# SUPPLEMENTAL MATERIAL

**Table S1. PRISMA checklist.**

| Section and Topic | Item # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | Title page |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | 1 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | 4-5 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 5 |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 6-7 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | 6 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | 6 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | 7 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they | 7 |

| Section and Topic | Item # | Checklist item | Reported on page # |
|---|---|---|---|
| | | worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | 6-9 |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | 6-9 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | 10 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | 9 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | 8-9 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | NA |
| | 13c | Describe any methods used to tabulate or visually display results | 9 |

| Section and Topic | Item # | Checklist item | Reported on page # |
|---|---|---|---|
| | | of individual studies and syntheses. | |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | 9 |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | 9 |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | 9 |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | 10 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | NA |
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | 10-11 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | NA |
| Study characteristics | 17 | Cite each included study and present its characteristics. | 14-17 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | 19-20 |
| Results of | 19 | For all outcomes, present, for each study: (a) summary statistics | 14-19 |

| Section and Topic | Item # | Checklist item | Reported on page # |
|---|---|---|---|
| individual studies | | for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | 19-20 |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | 14-19 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | 14-19 |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | 14-15 |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | 19-21 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | NA |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | 21-23 |
| | 23b | Discuss any limitations of the evidence included in the review. | 23 |
| | 23c | Discuss any limitations of the review processes used. | 23 |
| | 23d | Discuss implications of the results for practice, policy, and future research. | 24 |
| **OTHER INFORMATION** | | | |

| Section and Topic | Item # | Checklist item | Reported on page # |
|---|---|---|---|
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | 5 |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | 5 |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | 5 |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | 25 |
| Competing interests | 26 | Declare any competing interests of review authors. | 25 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | NA |

NA: not applicable

*From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

**Table S2. Characteristics of the CIMT measurement.**

| Study | Definition of CIMT | Area of CIM measurement | Calculation of the overall CIMT | Machine |
|---|---|---|---|---|
| Bao-Ge *et al.*[20] 2017 | inner surface of the inner membrane - external surface of the tunica media | 1 cm proximal to the CCA bifurcation in the left and right CCAs | mean of three separate values | 3.5–5 MHz convex probe and a high-resolution B-mode ultrasound scanner |
| Başyığıt *et al.*[34] 2012 | leading edge of the lumen intimal interface -leading edge of the media adventitia interface of the far wall | NI | mean of right and left values | high-resolution grey-scale Doppler ultrasonography |
| Diomedi *et al.*[24] 2004 | NI | 1.5 cm proximal to the CCA flow divider | mean of the maximum wall thickness for the near and far wall on the left and right side | continuous-wave Doppler and color flow B-mode Doppler ultrasound (Esaote Biomedica, Genova, Italy) with a high-resolution 7.5-MHz linear array-imaging probe |
| El Hadidy *et al.*[26] 2009 | NI | NI | NI | B mode grey scale ultrasound |
| Hamed *et al.*[21] 2008 | NI | 1 cm before carotid bifurcation | mean of the two sides | 5-MHz linear transducer of a color duplex flow imaging system (128 XP, Acuson Corp, Mountain View, Calif), modes: real-time B, color, and spectral Doppler |

| | | | | |
|---|---|---|---|---|
| Judaki *et al.*[35] 2017 | NI | NI | average of the measurements of left and right common CIMT | B-mode ultrasonography (Esaote, MylabTM 70 Co., Italy) using a high-resolution, 18-MHz linear array transducer |
| Karadag *et al.*[4] 2018 | distance between the lumen and the intima and the distance between the media and adventitia | 1 cm proximal to the carotid bifurcation | average value of the eight measurements on four with 1 mm distant adjacent localizations of the right and left carotid arteries | NI |
| Köksal *et al.*[22] 2004 | distance between the echoes arising from the intima-media interface and media-adventitia interface | 1 cm before the carotid bifurcation at the far wall of the CCA | At least 6 longitudinal and cross-sectional measurements of both CCAs were summarized and a mean CIMT was calculated | linear-array real-time ultrasound equipment with a 7.5-MHz transducer (GE LOGIQ MD 400, Milwaukee, Wisc., USA) |
| Mayr *et al.*[25] 2003 | lumen-intima interface - leading edge of the media-adventitia interface on the far wall | CCA proximal and distal segments on either side | NI | 10-MHz imaging probe and 5-MHz Doppler |
| Mete *et al.*[27] 2013 | viewable distance between the lumen-intima interface and the mediaadventitia interface | distal 1 cm of CCAs on both sides | CIMT measurements taken from both sides were averaged | grey scale high-resolution color Doppler ultrasound Esaote MyLab 50 (Genoa, Italy) equipped with a 5-12-MHz linear transducer |
| Shan *et al.*[36] 2018 | mean of the maximal intimamedia thickness of the near and far walls | 1 cm proximal to the flow divider on the distal wall of the CCA | The average of the left and right CIMT values | M-mode examinations, Philips iE33 Ultrasound System, Holland) |

