**Supplementary files to the manuscript**

**The global epidemiology of lean nonalcoholic fatty liver disease: a systematic review and meta-analysis**

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**File 1. Detailed description of the methods section**

**Search strategy and selection criteria**

The study evaluation and protocol description was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (http://www.prisma-statement.org/). A systematic search was performed in Pubmed, EMBASE, Web of Science and Cochrane databases to identify eligible studies published up to January 2020. The search terms were conducted as follows: “prevalence” OR “frequency” OR “incidence” OR “epidemiology” AND “non-alcoholic fatty liver disease” OR (non alcoholic fatty liver disease OR nonalcoholic fatty liver disease OR nonalcoholic fatty liver) OR non alcoholic steatohepatitis) OR NAFLD OR NASH. References of all publications identified as relevant were reviewed for further studies. All selected articles were reviewed for inclusion by two independent investigators and the presence of any disagreements was resolved by a third investigator.

Inclusion criteria of the eligible studies for the meta-analysis were as follows: (1) US, CT, MRI or liver biopsy were used for the diagnosis of NAFLD after exclusion of other known causes of liver diseases; (2) the studies provided sufficient information to estimate the pooled prevalence of lean NAFLD. We defined “lean NAFLD or overweight/obese NAFLD” according to both age and ethnic-specific BMI cutoffs: for adult Asians (≥18 years of age), lean NAFLD was defined as NAFLD and BMI <23 kg/m2, while overweight/obese NAFLD was defined as NAFLD and BMI ≥23 kg/m2; for adult non-Asians, lean NAFLD was defined as NAFLD and BMI <25 kg/m2, while overweight/obese NAFLD was defined as NAFLD and BMI ≥25 kg/m2; for children/adolescents (<18 years of age), lean NAFLD was defined as NAFLD and BMI <85th percentile, while overweight/obese NAFLD was defined as NAFLD and BMI ≥85th percentile; (3) studies with a sample size of at least 100 subjects; and (4) studies were published in English language.

The study exclusion criteria were as follows: (1) studies did not screen adults about excess alcohol consumption; (2) diagnosis of NAFLD did not exclude other known causes of liver disease; (3) lack of specific information for patients with NAFLD; (4) studies were carried out in populations with some pre-existing diseases, such as diabetes and human immunodeficiency virus (HIV) co-infection; (5) Screening population were all patients with abnormal liver function; (6) diagnosis of NAFLD was made only by abnormal liver function tests; (7) the study diagnosed NAFLD postmortem; and (8) abstracts or unpublished data.

**Study identification and data extraction**

According to the MOOSE guideline, all data were extracted by two independent investigators and any discrepancies in collection were resolved by a third investigator. From each study, the following characteristics were extracted: author name, publication year, study year, study design, region, selected population characteristics (such as BMI, mean age, sex, laboratory parameters, smoking, physical inactivity, complication), NAFLD diagnosis, number of participant, number of lean NAFLD. The authors of the studies without any available information were contacted for additional data when required. The checklist developed by the Briggs Institute Reviewer’s Manual was used to evaluate the overall quality of the included studies1.

**Statistical analysis**

All statistical analyses were performed using Open MetaAnalyst2. Based on the degree of heterogeneity, a random-effect or fixed-effect meta-analysis was conducted to estimate the pooled prevalence and its 95% confidence intervals (CI)3. In addition, we also estimated the average characteristics (clinical parameters, laboratory variables, male sex, smoking, physical inactivity, and complication rate) of lean NAFLD, lean non-NAFLD and overweight/obese NAFLD subjects across eligible studies, with 95% confidence intervals by random-effect or fixed-effect meta-analysis3, 4. The degree of heterogeneity between studies was evaluated using estimates of *I*2, which represents the estimated percentage of total variability that is due to heterogeneity rather than chance. *I*2 value of 25%, 50% and 75% indicates low, moderate or high heterogeneity, respectively.

Multivariable random-effects meta-regression and subgroup analyses were performed to determine potential sources of heterogeneity: type of population, mean age of participants, region of study, study type, sample size, study year, diagnostic methods used for diagnosing NAFLD. As a sensitivity analysis, we also assessed results when a logit transformation was applied to prevalence proportions.

To formally assess whether the prevalence of lean NAFLD had a sex difference, we used data from 14 studies to compare lean NAFLD prevalence between men and women within studies. By using random-effects meta-analysis, we then pooled these within-study estimates to analyze summary odds ratios with 95% confidence intervals.

The odds ratio (OR) was calculated for bivariate analysis and the continuous variable analysis was performed by estimating standardized mean difference (SMD).

Hypothesis testing was analyzed to determine whether or not the overall effect has statistical significance. The P-value of the test was calculated according to the Z value. *P-*value <0·05 was considered statistically significant.

