2017</td><td></td></im>	76.3	10.5	420	80.3	10.7	504	14.9%	-0.38 [-0.51, -0.25]	2017	
Binha 2020	88.9	6.5	37	87.3	6.1	83	5.3%	0.26 [-0.13, 0.64]	2020	
Zou 2020	69.8	21.92		72.1	21.58	3183	18.3%	-0.11 [-0.17, -0.04]	2020	-
_an 2022	83.8	11.1	1543	87.5	11.8	21654	18.6%	-0.31 [-0.37, -0.26]	2022	
Nang 2022	76.38	9.35	1034	79.48	9.72	4499	18.0%	-0.32 [-0.39, -0.25]	2022	
_i 2023	78.5	11.3	160	84	12.59	685	12.7%	-0.44 [-0.62, -0.27]	2023	
Subtotal (95% CI)			4856			31372	100.0%	-0.27 [-0.37, -0.16]		◆
Heterogeneity: Tau <sup>2</sup> :	= 0.01; Ch	i <sup>2</sup> = 46.0	)3, df =	6 (P < 0.0	00001); P	= 87%				
Fest for overall effect	Z = 5.02	(P < 0.0	0001)							
										-0.5 -0.25 0 0.25 0.5

Test for subgroup differences: Chi<sup>2</sup> = 0.18, df = 1 (P = 0.67), l<sup>2</sup> = 0%

**Figure 6.** Forest plot for lean NAFLD versus obese NAFLD for BP: (2.3.1) Systolic BP; (2.3.2) Diastolic BP. BP, blood pressure; NAFLD, non-alcoholic fatty liver disease.

	lear	NAFL	D	obe	se NAFL	D		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% Cl
Bhat 2013	84.9	5	30	97.7	5.1	120	3.0%	-2.51 [-3.00, -2.01]	2013	4
Kumar 2013	80.1	5.8	27	96.01	6.85	178	3.2%	-2.36 [-2.82, -1.89]	2013	4
Feng 2014	82.48	6.29	134	93.45	8.7	764	6.6%	-1.31 [-1.50, -1.11]	2014	
Fracanzani 2017	89.3	7.7	143	105.1	11	526	6.5%	-1.52 [-1.72, -1.32]	2017	<b>←</b>
Kim 2017	83.2	6.2	420	90.8	7.5	504	7.4%	-1.09 [-1.23, -0.96]	2017	
Cantero 2018	88.86	7.95	25	100.86	9.07	30	2.3%	-1.38 [-1.97, -0.78]	2018	·
Lum 2020	87	18.4	57	111.64	18	206	4.8%	-1.36 [-1.67, -1.04]	2020	<b>←</b>
Shah 2020	88.8	6.26	69	98.6	8.01	181	5.0%	-1.29 [-1.59, -0.99]	2020	
Sinha 2020	79.1	4.8	37	87.6	6.2	83	3.5%	-1.45 [-1.88, -1.02]	2020	<b>←</b> →
Zou 2020	99.9	9.96	1528	118.6	18.7	3183	8.2%	-1.14 [-1.21, -1.08]	2020	+
Semmler 2021	89.2	7.73	374	105.02	10.78	1612	7.6%	-1.54 [-1.66, -1.42]	2021	
Tan 2021	85.14	7.18	392	98.14	10.51	1420	7.6%	-1.31 [-1.43, -1.19]	2021	
Boonchai 2022	83	7.5	41	95.6	9.5	383	4.6%	-1.35 [-1.68, -1.01]	2022	<b>←</b> →→
Lan 2022	83.4	8.2	1543	92.8	8.7	21654	8.3%	-1.08 [-1.14, -1.03]	2022	+
Wang 2022	82.05	6.85	1034	91.95	7.61	4499	8.1%	-1.32 [-1.40, -1.25]	2022	+
Biswas 2023	86.7	6.67	127	98.69	8.64	924	6.6%	-1.42 [-1.62, -1.23]	2023	
Li 2023	88	5.93	160	99	8.15	685	6.7%	-1.41 [-1.60, -1.23]	2023	
Total (95% CI)			6141			36952	100.0%	-1.39 [-1.49, -1.28]		◆
Heterogeneity: Tau <sup>2</sup> =	= 0.04: C	$hi^2 = 1$	40.09.	df = 16 (F	< 0.00	001): I <sup>2</sup> =	89%			
Test for overall effect										-1 -0.5 0 0.5 1
										Favours [Lean NAFLD] Favours [Obese NAFLD]

