

## SUPPORTING INFORMATION

### **Systematic review with meta-analysis: the effects of probiotics in non-alcoholic fatty liver disease**

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**Supplemental table 1: Checklist of items in reporting a systematic review or meta-analysis (PRISMA statement)**

| Section/topic                      | Item | Checklist item   | Reported on page   |
|------------------------------------|------|--|--------------------|
| <b>Title</b>                       |      |  |                    |
| Title                              | 1    | Identify the report as a systematic review, meta-analysis, or both   | 1                  |
| <b>Abstract</b>                    |      |  |                    |
| Structured summary                 | 2    | Provide a structured summary including, as applicable, background, objectives, data sources, study eligibility criteria, participants, interventions, study appraisal and synthesis methods, results, limitations, conclusions and implications of key findings, systematic review registration number | 1-2                |
| <b>Introduction</b>                |      |  |                    |
| Rationale                          | 3    | Describe the rationale for the review in the context of what is already known  | 2                  |
| Objectives                         | 4    | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS)  | 2                  |
| <b>Methods</b>                     |      |  |                    |
| Protocol and registration          | 5    | Indicate if a review protocol exists, if and where it can be accessed (such as web address), and, if available, provide registration information including registration number   | NA                 |
| Eligibility criteria               | 6    | Specify study characteristics (such as PICOS, length of follow-up) and report characteristics (such as years considered, language, publication status) used as criteria for eligibility, giving rationale  | 3                  |
| Information sources                | 7    | Describe all information sources (such as databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched  | 3                  |
| Search                             | 8    | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated   | Supplementary data |
| Study selection                    | 9    | State the process for selecting studies (that is, screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)  | 3                  |
| Data collection process            | 10   | Describe method of data extraction from reports (such as piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators  | 4                  |
| Data items                         | 11   | List and define all variables for which data were sought (such as PICOS, funding sources) and any assumptions and simplifications made   | 4                  |
| Risk of bias in individual studies | 12   | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis  | 4                  |
| Summary measures                   | 13   | State the principal summary measures (such as risk ratio, difference in means)   | 4-5                |
| Synthesis of results               | 14   | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (such as I <sup>2</sup> statistic) for each meta-analysis   | 4-5                |
| Risk of bias across studies        | 15   | Specify any assessment of risk of bias that may affect the cumulative evidence (such as publication bias, selective reporting within studies)  | 4-5                |
| Additional analyses                | 16   | Describe methods of additional analyses (such as sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified  | 4-5                |
| <b>Results</b>                     |      |  |                    |
| Study selection                    | 17   | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram   | 5-6, Fig 1         |
| Study characteristics              | 18   | For each study, present characteristics for which data were extracted (such as study size, PICOS, follow-up period) and provide the citations  | Table 1            |

|                               |    |   |                    |
|-------------------------------|----|---|--------------------|
| Risk of bias within studies   | 19 | Present data on risk of bias of each study and, if available, any outcome-level assessment (see item 12).   | Supplementary data |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present for each study (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot | Fig 3              |
| Synthesis of results          | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency  | 5-21               |
| Risk of bias across studies   | 22 | Present results of any assessment of risk of bias across studies (see item 15)  | Supplementary data |
| Additional analysis           | 23 | Give results of additional analyses, if done (such as sensitivity or subgroup analyses, meta-regression) (see item 16)  | 5-21               |
| <b>Discussion</b>             |    |   |                    |
| Summary of evidence           | 24 | Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (such as health care providers, users, and policy makers)                    | 22-25              |
| Limitations                   | 25 | Discuss limitations at study and outcome level (such as risk of bias), and at review level (such as incomplete retrieval of identified research, reporting bias)  | 25                 |
| Conclusions                   | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research  | 26                 |
| <b>Funding</b>                |    |   |                    |
| Funding                       | 27 | Describe sources of funding for the systematic review and other support (such as supply of data) and role of funders for the systematic review  | 26                 |

## SEARCH STRATEGY (till to 2019.5.6)

### *PubMed*

#### **Query:**

(((((((((probiotic\*[Title/Abstract]) OR prebiotic\*[Title/Abstract]) OR synbiocit\*[Title/Abstract]) OR bifidobacter\*[Title/Abstract]) OR Lactobacill\*[Title/Abstract]) OR flora[Title/Abstract])) OR "Probiotics"[Mesh])) AND (((((((((((Non alcoholic Fatty Liver Disease[Title/Abstract]) OR NAFLD[Title/Abstract]) OR Nonalcoholic Fatty Liver Disease[Title/Abstract]) OR Fatty Liver, Nonalcoholic[Title/Abstract]) OR Fatty Livers, Nonalcoholic[Title/Abstract]) OR Liver, Nonalcoholic Fatty[Title/Abstract]) OR Livers, Nonalcoholic Fatty[Title/Abstract]) OR Nonalcoholic Fatty Liver[Title/Abstract]) OR Nonalcoholic Fatty Livers[Title/Abstract]) OR Nonalcoholic Steatohepatitis[Title/Abstract]) OR Nonalcoholic Steatohepatitides[Title/Abstract]) OR Steatohepatitides, Nonalcoholic[Title/Abstract]) OR Steatohepatitis, Nonalcoholic[Title/Abstract]) OR NASH[Title/Abstract] OR "Non-alcoholic Fatty Liver Disease"[Mesh])

**Result: 358**

### *Embase*

#### **Query:**

('nonalcoholic fatty liver'/exp OR 'non alcoholic fatty liver disease':ab,ti OR 'nafld':ab,ti OR 'nonalcoholic fatty liver disease':ab,ti OR 'fatty liver, nonalcoholic':ab,ti OR 'fatty livers, nonalcoholic':ab,ti OR 'liver, nonalcoholic fatty':ab,ti OR 'livers, nonalcoholic fatty':ab,ti OR 'nonalcoholic fatty liver':ab,ti OR 'nonalcoholic fatty livers':ab,ti OR 'nonalcoholic steatohepatitis':ab,ti OR 'nonalcoholic steatohepatitides':ab,ti OR 'steatohepatitides, nonalcoholic':ab,ti OR 'steatohepatitis, nonalcoholic':ab,ti OR 'nash':ab,ti) AND ('probiotic agent'/exp OR 'probiotic\*':ab,ti OR 'prebiotic\*':ab,ti OR 'synbiocit\*':ab,ti OR 'bifidobacter\*':ab,ti OR 'lactobacill\*':ab,ti OR 'flora':ab,ti)