**Reference**

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**File 2. References for included studies used to analyze the global prevalence of lean NAFLD**

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| **File 3. Extracted characteristics of all included studies.** | | | | | | | | |
| **Author** | **Country** | **Year** | **Study**  **design** | **Study**  **population** | **Excluded**  **Subgroups** | **Diagnostic**  **methods** | **Age**  **(years)** | **Total**  **(n)** |
| Fan,J.G. | China | 2005 | Cross-Sectional | Community  based | chronic viral hepatitis, cirrhosis or other severe diseases; pregnant; long-term using of estrogens, tamoxifen or corticosteroids | Ultrasound | 52.4±15·1 | 3175 |
| Church,T.S. | USA | 2006 | Cross-Sectional | Hospital  based | smoking men; history of myocardial infarction or stroke; diabetes; other chronic liver diseases; excessive alcohol use; missing data | Computed tompgraphy | 33-73 | 218 |
| Hsiao,P.J. | China | 2007 | Cross-Sectional | Population  based | under the age of 20 years; alcohol abuse; taking medications with tamoxifen or amiodarone; pregnant women; individuals with positive seromarkers for hepatitis B or C, and those with an aspartate aminotransferase (AST)/alanine aminotransferease (ALT) ratio >=12 | Ultrasound | NA | 16309 |
| Radu,C. | Romania | 2008 | Cross-Sectional | Hospital  based | none | Ultrasound | 54.3±13·5 | 3005 |
| Chen-Chung F. | China | 2009 | Cross-Sectional | Population  based | positive for HBsAg or anti-HCV | Ultrasound | 12-13 | 216 |
| Caballeria,L. | Spain | 2010 | Cross-Sectional | Health examination | other chronic liver diseases; excessive alcohol use; individuals with incapacitating diseases or cognitive deterioration; institutionalized patients | Ultrasound | 52.9±14.3 | 766 |
| Caserta,C.A. | Italy | 2010 | Cross-Sectional | Population  based | history of alcohol drinking or drug consumption; formerly diagnosed liver disease, or diabetes | Ultrasound | 11-13 | 642 |
| Das,K. | India | 2010 | Cross-Sectional | Population  based | migrant laborers; chronic hepatitis viral infections; alcohol and drug intake; comorbidities influence on the study implementation and outcome | Computed tomography | 35.5±12.4 | 1911 |
| Lazo,M. | USA | 2011 | Prospective | Population  based | none | Ultrasound | 42.7 | 11371 |
| Sinn,D.H. | Korea | 2012 | Cross-Sectional | Health examination | other chronic liver diseases; excessive alcohol use, history of malignancy; stroke; cardiovascular disease or hepatectomy; chronic use of medications other than vitamins; abnormal findings on ultrasound; serum glucose, insulin, c-peptide level outside of the homeostasis model assessment index calculation range | Ultrasound | 30-60 | 11476 |
| Younossi,Z.M. | USA | 2012 | Cross-Sectional | Population  based | none | Ultrasound | NA | 11613 |
| Goh,S.C. | Malaysia | 2013 | Cross-Sectional | Health examination | male who had admitted to regular drinking exceeding 140 g/week and female exceeding 70 g/week; known history of liver disease | Ultrasound | 46.0±15.3 | 1621 |
| Huang,S.C. | China | 2013 | Cross-Sectional | Community  based | history of alcohol drinking or drug consumption; formerly diagnosed liver disease, or diabetes | Ultrasound | 6-12 | 219 |
| Feng,Ren-Nan. | China | 2014 | Cross-Sectional | Health examination | previous/current excessive alcohol intake (male >20 g/d; female >10 g/d); hepatitis; malignancies; pregnancy; long-term use of estrogens, tamoxifen, or corticosteroids; absence of any of the anthropometric measurement, or laboratory analysis | Ultrasound | 20-70 | 1779 |
| Lawlor,D.A. | UK | 2014 | Cross-Sectional | Population  based | excessive alcohol use; missing data | Ultrasound | 17-18 | 1711 |
| Chan,R. | China | 2015 | Cross-Sectional | Population  based | active malignancy; metallic implants, or other contraindications to MRI; chronic liver disease; treatment with steatogenic drugs, medications associated with fatty liver changes; decompensated liver disease; excessive alcohol use; incomplete dietary data | Magnetic resonance | 48.1 | 793 |
| Du,T. | China | 2015 | Cross-Sectional | Community  based | taking medications for hypertension, diabetes, dyslipidemia, or hyperuricemia; excessive alcohol intake; chronic liver disease; missing information | Ultrasound | 49.7±4.0 | 10761 |
| Nishioji,K. | Japan | 2015 | Cross-Sectional | Health examination | hepatitis virus infection; autoimmune liver disease; treatment for thyroid disease, hormone therapy; excessive alcohol use; missing data | Ultrasound | 54.3 | 824 |
| Nishioji,K.2 | Japan | 2015 | Cross-Sectional | Health examination | other chronic liver diseases; excessive alcohol use; no uncontrolled biliary diseases | Ultrasound | NA | 3271 |
| Fukuda,T. | Japan | 2016 | Retrospective | Health examination | medical treatment; known liver disease; excessive alcohol use; diabetes; missing data | Ultrasound | 41.5±7.4 | 4629 |
| Seo,S.W. | USA | 2016 | Cross-Sectional | Population based | excessive alcohol use; have no data | Ultrasound | 37.3±0.3 | 4472 |
| Yang,M.H. | Korea | 2016 | Cross-Sectional | Health examination | alcohol use; history of chronic liver disease; missing data; hepatocellular carcinoma | Ultrasound | NA | 18369 |
| Honarvar,B. | Iran | 2017 | Cross-Sectional | Population  based | Pregnant women or those who had childbirth within the past six months; diabetes; alcoholic consumers, non-Iranian nationality | Ultrasound | 42 | 478 |
| Jinjuvadia,R. | USA | 2017 | Cross-Sectional | Population  based | chronic liver disease; excessive alcohol use or elevated transferrin level >50%; taking medications that might cause hepatic steatosis | Ultrasound | 42.1 | 11651 |
| Naderian,M. | Iran | 2017 | Cross-Sectional | Population  based | excessive alcohol use; active malignancy; history of chronic liver diseases | Ultrasound | NA | 927 |
| Yoshitaka,H. | Japan | 2017 | Prospective | Population  based | current use of any medication; known liver disease; previous CVD event; alcohol intake of more than 20g/d | Ultrasound | 48.01±8.7 | 1647 |
| Alam,S. | Bangladesh | 2018 | Cross-Sectional | Population  based | previously diagnosed cases of liver disease | Ultrasound | 34.2±12.7 | 2782 |
| Alferink,L.J. | Netherlands | 2019 | Cross-Sectional | Population  based | participants with secondary causes for steatosis | Ultrasound | 69.3±9.2 | 4609 |
| Alferink,L.J.2 | Netherlands | 2019 | Prospective | Population  based | participants with possible secondary causes; participants with more than 30% missing data; missing for steatosis | Ultrasound | 69.7±8·8 | 3882 |
| Niriella,M.A. | Sri Lanka | 2019 | Prospective | Community  based | alcohol overuse and other secondary causes | Ultrasound | NA | 2985 |
| Sinn,D.H.2 | Korea | 2019 | Retrospective | Health examination | history of liver cirrhosis or positive hepatitis B surface antigen or hepatitis C virus antibodies; history of cancer; alcohol intake ≥30 g/day in men or ≥20 g/day in women at any point during follow-up; underweight (BMI<18·5 kg/m2; missing data; diabetes | Ultrasound | 48.7±9.1 | 51463 |
| Wang,L. | Japan | 2019 | Retrospective | Health examination | known liver disease; ethanol consumption; medication usage; diabetes mellitus; fasting plasma glucose>6·1 mmol/L | Ultrasound | NA | 15464 |
| Yun,Yeojun. | Korea | 2019 | Cross-Sectional | Health examination | other liver diseases | Ultrasound | 43.6±8.2 | 268 |