| | | | | |
|---|---|---|---|---|
| Xu *et al.*[37] 2016 | leading edge of the media adventitia interface of the far wall - the leading edge of the lumen intimal interface | 1 and 2 cm away from the bifurcation, and the average of the two measurements | mean value between the right and left CCAs | Toshiba 790A color Doppler system (Toshiba Medical Systems Corporation, Ottawa, Tochigi, Japan) with a 10 MHz transducer |
| Feng *et al.*[23] 2018 | vertical distance from the edge of the first to the second echogenic line | 1.5 cm proximal to the carotid bifurcation | The average CIMT was obtained from three independent measurements in the bilateral CCAs | Doppler ultrasound machine (Siemens G50, Germany) with a 7.5MHz transducer |

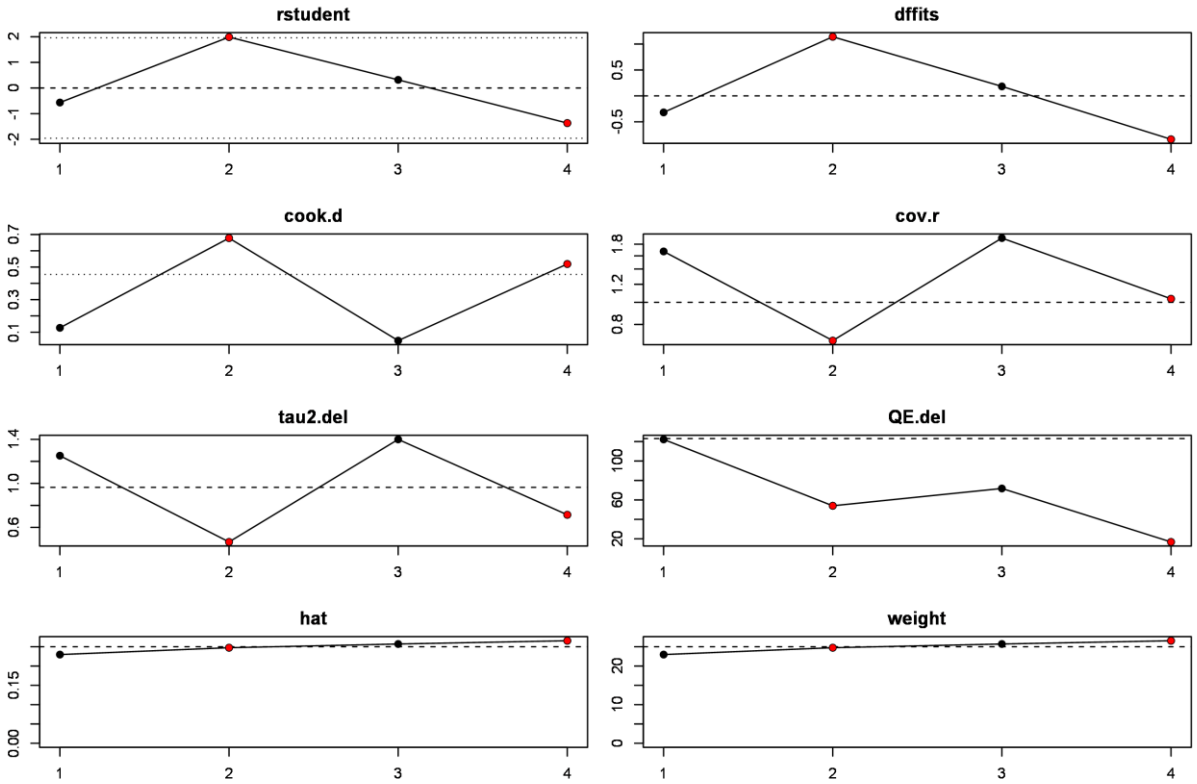
CIM: carotid intima-media, CIMT: carotid intima-media thickness, cm: centimeter, CCA: common carotid artery, NI: no information