**Result: 842**

**Query:**

D Search Hits

#1 MeSH descriptor: [Non-alcoholic Fatty Liver Disease] explode all trees 659

#2 Non alcoholic Fatty Liver Disease 1560

#3 NAFLD 1418

#4 Nonalcoholic Fatty Liver Disease 2014

#5 Fatty Liver, Nonalcoholic 2225

#6 Fatty Livers, Nonalcoholic 16

#7 Liver, Nonalcoholic Fatty 2225

#8 Livers, Nonalcoholic Fatty 16

#9 Nonalcoholic Fatty Liver 2225

#10 Nonalcoholic Fatty Livers16

#11 Nonalcoholic Steatohepatitis 892

#12 Nonalcoholic Steatohepatitides 0

#13 Steatohepatitides, Nonalcoholic 0

#14 Steatohepatitis, Nonalcoholic 892

#15 NASH 1545

#16 MeSH descriptor: [Probiotics] explode all trees 1776

#17 probiotic\* 5727

#18 prebiotic\* 1312

#19 synbiocit\* 0

#20 bifidobacter\* 2469

#21 Lactobacill\* 4461

#22 flora 3838

#23 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 3248

#24 #16 or #17 or #18 or #19 or #20 or #21 or #22 10806

#25 #23 and #24 128

**Result: 128**



## SUPPLEMENTARY FIGURES

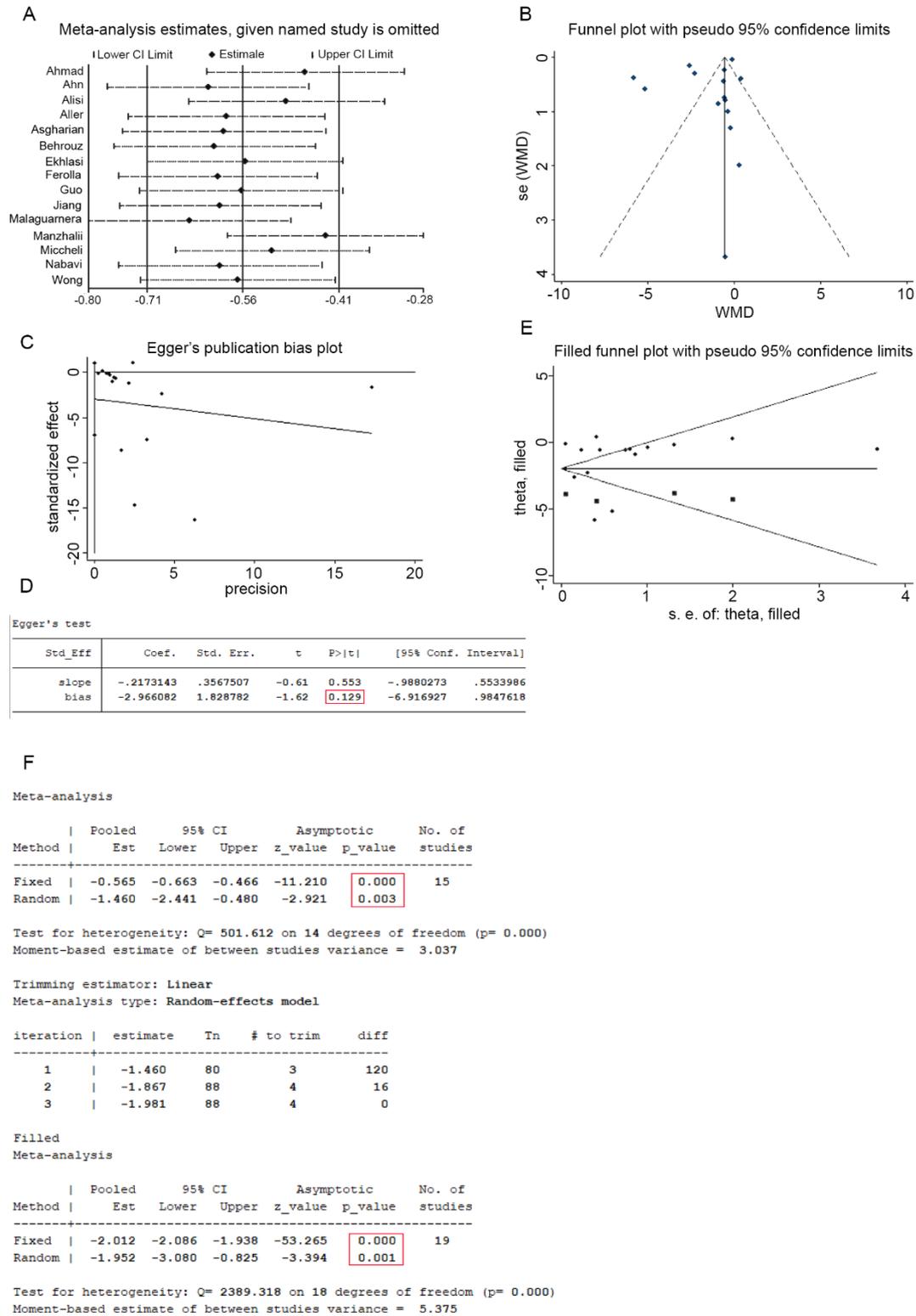


Figure S1: Supplementary data of body mass index (BMI), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).

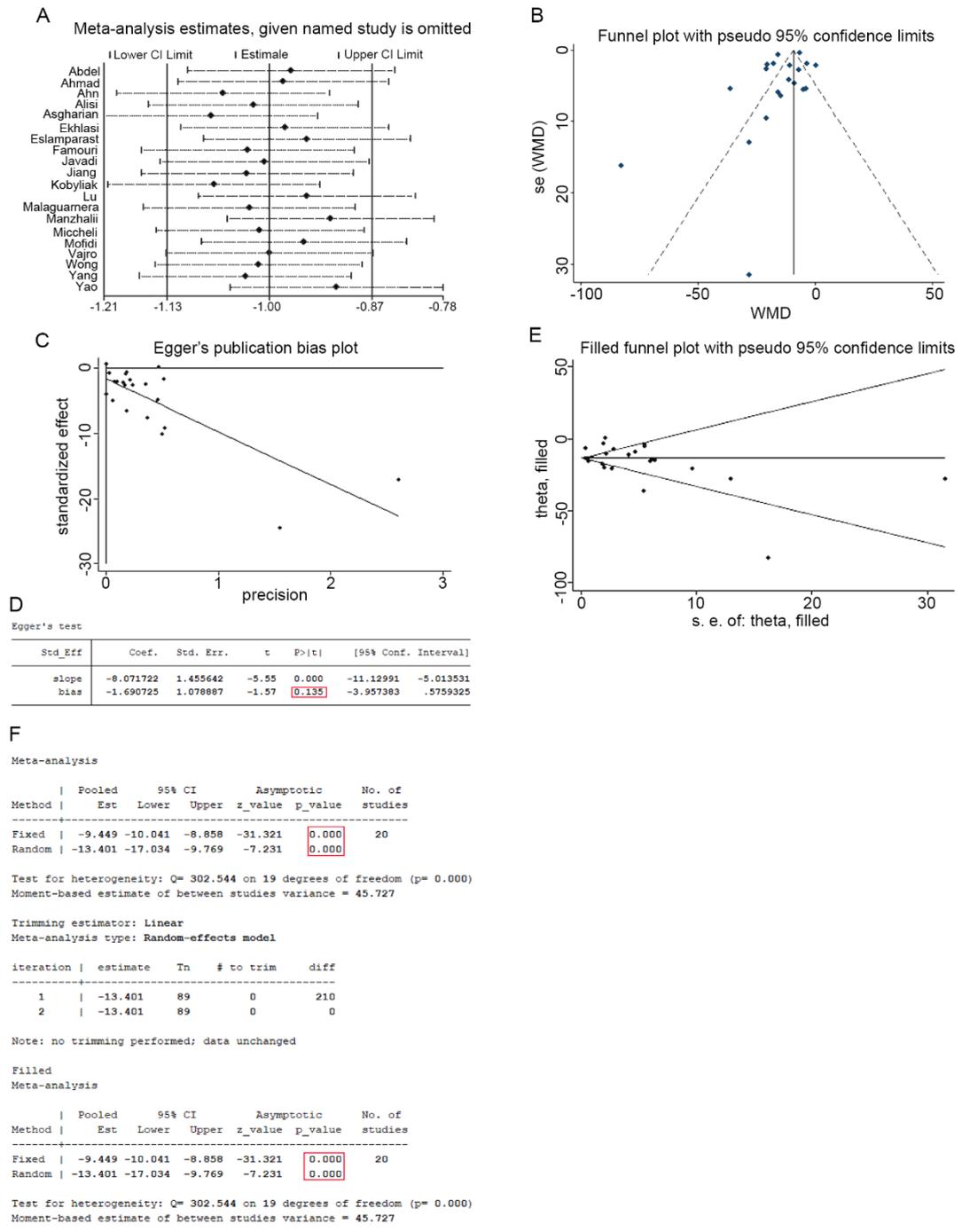
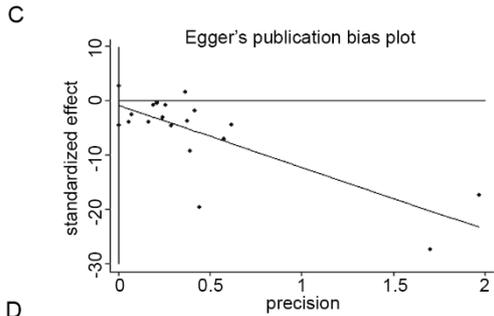
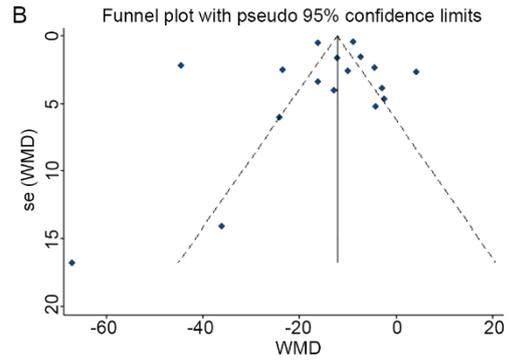
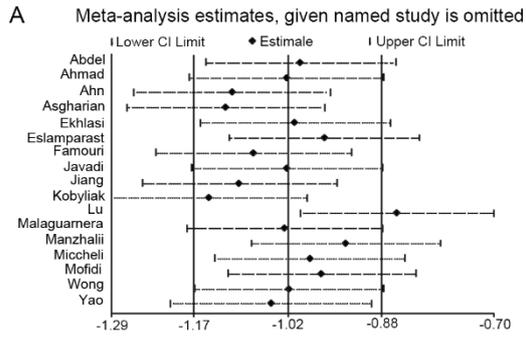