Data are expressed as mean ± SD, median or age range; NA: not available.

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| **File 4. Quality assessment of included studies in the global epidemiology of lean NAFLD using the JBI-Prevalence Critical Appraisal Checklist** | | | | | | | | | |
| **Study** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | **Q6** | **Q7** | **Q8** | **Q9** |
| Fan,J.G.2005 | Y | Y | Y | U | Y | Y | Y | Y | Y |
| Church,T.S.2006 | Y | NA | Y | Y | Y | Y | Y | Y | NA |
| Hsiao,P.J.2007 | U1 | Y | Y | Y | Y | Y | Y | Y | U |
| Radu,C.2008 | Y | U | Y | Y | Y | Y | Y | Y | U |
| Chen-Chung Fu.2009 | Y | U | Y | U | Y | Y | Y | Y | Y |
| Caballeria,L.2010 | Y | Y | Y | Y | U | Y | Y | U | Y |
| Caserta,C.A.2010 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Das,K.2010 | Y | Y | Y | Y | U | Y | Y | U | Y |
| Lazo,M.2011 | Y | NA | Y | Y | Y | Y | Y | Y | Y |
| Sinn,D.H.2012 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Younossi,Z.M.2012 | Y | NA | Y | Y | Y | Y | Y | Y | NA |
| Goh,S.C.2013 | Y | NA | Y | Y | Y | Y | Y | Y | NA |
| Huang,S.C.2013 | Y | U | Y | Y | Y | Y | Y | Y | U |
| Feng,Ren-Nan.2014 | Y | U | Y | Y | Y | Y | Y | Y | NA |
| Lawlor,D.A.2014 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Chan,R.2015 | Y | U | Y | Y | Y | Y | Y | Y | U |
| Du,T.2015 | Y | NA | Y | Y | Y | Y | Y | Y | NA |
| Nishioji,K.2015 | Y | U | Y | Y | Y | Y | Y | Y | U |
| Nishioji,K.2015 | Y | U | Y | Y | Y | Y | Y | Y | U |
| Fukuda,T.2016 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Seo,S.W.2016 | Y | NA | Y | Y | Y | Y | Y | Y | Y |
| Yang,M.H.2016 | Y | U | Y | Y | Y | Y | Y | Y | U |
| Honarvar,B.2017 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Jinjuvadia,R.2017 | Y | NA | Y | Y | Y | Y | Y | Y | NA |
| Naderian,M.2017 | Y | U | Y | Y | Y | Y | Y | Y | U |
| Yoshitaka,H.2017 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Alam,S.2018 | Y | Y | Y | Y | Y | Y | Y | Y | U |
| Alferink,L.J.2019 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Alferink,L.J.2019 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Niriella,M.A.2019 | Y | U | Y | Y | Y | Y | Y | Y | Y |
| Sinn,D.H.2019 | U | U | Y | Y | Y | Y | Y | Y | Y |
| Wang,L.2019 | Y | NA | Y | Y | Y | Y | Y | Y | NA |
| Yun,Yeojun.2019 | Y | U | Y | Y | Y | Y | Y | Y | U |
| 1Individuals with age <20 years were excluded. Whether the prevalence is different among this population is unknown. | | | | | | | | | |