**Table S3. Comparison between *H. pylori* positive and negative participants.**

| Study | N⁰ of patients | *H. pylori* positivity | | | | *H. pylori* negativity | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | N⁰ of patients | Sex (female%) | Age (mean±SD) | Overall CIMT (mean±SD) | N⁰ of patients | Sex (female%) | Age (mean±SD) | Overall CIMT (mean±SD) |
| Bao-Ge *et al.*[20] 2017 I. | 78 | 41 | 12.2 | 46.37±7.37* | 0.84±0.25* | 37 | 8.11 | 46.72±6.89* | 0.76±0.16* |
| Bao-Ge *et al.*[20] 2017 II. | 82 | 35 | 8.57 | 46.74±6.69* | 0.71±0.19* | 47 | 12.77 | 46.66±6.75* | 0.7±0.16* |
| Başyığıt *et al.*[34] 2012 | 61 | 30 | 53.33 | 40.9±10.3 | O: 0.71±0.1<br>L: 0.72±0.14<br>R: 0.7±0.09 | 31 | 51.61 | 42.3±9.4 | O: 0.65±0.06<br>L: 0.67±0.08<br>R: 0.64±0.06 |
| Diomedi *et al.*[24] 2004 | 124 | 85 | 36.47 | 68.8±9.8 | 1.13±0.26 | 39 | 46.15 | 66.9±15.8 | 1.01±0.17 |
| El Hadidy *et al.*[26] 2009 | 60 | 23 | 82.61 | NI | L: 8.08±1.54<br>R: 7.78±1.41 | 37 | 67.57 | NI | L: 8.21±1.62<br>R: 8.16±1.69 |
| Hamed *et al.*[21] 2008 I. | 80 | 68 | 48.53 | 47.6±9.1 | 0.84±0,17 | 12 | 66.67 | 48.2±9.3 | 0.78±0.1 |
| Hamed *et al.*[21] 2008 II. | 60 | 46 | 39.13 | 46.2±9.7 | 0.62±0.08 | 14 | 42.86 | 50.2±6.5 | 0.58±0.1 |
| Judaki *et al.*[35] 2017 | 80 | 40 | 55 | 45.64±8.32 | 0.58±0.13 | 40 | 42.5 | 46.52±5.52 | 0.48±0.32 |
| Karadag *et al.*[4] 2018 | 45 | 24 | 50 | 50±8.2 | 0.78±0.11 | 21 | 57.14 | 52±7.9 | 0.67±0.08 |
| Köksal *et al.*[22] 2004 I. | 84 | 63 | 73.02 | 46.7±14.7 | 0.85±0.38 | 21 | 66.67 | 45.1±7.1 | 0.88±0.3 |
| Köksal *et al.*[22] 2004 II. | 50 | 30 | 66.67 | 45±11 | 0.56±0.19 | 20 | 70 | 45±10 | 0.67±0.13 |
| Mayr *et al.*[25] 2003 | 421 | 285 | 47 | 56.6† | 0.986±0.184 | 136 | 49 | 55.7† | 0.991±0.189 |
| Mete *et al.*[27] 2013 | 134 | 103 | 57.29 | 49.8±8.7 | O: 0.73 (0.34-1.35)‡<br>L: 0.74 (34-1.6)‡<br>R: 0.72 (34-1.2)‡ | 31 | 61.29 | 50.2±9.33 | O: 0.57 (0.44-0.70)‡<br>L: 0.55 (0.44-0.67)‡<br>R: 0.57 (0.4-0.85)‡ |
| Shan *et al.*[36] 2018 | 395 | 186 | NI | NI | L: 0.65±0.01<br>R: 0.65±0.01 | 209 | NI | NI | L: 0.63±0.01<br>R: 0.61±0.01 |
| Xu *et al.*[37] 2016 | 364 | 208 | 46.15 | 63.2±10.4 | 1.12±0.18 | 156 | 48.1 | 62.8±11.7 | 0.93±0.15 |
| Feng *et al.*[23] 2018 I. | 89 | 51 | 19.61 | 46.1±0.58* | 0.84±0.009* | 38 | 21.05 | 46.79±0.63* | 0.76±0.013* |
| Feng *et al.*[23] 2018 II. | 91 | 42 | 21.43 | 46.64±0.54* | 0.75±0.011* | 49 | 22.45 | 46.61±0.53* | 0.75±0.009* |