**Figure 7.** Forest plot for lean NAFLD versus obese NAFLD for waist circumference. NAFLD, non-alcoholic fatty liver disease.

individuals. The sensitivity analysis also reiterated the more favorable lipid profiles and anthropometric measures in the LN group, with higher HDL levels (SMD 0.27, 95% CI 0.18–0.35, p < 0.00001) and lower triglycerides (SMD -0.19, 95% CI -0.26 to -0.12, p < 0.00001), LDL (SMD -0.13, 95% CI -0.19 to -0.06, p < 0.0001), and WC (SMD -1.33, 95% CI -1.40-1.26, p < 0.00001). The systolic (SMD -0.29, 95% CI -0.35 to -0.23, p < 0.00001) and diastolic (SMD -0.33, 95% CI -0.36 to -0.29, p < 0.00001) BP and FBS (SMD -0.06, 95% CI -0.13-0.02, p = 0.13) remained almost similar as well (Supplemental Figures S1-S5).

## Publication bias

The presence of publication bias for prevalence, DM, HTN, dyslipidemia, MS, lipid profiles, WC, systolic and diastolic BPs, and FBS was assessed using a funnel plot, revealing an asymmetric distribution on visualization and suggesting evidence

	Lea	n Nafld		Obe	ese Nafi	ld		Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% Cl
Bhat 2013	87.5	14.4	30	88.1	17.3	120	2.6%	-0.04 [-0.44, 0.36]	2013	· · · · · · · · · · · · · · · · · · ·
Kumar 2013	94.2	8.4	27	102.08	19.78	178	2.5%	-0.42 [-0.83, -0.01]	2013	·
Feng 2014	106.38	33.33	134	103.68	25.56	764	8.3%	0.10 [-0.08, 0.28]	2014	
Kim 2017	103.6	19	420	106.9	24.4	504	11.7%	-0.15 [-0.28, -0.02]	2017	·
Cantero 2018	93.4	16.23	25	105.99	20.29	30	1.5%	-0.67 [-1.22, -0.12]	2018	<b>←</b>
Shah 2020	129.52	26.07	69	120.74	24.25	181	4.7%	0.35 [0.07, 0.63]	2020	<b>_</b>
Sinha 2020	127.8	30.8	37	135.1	29.5	83	2.7%	-0.24 [-0.63, 0.15]	2020	+
Zou 2020	120.1	51.81	1528	120.8	54.67	3183	17.3%	-0.01 [-0.07, 0.05]	2020	
Navarozza 2021	112.4	29.4	60	119.4	39	486	5.0%	-0.18 [-0.45, 0.08]	2021	·
Lan 2022	93.6	17.33	1543	95.4	18.67	21654	17.9%	-0.10 [-0.15, -0.05]	2022	
Wang 2022	94.14	18.72	1034	94.32	16.92	4499	16.8%	-0.01 [-0.08, 0.06]	2022	
Li 2023	98.82	9.87	160	98.46	9.87	685	8.9%	0.04 [-0.14, 0.21]	2023	
Total (95% CI)			5067			32367	100.0%	-0.05 [-0.12, 0.02]		
Heterogeneity: Tau <sup>2</sup> =	0.01; Ch	i <sup>z</sup> = 29.7	71, df =	11 (P = 0	.002); 12	= 63%				-0.2 -0.1 0 0.1 0.2
Test for overall effect:	Z=1.36	(P = 0.1	8)							Favours [Lean NAFLD] Favours [Obese NAFLD]

**Figure 8.** Forest plot for lean NAFLD versus obese NAFLD for fasting blood sugar. NAFLD, non-alcoholic fatty liver disease.

of publication bias (Supplemental Figures S6–S16).