**Questions:**

1. Was the sample frame appropriate to address the target population?

2. Were study participants sampled in an appropriate way?

3. Was the sample size adequate?

4. Were the study subjects and the setting described in detail?

5. Was the data analysis conducted with sufficient coverage of the identified sample?

6. Were valid methods used for the identification of the condition?

7. Was the condition measured in a standard, reliable way for all participants?

8. Was there appropriate statistical analysis?

9. Was the response rate adequate, and if not, was the low response rate managed appropriately?

**Abbreviations**

Y: Yes

N: No

U: Unclear

NA: Not applicable

Prevalence Critical Appraisal Tool by:

Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and incidence data. Int J Evid Based Healthc 2015;13:147-153.

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| **File 5. The prevalence of NAFLD in different populations over time in recent years** | | | |
| **Populations** | **Pooled average prevalence (95%CI)** | | |
|  | <2001 | 2001-2010 | >2010 |
| NAFLD in overall subjets | 16.4(10.9-21.9) | 26.6(15.6-37.7) | 32.8(29.3-36.3) |
| Lean NAFLD in overall subjets | 2.8(1.6-4.0) | 4.2(3.1-5.4) | 4.8(4.1-5.6) |
| Overweight/obese NAFLD in overall subjets | 13.6(9.1-18.1) | 22.2(11.0-33.4) | 27.6(24.5-30.8) |
| Lean non-NAFLD in overall subjets | 46(38.2-53.9) | 47.3(35.4-59.1) | 38.8(33.8-43.7) |
| Overweight/obese non-NAFLD in overall subjets | 36.7(30.3-43.2) | 27.8(22.2-33.4) | 27.1(22-32.1) |
| NAFLD in lean subjets | 6.1(2.9-9.3) | 10.3(6.3-14.2) | 11.8(10.0-13.7) |
| NAFLD in overweight/obese subjets | 27.1(23.3-30.8) | 41.8(30.2-53.5) | 51.3(45.9-56.6) |

CI: confidential interval.

The study year is defined as the main time for which data were collected.

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| **File 6. Prevalence of lean NAFLD in each study country (*n* ≥2 studies).** | | | | | |
| **Country** | **Studies (n)** | **Prevalence (%)** | **95% CI** | **Heterogeneity *I*2-statistics** | ***P*-value** |
| USA | 5 | 3.1 | 2.3-3.8 | 93.4% | <0.001 |
| Netherlands | 2 | 3.5 | 3.1-3.8 | 0.0% | 0.815 |
| Japan | 5 | 3.8 | 3.2-9.1 | 83.2% | <0.001 |
| Iran | 2 | 4.3 | 1.2-7.5 | 88.8% | 0.003 |
| Korea | 4 | 5.0 | 4.4-5.6 | 89.3% | <0.001 |
| China | 7 | 5.5 | 2.5-8.5 | 99.3% | <0.001 |

CI: confidential interval.

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| **File 7. Subgroup analysis - global prevalence of lean NAFLD.** | | | | | | | |
| **Category** | **Subgroups** | **Studies**  **(n)** | **Total (n)** | **Cases (n)** | **Pooled estimate**  **(95% CI)** | **Heterogeneity *I*2 (%)** | **P-value** |
| Total |  |  | 205307 | 9357 | 0.041 (0.034-0.048) | 98.3 | <0.001 |
| Type of population | Population based | 16 | 75014 | 3701 | 0.043 (0.030-0.099) | 98.9 | <0.001 |
| Community based | 4 | 17140 | 694 | 0.030 (0.007-0.053) | 98.5 | <0.001 |
| Health examination | 11 | 109930 | 4854 | 0.044 (0.038-0.050) | 94.4 | <0.001 |
| Hospital based | 2 | 3223 | 108 | 0.020 (-0.01-0.051) | 96.6 | <0.001 |
| Mean age of population | <18 years old | 4 | 2788 | 39 | 0.023 (0.004-0.042) | 89.2 | <0.001 |
| 18-44 years old | 7 | 37294 | 1363 | 0.038 (0.032-0.043) | 86.4 | <0.001 |
| 45-59 years old | 10 | 74323 | 3209 | 0.044 (0.032-0.055) | 97.3 | <0.001 |
| >59 years old | 2 | 8491 | 293 | 0.035 (0.031-0.038) | 0.0 | 0.815 |

CI: confidential interval.