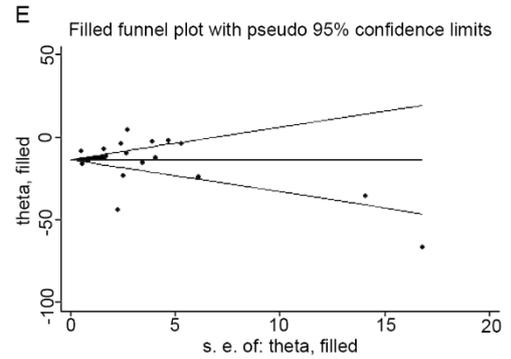
Figure S2: Supplementary data of alanine aminotransferase (ALT), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).



**D**

Egger's test

| Std_Eff | Coef.     | Std. Err. | t     | P> t  | [95% Conf. Interval] |
|---------|-----------|-----------|-------|-------|----------------------|
| slope   | -11.40297 | 2.405359  | -4.74 | 0.000 | -16.52987 -6.276069  |
| bias    | -0.819056 | 1.712781  | -0.48 | 0.639 | -4.469761 2.831649   |



**F**

Meta-analysis

| Method | Pooled Est | 95% CI Lower | 95% CI Upper | Asymptotic z_value | p_value | No. of studies |
|--------|------------|--------------|--------------|--------------------|---------|----------------|
| Fixed  | -12.196    | -12.864      | -11.529      | -35.807            | 0.000   | 17             |
| Random | -13.539    | -17.862      | -9.217       | -6.139             | 0.000   |                |

Test for heterogeneity: Q= 398.324 on 16 degrees of freedom (p= 0.000)  
Moment-based estimate of between studies variance = 65.353

Trimming estimator: Linear  
Meta-analysis type: Random-effects model

| iteration | estimate | In | # to trim | diff |
|-----------|----------|----|-----------|------|
| 1         | -13.539  | 77 | 0         | 153  |
| 2         | -13.539  | 77 | 0         | 0    |

Note: no trimming performed; data unchanged

Filled  
Meta-analysis

| Method | Pooled Est | 95% CI Lower | 95% CI Upper | Asymptotic z_value | p_value | No. of studies |
|--------|------------|--------------|--------------|--------------------|---------|----------------|
| Fixed  | -12.196    | -12.864      | -11.529      | -35.807            | 0.000   | 17             |
| Random | -13.539    | -17.862      | -9.217       | -6.139             | 0.000   |                |

Test for heterogeneity: Q= 398.324 on 16 degrees of freedom (p= 0.000)  
Moment-based estimate of between studies variance = 65.353

Figure S3: Supplementary data of aspartate transaminase (AST), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).

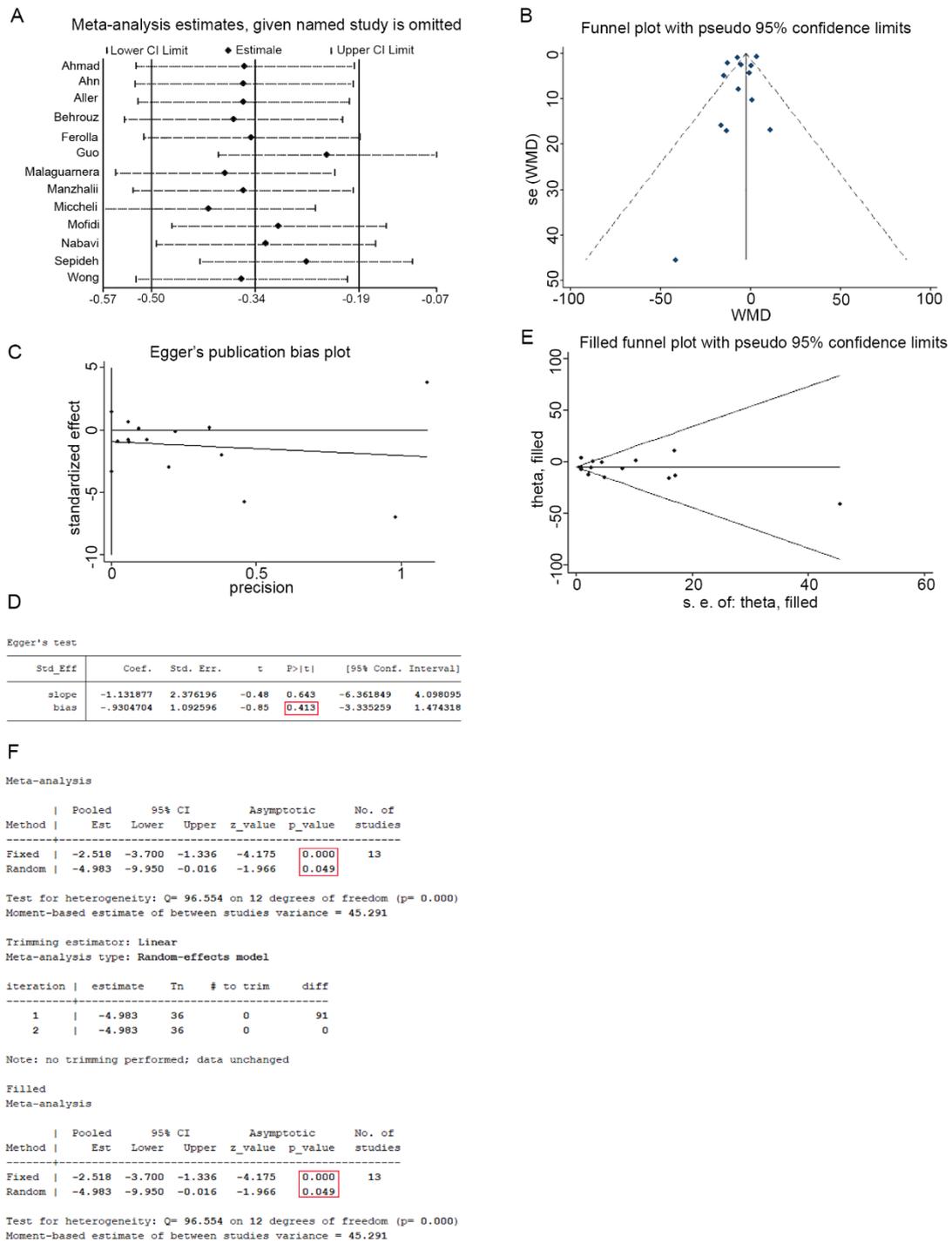


Figure S4: Supplementary data of fasting blood sugar (FBS), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).