# Discussion

Lean NAFLD represents a unique subtype of NAFLD, distinguishing itself from conventional NAFLD primarily seen in overweight or obese individuals or those with features resembling MS. This study seeks to provide a comprehensive global overview of NAFLD prevalence in lean individuals and explores the extent of associated metabolic dysfunction. Unlike prior research, this analysis stands out by its specific emphasis on investigating the correlation between different ethnic groups and the occurrence of NAFLD in lean people. It is worth noting that while LN constitutes a small percentage of the population in Western regions, it comprises a significant onethird of all NAFLD cases in the Eastern regions, where roughly 14% of the overall population is impacted by this condition.<sup>1</sup>

In our analysis, the prevalence of NAFLD varies among lean and non-lean populations in different regions. In already diagnosed NAFLD cases, Asian populations show a higher prevalence among non-lean individuals (88%), while in Europe and North America, NAFLD is more evenly distributed between lean and non-lean individuals. In the general population, the prevalence of NAFLD is generally higher among nonlean individuals, with the highest rates in Europe, followed by Asia and the lowest in North America. These findings underscore the importance of understanding regional and population-specific factors in NAFLD prevalence, with lifestyle, diet, and healthcare access playing significant roles. However, when examining the results by region, significant variations emerge. The criteria for classifying someone as obese or lean may differ across populations. It is crucial to consider that this outcome may be partly due to chance, as the American population had a much larger sample size than the others, and the healthcare facilities among the Asian population might not be state-of-the-art and accessible to all. Therefore, it is reasonable to assume that a significant portion of the population may have NAFLD but remains undiagnosed.<sup>34–37</sup>

The current analysis revealed that lean individuals with NAFLD have a notably lower metabolic burden compared to overweight and obese individuals. While metabolic dysregulation plays a decisive role in the development of NAFLD, it represents just one facet of the complex picture. Our findings indicate that metabolic dysfunction in NAFLD is influenced by body weight, with conditions such as DM, HTN, and dyslipidemia exhibiting a more pronounced impact on individuals with ON than those with a leaner form of the disease. Furthermore, our data show that fasting blood glucose levels are generally lower in lean people with NAFLD than in their overweight or obese counterparts. Additionally, in our analysis, lean individuals diagnosed with NAFLD typically exhibit lower BP levels in contrast to ON, and it is noteworthy that BMI serves as a substantial indicator for predicting the presence of HTN.38 Recent research has pinpointed specific genetic factors, notably PNPLA3 and TM6SF2, as pivotal contributors to the evolution and course of NAFLD. These genetic elements are instrumental in understanding the close associations between NAFLD, MS, DM, and cardiovascular diseases.<sup>39</sup> Moreover, IR plays a critical role in this intricate web. It enhances the production of lipids in the liver while impeding the body's ability to control the breakdown of fats stored in adipose tissue. This dual effect results in the disproportionate deposit of fat in the liver, a hallmark of NAFLD. In essence, these genetic and metabolic factors intersect to shape the pathophysiology of NAFLD and its intricate relationships with MS, DM, and cardiovascular diseases, providing crucial insights into these interconnected health issues.<sup>39,40</sup>

According to a study conducted in Hong Kong, two primary factors were significantly associated with LN: modifications in waist size and the concentration of triglycerides in the blood.<sup>41</sup> In our analysis, in comparison to the LN group, the ON group displayed significantly more pronounced deviations in lipid profile components. Lipid profile abnormalities are integral to MS, with NAFLD being closely associated. Factors contributing to these abnormalities include sedentary lifestyles, genetic polymorphisms, de novo synthesis of triglycerides and free fatty acids, and dietary habits. Notably, lean individuals with NAFLD often exhibit better lipid profiles than their obese counterparts. This is primarily due to differences in fat distribution, insulin sensitivity, and their collective influence on lipid metabolism. LN is characterized by a more liver-centric fat distribution, resulting in less systemic adiposity and fewer harmful fatty acids released into the bloodstream. Additionally, lean individuals typically have better insulin sensitivity, further aiding in maintaining a healthier lipid profile and, hence, a more favorable metabolic profile.<sup>33,42,43</sup>

The average WC for LN was  $85.9 \pm 7.1$  cm. Our analysis reveals that the non-lean population tends to have a higher WC. The WC of the lean population falls close to the international guidelines' borderline values (95 cm for men and 80 cm for women). While having an apple-shaped body characterized by a high WC is considered a risk factor for DM in individuals with normal BMI, there is limited evidence linking this to NAFLD in lean individuals, as their WC is near the borderline range. It is important to note that there is no universal WC threshold worldwide, and these parameters can differ among various races and ethnicities. Notably, lean individuals who are diagnosed with NAFLD and have higher WCs (exceeding 102 and 88 cm in men and women,

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respectively) exhibit a greater risk of developing DM, carotid plaque, and fibrosis when compared to individuals without NAFLD.<sup>16,44</sup> The intensity of LN is positively linked to accumulation of fat in the viscera, and it is suggested that visceral adiposity, rather than total fat, may contribute to the risk of LN.<sup>42,43</sup> Consequently, measuring WC provides an additional means to assess metabolic risks associated with BMI.