**File 8. References for included studies used to compare the prevalence of lean NAFLD between men and women**

1. Chen-Chung Fu M-CC, Yin-Ming Li,Tso-Tsai Liu,Li-Yu Wang,. The Risk Factors for Ultrasound-diagnosed Non-alcoholic Fatty Liver Disease Among Adolescents. *Ann Acad Med Singapore* 2009; **38**: 1.

2. Caserta CA, Pendino GM, Amante A, et al. Cardiovascular risk factors, nonalcoholic fatty liver disease, and carotid artery intima-media thickness in an adolescent population in southern Italy. *American journal of epidemiology* 2010; **171**: 1195-202.

3. Younossi ZM, Stepanova M, Negro F, et al. Nonalcoholic fatty liver disease in lean individuals in the United States. *Medicine* 2012; **91**: 319-27.

4. Feng R-N, Du S-S, Wang C, et al. Lean-non-alcoholic fatty liver disease increases risk for metabolic disorders in a normal weight Chinese population. *World journal of gastroenterology* 2014; **20**: 17932-40.

5. Nishioji K, Mochizuki N, Kobayashi M, et al. The Impact of PNPLA3 rs738409 Genetic Polymorphism and Weight Gain≥10 kg after Age 20 on Non-Alcoholic Fatty Liver Disease in Non-Obese Japanese Individuals. *PloS one* 2015; **10**: e0140427.

6. Nishioji K, Sumida Y, Kamaguchi M, et al. Prevalence of and risk factors for non-alcoholic fatty liver disease in a non-obese Japanese population, 2011-2012. *Journal of gastroenterology* 2015; **50**: 95-108.

7. Fukuda T, Hamaguchi M. The impact of non-alcoholic fatty liver disease on incident type 2 diabetes mellitus in non-overweight individuals. 2016; **36**: 275-83.

8. Honarvar B, Lankarani KB, Keshani P, Rafiee T. Dietary Determinants of Non-Alcoholic Fatty Liver Disease in Lean and Non-Lean Adult Patients: A Population-Based Study in Shiraz, Southern Iran. *Hepatitis monthly* 2017; **17**: e44962.

9. Yoshitaka H, Hamaguchi M, Kojima T, Fukuda T, Ohbora A, Fukui M. Nonoverweight nonalcoholic fatty liver disease and incident cardiovascular disease: A post hoc analysis of a cohort study. *Medicine* 2017; **96**: e6712.

10. Alam S, Fahim SM, Chowdhury MAB. Prevalence and risk factors of non-alcoholic fatty liver disease in Bangladesh. 2018; **2**: 39-46.

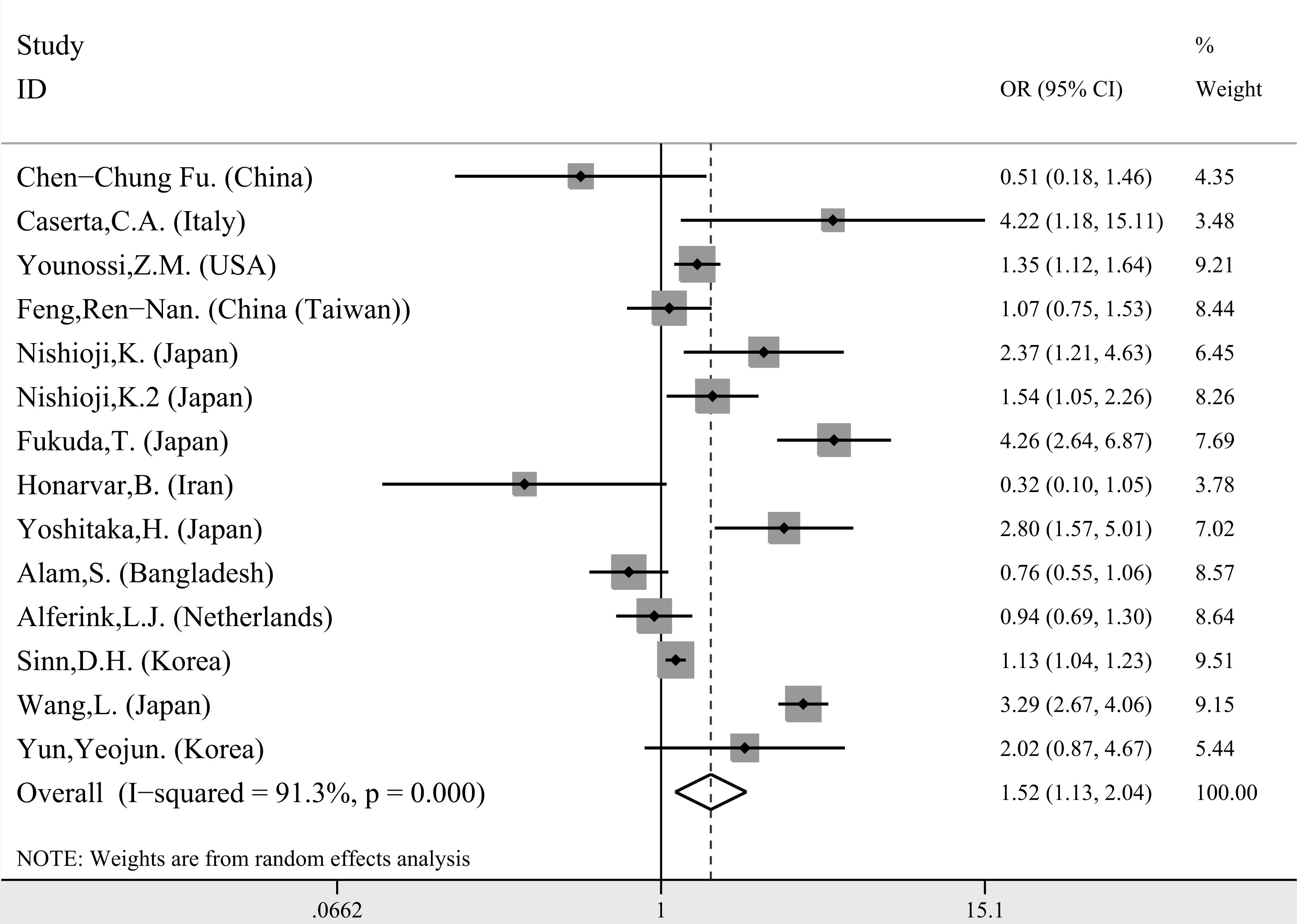
11. Alferink LJM, Trajanoska K, Erler NS, et al. Nonalcoholic Fatty Liver Disease in The Rotterdam Study: About Muscle Mass, Sarcopenia, Fat Mass, and Fat Distribution. *Journal Of Bone And Mineral Research* 2019; **34**: 1254-63.