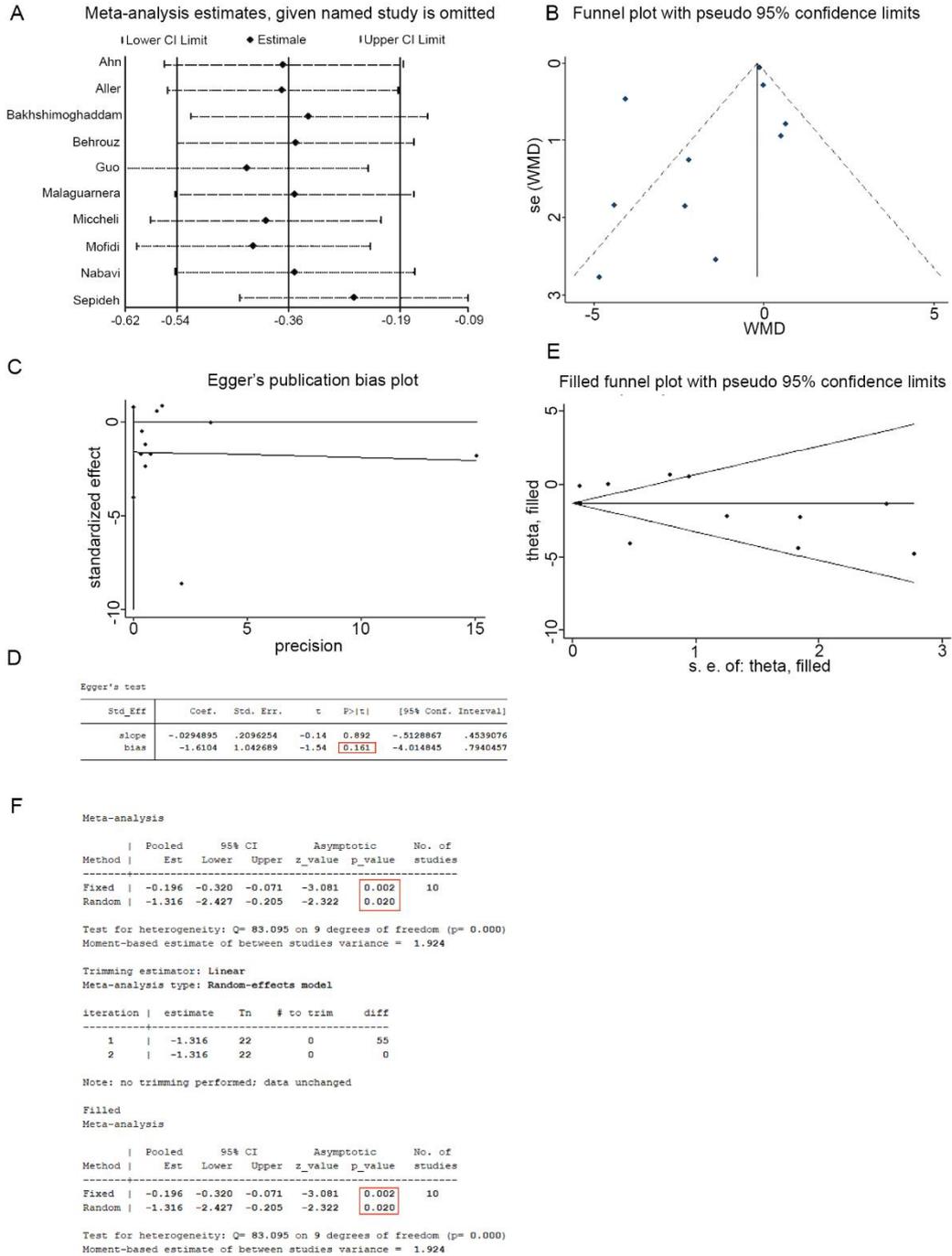


Figure S5: Supplementary data of insulin, showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).

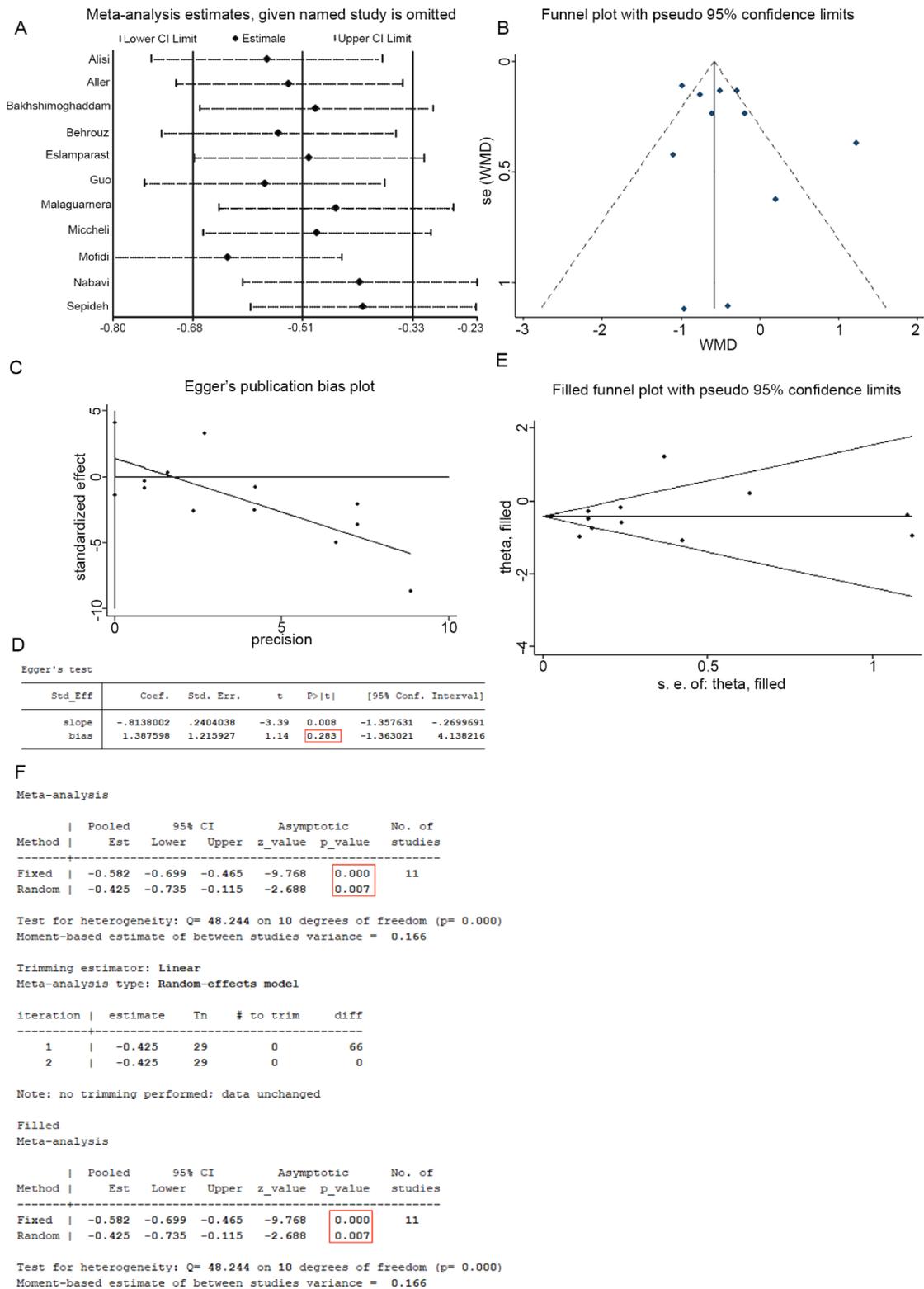


Figure S6: Supplementary data of homeostasis model assessment- insulin resistance (HOMA-IR), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).