Numerous studies have consistently found that lean individuals diagnosed with NAFLD experience a lesser incidence of DM, HTN, hypertriglyceridemia, obesity, and MS.15,16,45 However, in the advanced stages of the disease, LN patients tend to exhibit increase in fibrosis scores, cardiovascular morbidity, and all-cause mortality rates compared to their non-lean counterparts with NAFLD.9,29,46 Additionally, when using magnetic resonance elastography to assess fibrosis in NAFLD, the lean group displayed a reduced occurrence of substantial fibrosis but a heightened incidence of severe fibrosis.47 Recent studies have predominantly focused on evaluating LN based on genetics and ethnicity. However, the available evidence on this topic remains limited.

# Limitation

This analysis represents the most extensive investigation of the prevalence of NAFLD in lean individuals, along with its associated metabolic dysregulation. However, it is essential to acknowledge certain limitations in our study. Liver biopsy is the established benchmark for making a diagnosis of fatty liver; it is crucial to acknowledge that a selection bias could influence the outcomes of the sensitivity analysis. This bias arises from the fact that patients who opt for biopsies are more inclined to have a more advanced or severe form of the disease. Moreover, the literature could greatly benefit from examining the outlook or prognosis disparities between individuals with lean and non-lean NAFLD. However, our study's scope is limited due to the absence of reported mortality outcomes in lean and ON from existing studies. In future research, investigating these mortality outcomes could provide valuable insights into the overall impact of NAFLD in both lean and obese individuals. Another limitation of our study is the unavailability of genderbased data. Anthropometric measures such as BMI, weight, and WC can significantly differ between genders. Additionally, genetics and

ethnicity also contribute to variations in these anthropometric measures. Therefore, the lack of gender-specific data might hinder a comprehensive understanding of the impact of these factors on our study results.

#### Conclusion

This study delves into the unique subtype of NAFLD known as LN, differentiating it from the typical form associated with overweight or obese individuals. Notably, LN's prevalence varies between Western and Eastern regions. While Western populations see it as a small fraction, it constitutes one-third of all NAFLD cases in the East. The prevalence of NAFLD among lean and non-lean individuals varies by region. Lean people with NAFLD generally experience lower metabolic burdens than their overweight and obese counterparts. This metabolic distinction is influenced by factors like body weight, genetics (e.g. PNPLA3 and TM6SF2), and IR. Lean NAFLD is characterized by a liver-centric fat distribution, resulting in more favorable lipid profiles and metabolic outcomes. While lean individuals with NAFLD experience fewer metabolic abnormalities initially, they may face higher fibrosis scores and increased cardiovascular risks in advanced stages. The connection between genetics, metabolism, and NAFLD provides crucial insights into the condition's complex relationships with MS, DM, and cardiovascular diseases. Further research is needed to enhance our understanding and management of this unique condition.

## Declarations

*Ethics approval and consent to participate* Not applicable.

*Consent for publication* Not applicable.

#### Author contributions

**Hareer Fatima:** Conceptualization; Writing – original draft; Writing – review & editing.

**Hussain Sohail Rangwala:** Project administration; Writing – original draft; Writing – review & editing.

**Muhammad Saqlain Mustafa:** Formal analysis; Investigation; Methodology; Writing – review & editing. **Muhammad Ashir Shafique:** Conceptualization; Writing – original draft; Writing – review & editing.

**Syed Raza Abbas:** Data curation; Writing – original draft.

**Burhanuddin Sohail Rangwala:** Conceptualization; Writing – original draft; Writing – review & editing.

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#### Competing interests

The authors declare that there is no conflict of interest.

#### Availability of data and materials

Data available within the article. The authors confirm that the data supporting the findings of this study are available within the article.

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#### Supplemental material

Supplemental material for this article is available online.

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