12. Sinn DH, Kang D, Choi SJ, et al. Lean non-alcoholic fatty liver disease and development of diabetes: a cohort study. *European Journal Of Endocrinology* 2019; **181**: 185-92.

13. Wang L. Ultrasound-Diagnosed Nonalcoholic Fatty Liver Disease Independently Predicts a Higher Risk of Developing Diabetes Mellitus in Nonoverweight Individuals. *Academic radiology* 2019; **26**: 863-8.

14. Yun Y, Kim H-N, Lee E-j, et al. Fecal and blood microbiota profiles and presence of nonalcoholic fatty liver disease in obese versus lean subjects. *PloS one* 2019; **14**: e0213692.

**File 9. Meta-analysis of within-study comparisons of lean NAFLD prevalence in men vs. women**

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**File 10. References for included studies used to analyze the prevalence of lean NAFLD in Asia**

1. Fan JG, Zhu J, Li XJ, et al. Prevalence of and risk factors for fatty liver in a general population of Shanghai, China. Journal of hepatology 2005; 43: 508-14.

2. Hsiao PJ, Kuo KK, Shin SJ, et al. Significant correlations between severe fatty liver and risk factors for metabolic syndrome. Journal of gastroenterology and hepatology 2007; 22: 2118-23.

3. Chen-Chung Fu M-CC, Yin-Ming Li,Tso-Tsai Liu,Li-Yu Wang,. The Risk Factors for Ultrasound-diagnosed Non-alcoholic Fatty Liver Disease Among Adolescents. Ann Acad Med Singapore 2009; 38: 1.

4. Das K, Das K, Mukherjee PS, et al. Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease. Hepatology 2010; 51: 1593-602.

5. Sinn DH, Gwak GY, Park HN, et al. Ultrasonographically detected non-alcoholic fatty liver disease is an independent predictor for identifying patients with insulin resistance in non-obese, non-diabetic middle-aged Asian adults. The American journal of gastroenterology 2012; 107: 561-7.

6. Goh SC, Ho EL, Goh KL. Prevalence and risk factors of non-alcoholic fatty liver disease in a multiracial suburban Asian population in Malaysia. Hepatology international 2013; 7: 548-54.

7. Huang SC, Yang YJ. Serum retinol-binding protein 4 is independently associated with pediatric NAFLD and fasting triglyceride level. Journal of pediatric gastroenterology and nutrition 2013; 56: 145-50.

8. Feng R-N, Du S-S, Wang C, et al. Lean-non-alcoholic fatty liver disease increases risk for metabolic disorders in a normal weight Chinese population. World journal of gastroenterology 2014; 20: 17932-40.

9. Chan R, Wong VW, Chu WC, et al. Diet-Quality Scores and Prevalence of Nonalcoholic Fatty Liver Disease: A Population Study Using Proton-Magnetic Resonance Spectroscopy. PloS one 2015; 10: e0139310.

10. Du T, Yu X, Yuan G, Zhang J, Sun X. Combined influence of nonalcoholic fatty liver and body size phenotypes on diabetes risk. Cardiovascular diabetology 2015; 14: 144.

11. Nishioji K, Mochizuki N, Kobayashi M, et al. The Impact of PNPLA3 rs738409 Genetic Polymorphism and Weight Gain≥10 kg after Age 20 on Non-Alcoholic Fatty Liver Disease in Non-Obese Japanese Individuals. PloS one 2015; 10: e0140427.

12. Nishioji K, Sumida Y, Kamaguchi M, et al. Prevalence of and risk factors for non-alcoholic fatty liver disease in a non-obese Japanese population, 2011-2012. Journal of gastroenterology 2015; 50: 95-108.