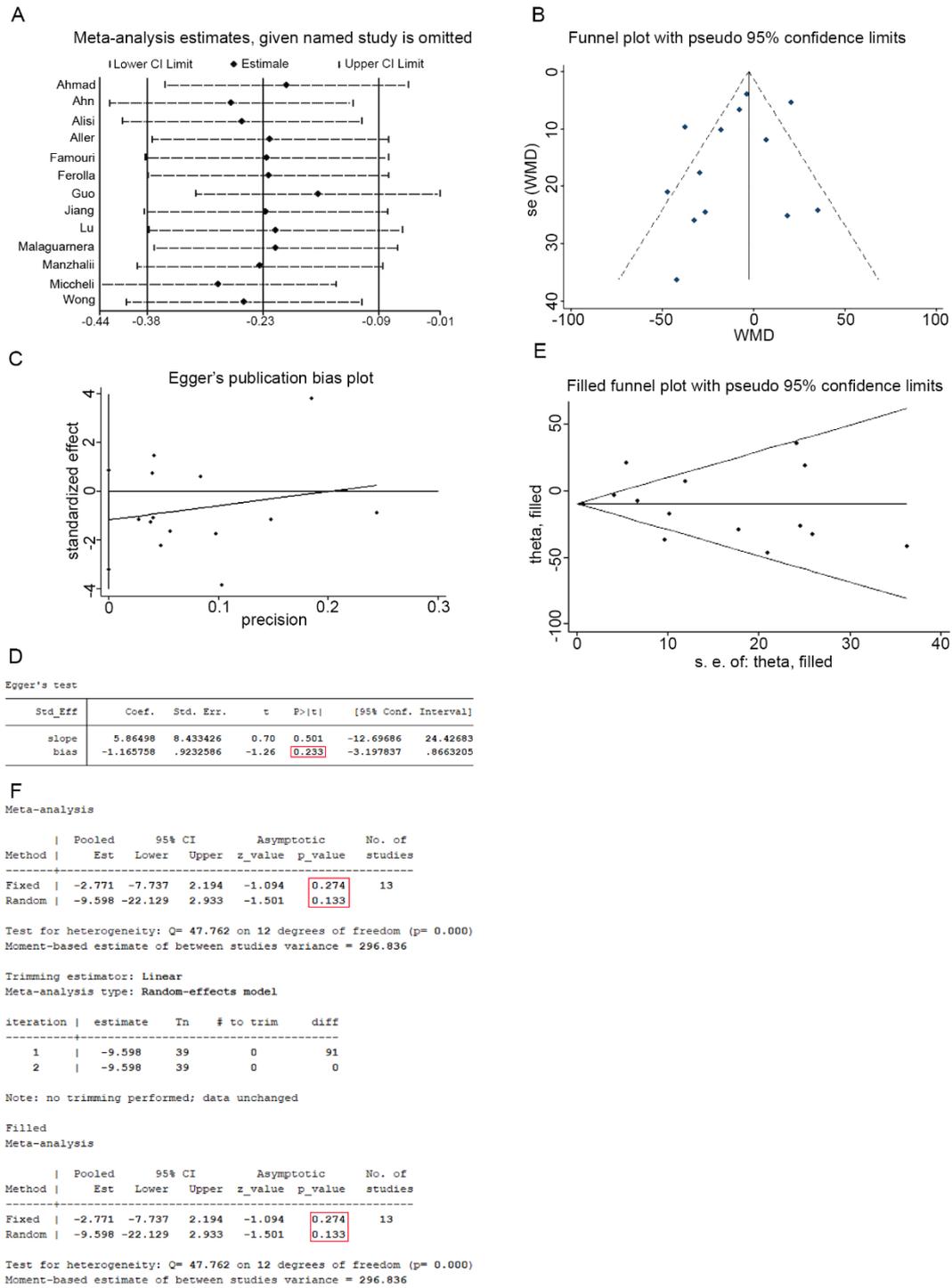
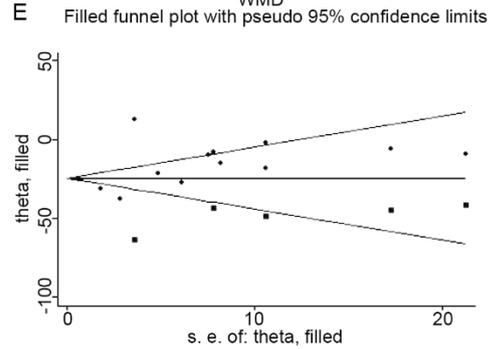
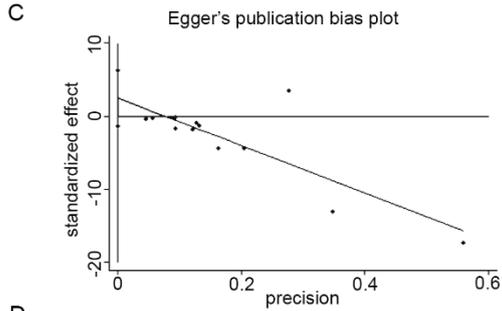
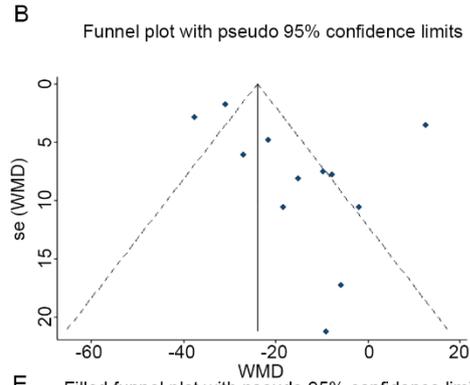
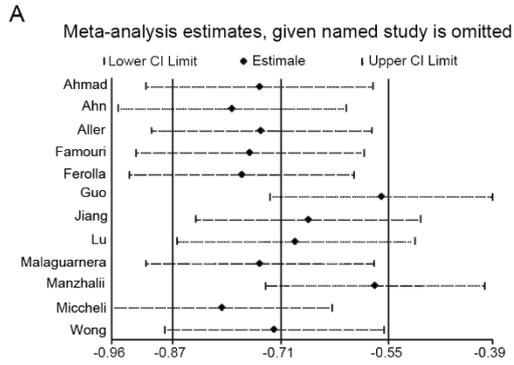


Figure S7: Supplementary data of triglycerides (TG), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).