13. Fukuda T, Hamaguchi M. The impact of non-alcoholic fatty liver disease on incident type 2 diabetes mellitus in non-overweight individuals. 2016; 36: 275-83.

14. Yang MH, Sung J, Gwak GY. The associations between apolipoprotein B, A1, and the B/A1 ratio and nonalcoholic fatty liver disease in both normal-weight and overweight Korean population. Journal of clinical lipidology 2016; 10: 289-98.

15. Honarvar B, Lankarani KB, Keshani P, Rafiee T. Dietary Determinants of Non-Alcoholic Fatty Liver Disease in Lean and Non-Lean Adult Patients: A Population-Based Study in Shiraz, Southern Iran. Hepatitis monthly 2017; 17: e44962.

16. Naderian M, Kolahdoozan S, Sharifi AS, et al. Assessment of Lean Patients with Non-alcoholic Fatty Liver Disease in a Middle Income Country; Prevalence and Its Association with Metabolic Disorders: A Cross-sectional Study. Archives of Iranian medicine 2017; 20: 211-7.

17. Yoshitaka H, Hamaguchi M, Kojima T, Fukuda T, Ohbora A, Fukui M. Nonoverweight nonalcoholic fatty liver disease and incident cardiovascular disease: A post hoc analysis of a cohort study. Medicine 2017; 96: e6712.

18. Alam S, Fahim SM, Chowdhury MAB. Prevalence and risk factors of non-alcoholic fatty liver disease in Bangladesh. 2018; 2: 39-46.

19. Niriella MA, Kasturiratne A, Pathmeswaran A, et al. Lean non-alcoholic fatty liver disease (lean NAFLD): characteristics, metabolic outcomes and risk factors from a 7-year prospective, community cohort study from Sri Lanka. Hepatology international 2019; 13: 314-22.

20. Sinn DH, Kang D, Choi SJ, et al. Lean non-alcoholic fatty liver disease and development of diabetes: a cohort study. European Journal Of Endocrinology 2019; 181: 185-92.

21. Wang L. Ultrasound-Diagnosed Nonalcoholic Fatty Liver Disease Independently Predicts a Higher Risk of Developing Diabetes Mellitus in Nonoverweight Individuals. Academic radiology 2019; 26: 863-8.

22. Yun Y, Kim H-N, Lee E-j, et al. Fecal and blood microbiota profiles and presence of nonalcoholic fatty liver disease in obese versus lean subjects. PloS one 2019; 14: e0213692.

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| **File 11. The prevalence of NAFLD in different populations over time in recent years in Asia** | | | |
| **Population** | **Pooled average prevalence (95%CI)** | | |
|  | <2001 | 2001-2010 | >2010 |
| Lean NAFLD in overall subjets | 3.5 (2.4-4.7) | 4.6 (3.2-5.9) | 5.4 (4.4-6.4) |
| NAFLD in lean subjets | 5.7 (3.4-8.0) | 11.2 (6.4-15.9) | 12.0 (9.6-14.4) |

CI: confidential interval.

The study year is defined as the main time for which data were collected.

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| **File 12. Subgroup analysis - prevalence of lean NAFLD in Asia** | | | | | | | |
| **Category** | **Subgroups** | **Studies**  **(n)** | **Total (n)** | **Cases (n)** | **Pooled estimate**  **(95% CI)** | **Heterogeneity *I*2 (%)** | **P-value** |
| Total |  | 22 | 205089 | 9356 | 0.048 (0.040-0.056) | 97.9 | <0.001 |
| Type of population | Population based | 8 | 25063 | 1981 | 0.057 (0.036-0.077) | 96.5 | <0.001 |
| Community based | 4 | 17140 | 694 | 0.030 (0.007-0.053) | 98.5 | <0.001 |
| Health examination | 10 | 109164 | 4832 | 0.045 (0.039-0.052) | 94.8 | <0.001 |
| Hospital based | - | - | - | - | - | - |
| Mean age of population | <18 years old | 2 | 435 | 19 | 0.042 (0.001-0.092) | 85.5 | <0.001 |
| 18-44 years old | 4 | 9800 | 387 | 0.039 (0.026-0.062) | 89.1 | <0.001 |
| 45-59 years old | 8 | 67377 | 3045 | 0.047 (0.034-0.060) | 97.9 | <0.001 |
| >59 years old | - | - | - | - | - | - |
| Sex of population | Male | 11 | 44087 | 2143 | 0.051 (0.043-0.058) | 83.6 | <0.001 |
|  | Female | 11 | 38734 | 1382 | 0.039 (0.027-0.050) | 96.5 | <0.001 |

CI: confidential interval.

**File 13. References for included studies used to compare the prevalence of lean NAFLD between men and women in Asia**

1. Chen-Chung Fu M-CC, Yin-Ming Li,Tso-Tsai Liu,Li-Yu Wang,. The Risk Factors for Ultrasound-diagnosed Non-alcoholic Fatty Liver Disease Among Adolescents. Ann Acad Med Singapore 2009; 38: 1.

2. Feng R-N, Du S-S, Wang C, et al. Lean-non-alcoholic fatty liver disease increases risk for metabolic disorders in a normal weight Chinese population. World journal of gastroenterology 2014; 20: 17932-40.

3. Nishioji K, Mochizuki N, Kobayashi M, et al. The Impact of PNPLA3 rs738409 Genetic Polymorphism and Weight Gain≥10 kg after Age 20 on Non-Alcoholic Fatty Liver Disease in Non-Obese Japanese Individuals. PloS one 2015; 10: e0140427.

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5. Fukuda T, Hamaguchi M. The impact of non-alcoholic fatty liver disease on incident type 2 diabetes mellitus in non-overweight individuals. 2016; 36: 275-83.

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11. Yun Y, Kim H-N, Lee E-j, et al. Fecal and blood microbiota profiles and presence of nonalcoholic fatty liver disease in obese versus lean subjects. PloS one 2019; 14: e0213692.

**File 14. References for included studies used to compare the characteristics between lean NAFLD and lean non-NAFLD subjects**

1. Radu C, Grigorescu M, Crisan D, Lupsor M, Constantin D, Dina L. Prevalence and associated risk factors of non-alcoholic fatty liver disease in hospitalized patients. J Gastrointestin Liver Dis. 2008 Sep;Sect. 255-60.

2. Younossi ZM, Stepanova M, Negro F, et al. Nonalcoholic fatty liver disease in lean individuals in the United States. *Medicine* 2012; **91**: 319-27.

3. Feng R-N, Du S-S, Wang C, et al. Lean-non-alcoholic fatty liver disease increases risk for metabolic disorders in a normal weight Chinese population. *World journal of gastroenterology* 2014; **20**: 17932-40.

4. Du T, Yu X, Yuan G, Zhang J, Sun X. Combined influence of nonalcoholic fatty liver and body size phenotypes on diabetes risk. *Cardiovascular diabetology* 2015; **14**: 144.

5. Nishioji K, Mochizuki N, Kobayashi M, et al. The Impact of PNPLA3 rs738409 Genetic Polymorphism and Weight Gain≥10 kg after Age 20 on Non-Alcoholic Fatty Liver Disease in Non-Obese Japanese Individuals. *PloS one* 2015; **10**: e0140427.

6. Fukuda T, Hamaguchi M. The impact of non-alcoholic fatty liver disease on incident type 2 diabetes mellitus in non-overweight individuals. 2016; **36**: 275-83.

7. Naderian M, Kolahdoozan S, Sharifi AS, et al. Assessment of Lean Patients with Non-alcoholic Fatty Liver Disease in a Middle Income Country; Prevalence and Its Association with Metabolic Disorders: A Cross-sectional Study. *Archives of Iranian medicine* 2017; **20**: 211-7.

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9. Alferink LJM, Trajanoska K, Erler NS, et al. Nonalcoholic Fatty Liver Disease in The Rotterdam Study: About Muscle Mass, Sarcopenia, Fat Mass, and Fat Distribution. *Journal Of Bone And Mineral Research* 2019; **34**: 1254-63.

10. Sinn DH, Kang D, Choi SJ, et al. Lean non-alcoholic fatty liver disease and development of diabetes: a cohort study. *European Journal Of Endocrinology* 2019; **181**: 185-92.

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12. Yun Y, Kim H-N, Lee E-j, et al. Fecal and blood microbiota profiles and presence of nonalcoholic fatty liver disease in obese versus lean subjects. *PloS one* 2019; **14**: e0213692.

**File 15. References for included studies used to compare the characteristics between lean NAFLD and overweight/obese NAFLD subjects**

1. Radu C, Grigorescu M, Crisan D, Lupsor M, Constantin D, Dina L. Prevalence and associated risk factors of non-alcoholic fatty liver disease in hospitalized patients. J Gastrointestin Liver Dis. 2008 Sep;Sect. 255-60.

2. Das K, Das K, Mukherjee PS, et al. Nonobese population in a developing country has a high prevalence of nonalcoholic fatty liver and significant liver disease. Hepatology 2010; 51: 1593-602.

3. Younossi ZM, Stepanova M, Negro F, et al. Nonalcoholic fatty liver disease in lean individuals in the United States. Medicine 2012; 91: 319-27.

4. Feng R-N, Du S-S, Wang C, et al. Lean-non-alcoholic fatty liver disease increases risk for metabolic disorders in a normal weight Chinese population. World journal of gastroenterology 2014; 20: 17932-40.

5. Du T, Yu X, Yuan G, Zhang J, Sun X. Combined influence of nonalcoholic fatty liver and body size phenotypes on diabetes risk. Cardiovascular diabetology 2015; 14: 144.

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11. Niriella MA, Kasturiratne A, Pathmeswaran A, et al. Lean non-alcoholic fatty liver disease (lean NAFLD): characteristics, metabolic outcomes and risk factors from a 7-year prospective, community cohort study from Sri Lanka. Hepatology international 2019; 13: 314-22.

12. Sinn DH, Kang D, Choi SJ, et al. Lean non-alcoholic fatty liver disease and development of diabetes: a cohort study. European Journal Of Endocrinology 2019; 181: 185-92.

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