**D**

Egger's test

| Std_Eff | Coef.     | Std. Err. | t     | P> t  | [95% Conf. Interval] |
|---------|-----------|-----------|-------|-------|----------------------|
| slope   | -32.52605 | 7.330475  | -4.44 | 0.001 | -48.85937 -16.19273  |
| bias    | 2.494808  | 1.708969  | 1.46  | 0.175 | -1.313014 6.302629   |

**F**

Meta-analysis

| Method | Pooled Est | 95% CI Lower | 95% CI Upper | Asymptotic z_value | Asymptotic p_value | No. of studies |
|--------|------------|--------------|--------------|--------------------|--------------------|----------------|
| Fixed  | -23.999    | -26.426      | -21.572      | -19.382            | 0.000              | 12             |
| Random | -15.375    | -26.501      | -4.250       | -2.709             | 0.007              |                |

Test for heterogeneity:  $Q = 155.233$  on 11 degrees of freedom ( $p = 0.000$ )  
Moment-based estimate of between studies variance = 310.327

Trimming estimator: Linear  
Meta-analysis type: Random-effects model

| iteration | estimate | Tn | # to trim | diff |
|-----------|----------|----|-----------|------|
| 1         | -15.375  | 42 | 1         | 78   |
| 2         | -20.694  | 58 | 3         | 32   |
| 3         | -22.965  | 63 | 4         | 10   |
| 4         | -25.120  | 68 | 5         | 10   |
| 5         | -25.469  | 68 | 5         | 0    |

Filled  
Meta-analysis

| Method | Pooled Est | 95% CI Lower | 95% CI Upper | Asymptotic z_value | Asymptotic p_value | No. of studies |
|--------|------------|--------------|--------------|--------------------|--------------------|----------------|
| Fixed  | -28.834    | -31.082      | -26.585      | -25.132            | 0.000              | 17             |
| Random | -24.490    | -35.438      | -13.542      | -4.384             | 0.000              |                |

Test for heterogeneity:  $Q = 270.640$  on 16 degrees of freedom ( $p = 0.000$ )  
Moment-based estimate of between studies variance = 431.164

Figure S8: Supplementary data of total cholesterol (TC), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).

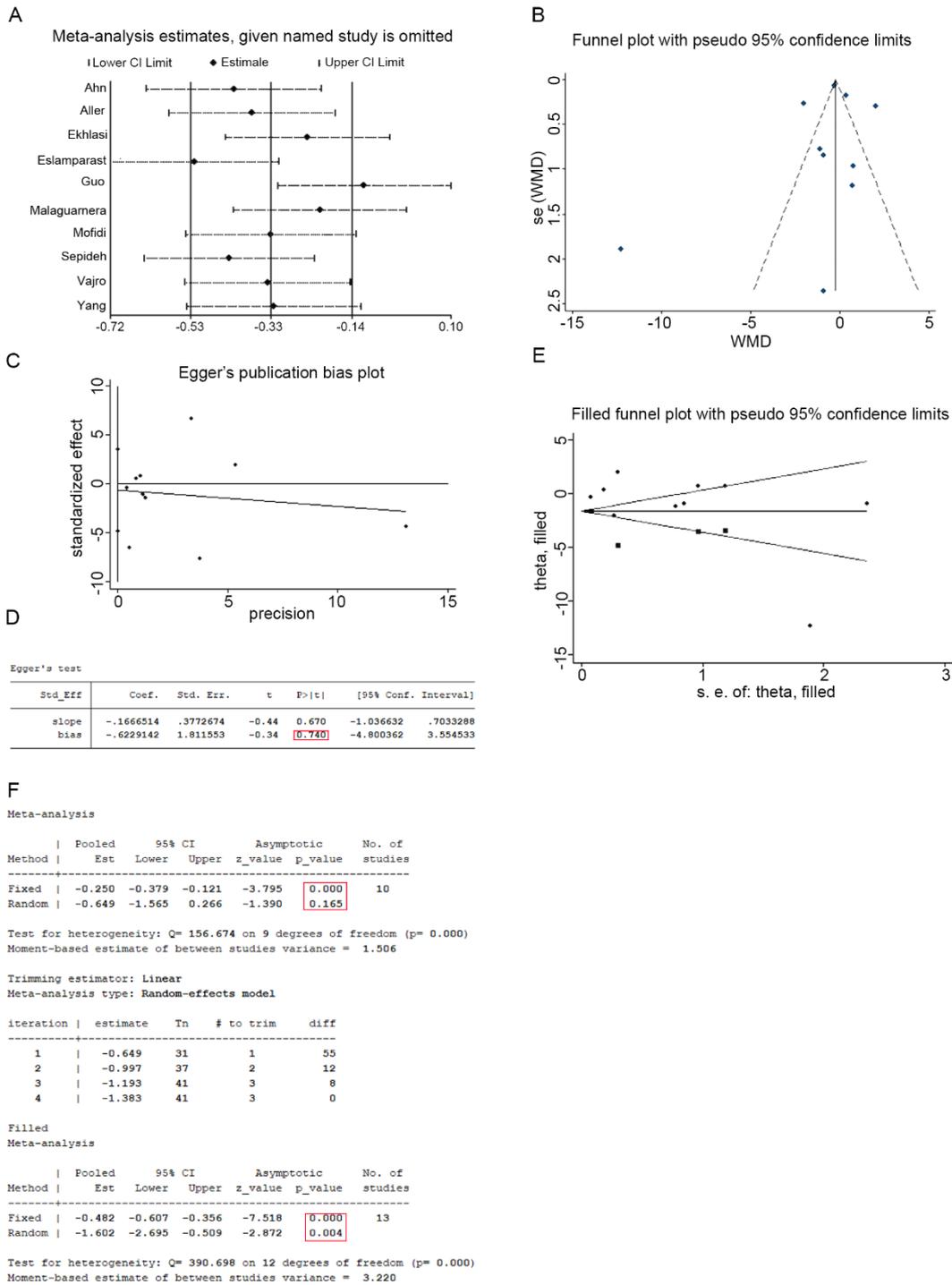


Figure S9: Supplementary data of tumor necrosis factor – alpha (*Tnf- $\alpha$* ), showing the interpretation of single study (A), funnel plot (B), Egger's tests (C, D), trim-and-fill computation (E, F).

Supplemental table 2: Evidence quality assessment

**Question:** Should probiotics be used for NAFLD?

**Item:** BMI

| Quality assessment                            |                   |                      |                      |                         |                        |                                 | No of patients |         | Effect            |                                    | Quality          | Importance |
|---|-------------------|----------------------|----------------------|-------------------------|------------------------|---------------------------------|----------------|---------|-------------------|------------------------------------|------------------|------------|
| No of studies                                 | Design            | Risk of bias         | Inconsistency        | Indirectness            | Imprecision            | Other considerations            | Probiotics     | Control | Relative (95% CI) | Absolute                           |                  |            |
| <b>BMI (Better indicated by lower values)</b> |                   |                      |                      |                         |                        |                                 |                |         |                   |                                    |                  |            |
| 15  | randomised trials | serious <sup>1</sup> | serious <sup>2</sup> | no serious indirectness | no serious imprecision | strong association <sup>3</sup> | 410            | 408     | -                 | MD 0.56 lower (0.66 to 0.47 lower) | ⊕⊕⊕⊕<br>MODERATE | IMPORTANT  |

<sup>1</sup> Studies included possess several bias

<sup>2</sup> Studies included reported inconsistency results

<sup>3</sup> Studies included are more than 10

**Item:** Liver function

| Quality assessment                            |                   |                      |                          |                         |                        |                                      | No of patients |         | Effect            |                                     | Quality          | Importance |
|---|-------------------|----------------------|--------------------------|-------------------------|------------------------|--------------------------------------|----------------|---------|-------------------|-------------------------------------|------------------|------------|
| No of studies                                 | Design            | Risk of bias         | Inconsistency            | Indirectness            | Imprecision            | Other considerations                 | Probiotics     | Control | Relative (95% CI) | Absolute                            |                  |            |
| <b>ALT (Better indicated by lower values)</b> |                   |                      |                          |                         |                        |                                      |                |         |                   |                                     |                  |            |
| 20  | randomised trials | serious <sup>1</sup> | no serious inconsistency | no serious indirectness | no serious imprecision | very strong association <sup>2</sup> | 561            | 555     | -                 | MD 13.4 lower (17.03 to 9.77 lower) | ⊕⊕⊕⊕<br>HIGH     | CRITICAL   |
| <b>AST (Better indicated by lower values)</b> |                   |                      |                          |                         |                        |                                      |                |         |                   |                                     |                  |            |
| 17  | randomised trials | serious <sup>1</sup> | serious <sup>3</sup>     | no serious indirectness | no serious imprecision | strong association <sup>4</sup>      | 499            | 493     | -                 | MD 12.2 lower (12.86                | ⊕⊕⊕⊕<br>MODERATE | CRITICAL   |

|   |                       |                          |                                 |                                   |                                  |      |     |     |   |   |             |              |
|---|-----------------------|--------------------------|---------------------------------|-----------------------------------|----------------------------------|------|-----|-----|---|---|-------------|--------------|
|   |                       |                          |                                 |                                   |                                  |      |     |     |   | to<br>11.53<br>lower)                             |             |              |
| <b>GGT (Better indicated by lower values)</b>               |                       |                          |                                 |                                   |                                  |      |     |     |   |   |             |              |
| 7   | randomi<br>sed trials | serio<br>us <sup>5</sup> | serious <sup>3</sup>            | no<br>serious<br>indirectne<br>ss | no<br>serious<br>imprecisi<br>on | none | 248 | 240 | - | MD<br>6.44<br>lower<br>(7.46<br>to 5.41<br>lower) | ⊕⊕○○<br>LOW | CRITICA<br>L |
| <b>LSM (Better indicated by lower values)</b>               |                       |                          |                                 |                                   |                                  |      |     |     |   |   |             |              |
| 4   | randomi<br>sed trials | serio<br>us <sup>5</sup> | no serious<br>inconsisten<br>cy | no serious<br>indirectne<br>ss    | Serious <sup>5</sup>             | none | 99  | 103 | - | MD<br>0.65<br>lower<br>(0.76<br>to 0.55<br>lower) | ⊕⊕○○<br>LOW | CRITICA<br>L |
| <b>Hepatic steatosis (Better indicated by lower values)</b> |                       |                          |                                 |                                   |                                  |      |     |     |   |   |             |              |
| 4   | randomi<br>sed trials | serio<br>us <sup>5</sup> | no serious<br>inconsisten<br>cy | no serious<br>indirectne<br>ss    | Serious <sup>5</sup>             | none | 131 | 128 | - | not<br>pooled                                     | ⊕⊕○○<br>LOW | CRITICA<br>L |

<sup>1</sup> Studies included possess several bias

<sup>2</sup> Studies included are more than 20

<sup>3</sup> Studies included reported inconsistency results

<sup>4</sup> Studies included are more than 10

<sup>5</sup> Studies included are less than 5

### Item: Glycemic indices

| Quality assessment                            |                       |                          |                      |                                   |                                  |                                    | No of patients |         | Effect            |  | Quality              | Importance    |
|---|-----------------------|--------------------------|----------------------|-----------------------------------|----------------------------------|------------------------------------|----------------|---------|-------------------|--|----------------------|---------------|
| No of studies                                 | Design                | Risk of bias             | Inconsistency        | Indirectness                      | Imprecision                      | Other considerations               | Probiotics     | Control | Relative (95% CI) | Absolute   |                      |               |
| <b>FBS (Better indicated by lower values)</b> |                       |                          |                      |                                   |                                  |                                    |                |         |                   |  |                      |               |
| 13  | randomi<br>sed trials | serio<br>us <sup>1</sup> | serious <sup>2</sup> | no<br>serious<br>indirectne<br>ss | no<br>serious<br>imprecisi<br>on | strong<br>association <sup>3</sup> | 346            | 347     | -                 | MD<br>2.52<br>lower<br>(3.7 to<br>1.34<br>lower) | ⊕⊕⊕○<br>MODER<br>ATE | IMPORT<br>ANT |

| Insulin (Better indicated by lower values) |                   |                      |                          |                         |                        |                                 |     |     |   |                                     |                  |           |
|--|-------------------|----------------------|--------------------------|-------------------------|------------------------|---------------------------------|-----|-----|---|-------------------------------------|------------------|-----------|
| 10   | randomised trials | serious <sup>1</sup> | no serious inconsistency | no serious indirectness | no serious imprecision | strong association <sup>3</sup> | 271 | 273 | - | MD 0.2 lower (0.32 to 0.07 lower)   | ⊕⊕⊕⊕<br>HIGH     |           |
| GLP-1 (Better indicated by lower values)   |                   |                      |                          |                         |                        |                                 |     |     |   |                                     |                  |           |
| 2  | randomised trials | serious <sup>1</sup> | no serious inconsistency | no serious indirectness | serious <sup>4</sup>   | none                            | 37  | 38  | - | MD 1.37 higher (1.24 to 1.5 higher) | ⊕⊕○○<br>LOW      | IMPORTANT |
| HOMA-IR (Better indicated by lower values) |                   |                      |                          |                         |                        |                                 |     |     |   |                                     |                  |           |
| 12   | randomised trials | serious <sup>1</sup> | serious <sup>2</sup>     | no serious indirectness | no serious imprecision | strong association <sup>3</sup> | 317 | 317 | - | MD 0.58 lower (0.7 to 0.47 lower)   | ⊕⊕⊕○<br>MODERATE | IMPORTANT |

<sup>1</sup> Studies included possess several bias

<sup>2</sup> Studies included reported inconsistency results

<sup>3</sup> Studies included are more than 10

<sup>4</sup> Studies included are less than 5

### Item: Lipid profiles

| Quality assessment                       |                   |                      |                      |                         |                        |                      | No of patients |         | Effect            |  | Quality     | Importance |
|--|-------------------|----------------------|----------------------|-------------------------|------------------------|----------------------|----------------|---------|-------------------|--|-------------|------------|
| No of studies                            | Design            | Risk of bias         | Inconsistency        | Indirectness            | Imprecision            | Other considerations | Probiotics     | Control | Relative (95% CI) | Absolute                                   |             |            |
| HDL-C (Better indicated by lower values) |                   |                      |                      |                         |                        |                      |                |         |                   |  |             |            |
| 9  | randomised trials | serious <sup>1</sup> | serious <sup>2</sup> | no serious indirectness | no serious imprecision | none                 | 243            | 240     | -                 | MD 1.36 higher (0.01 lower to 2.73 higher) | ⊕⊕○○<br>LOW | IMPORTANT  |
| LDL-C (Better indicated by lower values) |                   |                      |                      |                         |                        |                      |                |         |                   |  |             |            |

|  |                   |                      |                      |                         |                        |                                 |     |     |   |  |                  |           |
|--|-------------------|----------------------|----------------------|-------------------------|------------------------|---------------------------------|-----|-----|---|--|------------------|-----------|
| 8  | randomised trials | serious <sup>1</sup> | serious <sup>2</sup> | no serious indirectness | no serious imprecision | none                            | 212 | 208 | - | MD 0.31 higher (3.52 lower to 4.15 higher) | ⊕⊕○○<br>LOW      | IMPORTANT |
| <b>Triglyceride (Better indicated by lower values)</b> |                   |                      |                      |                         |                        |                                 |     |     |   |  |                  |           |
| 13   | randomised trials | serious <sup>1</sup> | serious <sup>2</sup> | no serious indirectness | no serious imprecision | strong association <sup>3</sup> | 383 | 383 | - | MD 2.77 lower (7.74 lower to 2.19 higher)  | ⊕⊕⊕○<br>MODERATE | IMPORTANT |
| <b>Cholesterol (Better indicated by lower values)</b>  |                   |                      |                      |                         |                        |                                 |     |     |   |  |                  |           |
| 12   | randomised trials | serious <sup>1</sup> | serious <sup>2</sup> | no serious indirectness | no serious imprecision | strong association <sup>3</sup> | 361 | 361 | - | MD 24 lower (26.43 to 21.57 lower)         | ⊕⊕⊕○<br>MODERATE | IMPORTANT |

<sup>1</sup> Studies included possess several bias

<sup>2</sup> Studies included reported inconsistency results

<sup>3</sup> Studies included are more than 10

### Item: Inflammation factors

| Quality assessment                              |                   |                      |                      |                         |                        |  | No of patients |         | Effect            |  | Quality    | Importance |
|---|-------------------|----------------------|----------------------|-------------------------|------------------------|--|----------------|---------|-------------------|--|------------|------------|
| No of studies                                   | Design            | Risk of bias         | Inconsistency        | Indirectness            | Imprecision            | Other considerations                           | Probiotics     | Control | Relative (95% CI) | Absolute                                 |            |            |
| <b>TNF-a (Better indicated by lower values)</b> |                   |                      |                      |                         |                        |  |                |         |                   |  |            |            |
| 10  | randomised trials | serious <sup>1</sup> | serious <sup>2</sup> | no serious indirectness | no serious imprecision | reporting bias strong association <sup>4</sup> | 239            | 240     | -                 | MD 0.25 lower (0.38 lower to 0.12 lower) | ⊕⊕○<br>LOW | IMPORTANT  |
| <b>IL-6 (Better indicated by lower values)</b>  |                   |                      |                      |                         |                        |  |                |         |                   |  |            |            |
| 4   | randomised trials | serious <sup>1</sup> | serious <sup>2</sup> | no serious indirectness | Serious <sup>4</sup>   | none   | 95             | 100     | -                 | MD                                       | ⊕○○        | IMPORTANT  |

|   |                   |                      |                          |                         |                      |      |     |     |   |   |                      |               |
|---|-------------------|----------------------|--------------------------|-------------------------|----------------------|------|-----|-----|---|---|----------------------|---------------|
|   | sed trials        | s <sup>1</sup>       |                          | indirectness            |                      |      |     |     |   | 0.08<br>lower<br>(0.37<br>lower<br>to 0.21<br>higher) | O<br>VER<br>Y<br>LOW | NT            |
| <b>CRP (Better indicated by lower values)</b> |                   |                      |                          |                         |                      |      |     |     |   |   |                      |               |
| 4   | randomized trials | serious <sup>1</sup> | no serious inconsistency | no serious indirectness | Serious <sup>4</sup> | none | 117 | 111 | - | MD<br>1.27<br>lower<br>(2.1 to<br>0.44<br>lower)      | ⊕⊕O<br>O<br>LOW      | IMPORTA<br>NT |

<sup>1</sup> Studies included possess several bias

<sup>2</sup> Studies included reported inconsistency results

<sup>3</sup> Studies included are more than 10

<sup>4</sup> Studies included are less than 5

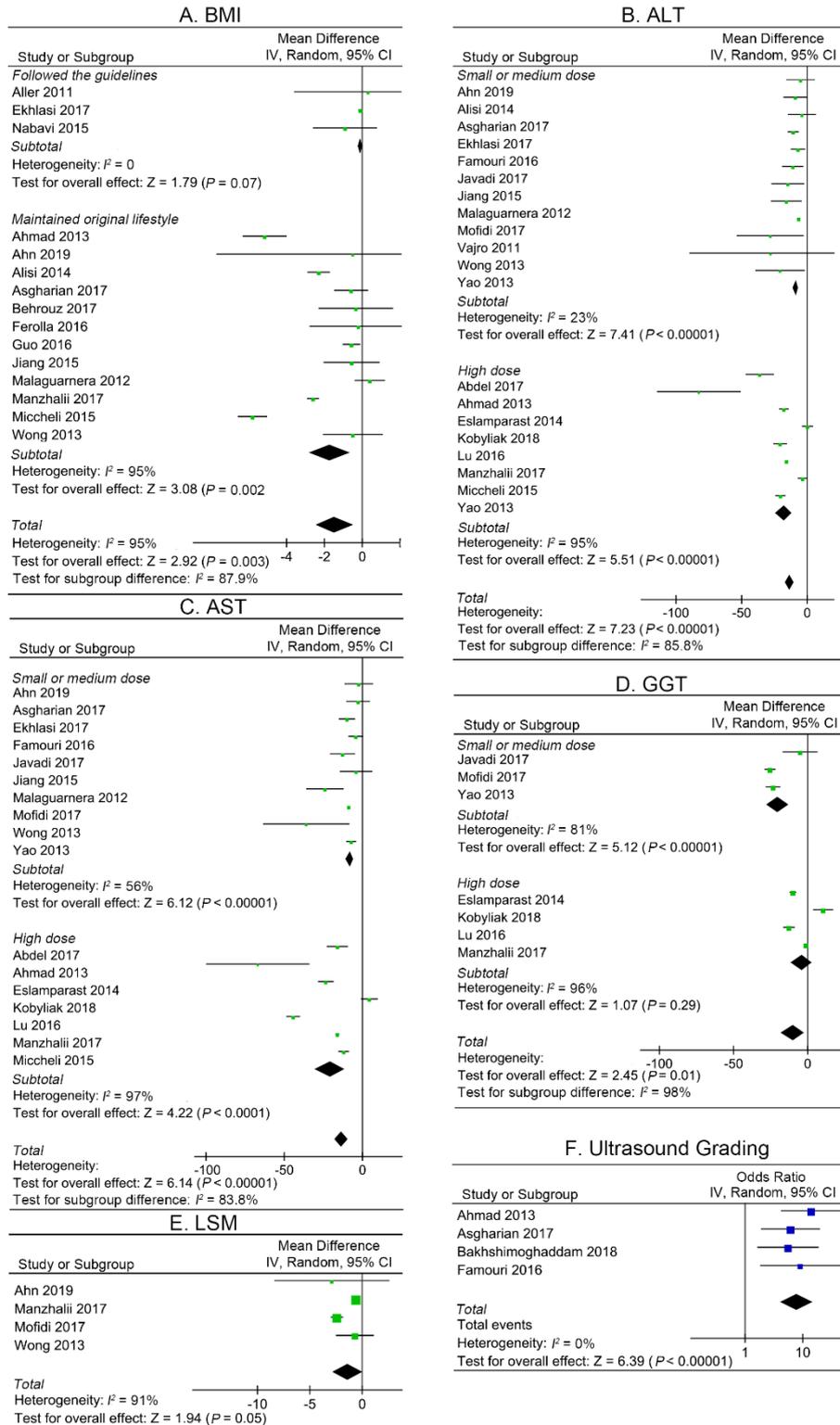


Figure S10: Forest plots of comparison for the effects of probiotics in NAFLD patients, showing (A) body mass index (BMI), (B) alanine aminotransferase (ALT), (C) aspartate transaminase (AST), (D) gamma -glutamyl transpeptidase (GGT), and subgroup analyses by probiotic strains of each index.