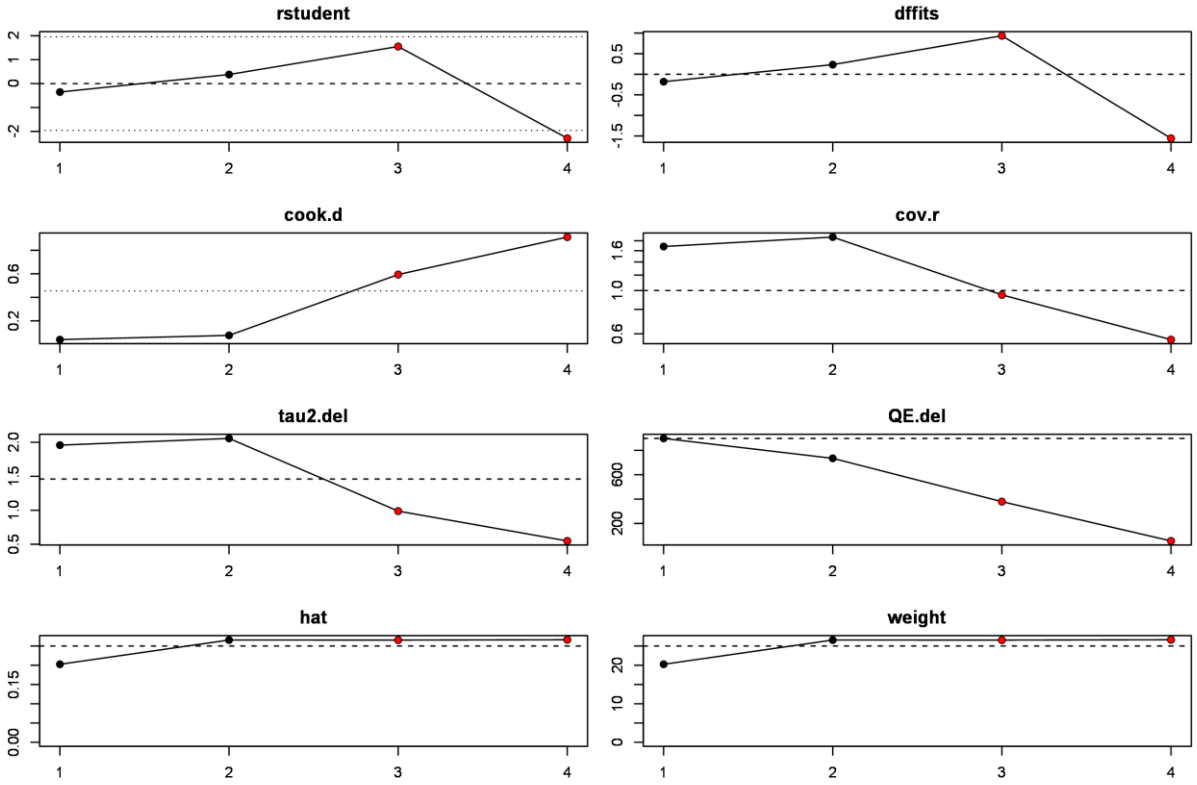
*mean±SE, † mean without SD, ‡ median (min-max), HP: *H. pylori*, SD: standard deviation, SE: standard error, NI: no information, CIMT: carotid intima-media thickness, O: overall, L: left, R: right

**Figure S1. Influence diagnostics of the four included studies in the right carotid intima-media thickness analyses with various methods (Externally Standardized Residuals (rstudent), DFFITS value, Cook's Distance, Covariance Ratio, tau2, Qvalues, Hat & Weight).**




1: Başyığıt *et al.* [23] (2012), 2: El Hadidy *et al.* [26] (2009), 3: Mete *et al.* [27] (2013), 4: Shan *et al.* [36] (2018).

**Figure S2. Influence diagnostics of the four included studies in the left carotid intima-media thickness analyses with various methods (Externally Standardized Residuals (rstudent), DFFITS value, Cook's Distance, Covariance Ratio, tau2, Qvalues, Hat & Weight).**




1: Başyığıt *et al.* [23] (2012), 2: El Hadidy *et al.* [26] (2009), 3: Mete *et al.* [27] (2013), 4: Shan *et al.* [36] (2018).

**Figure S3. Sensitivity analyses of the four included studies in the right and in the left carotid intima-media thickness analyses.**

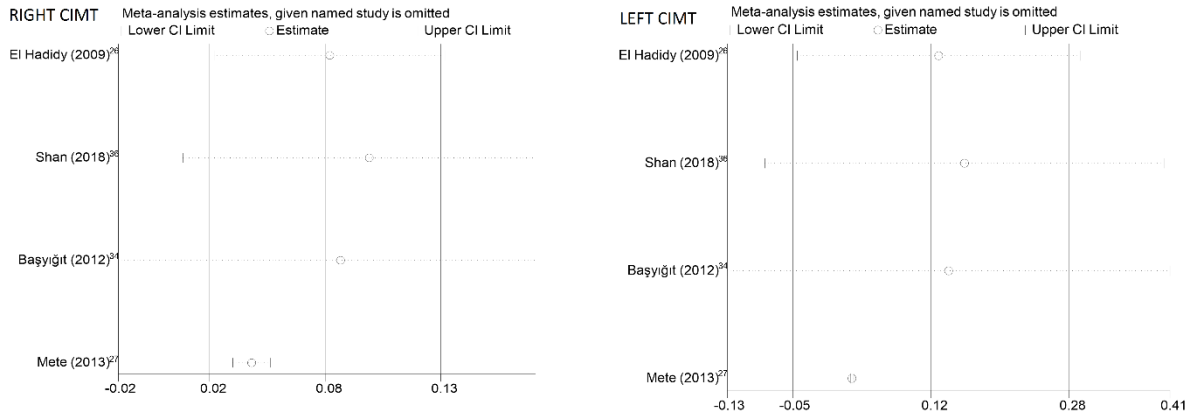
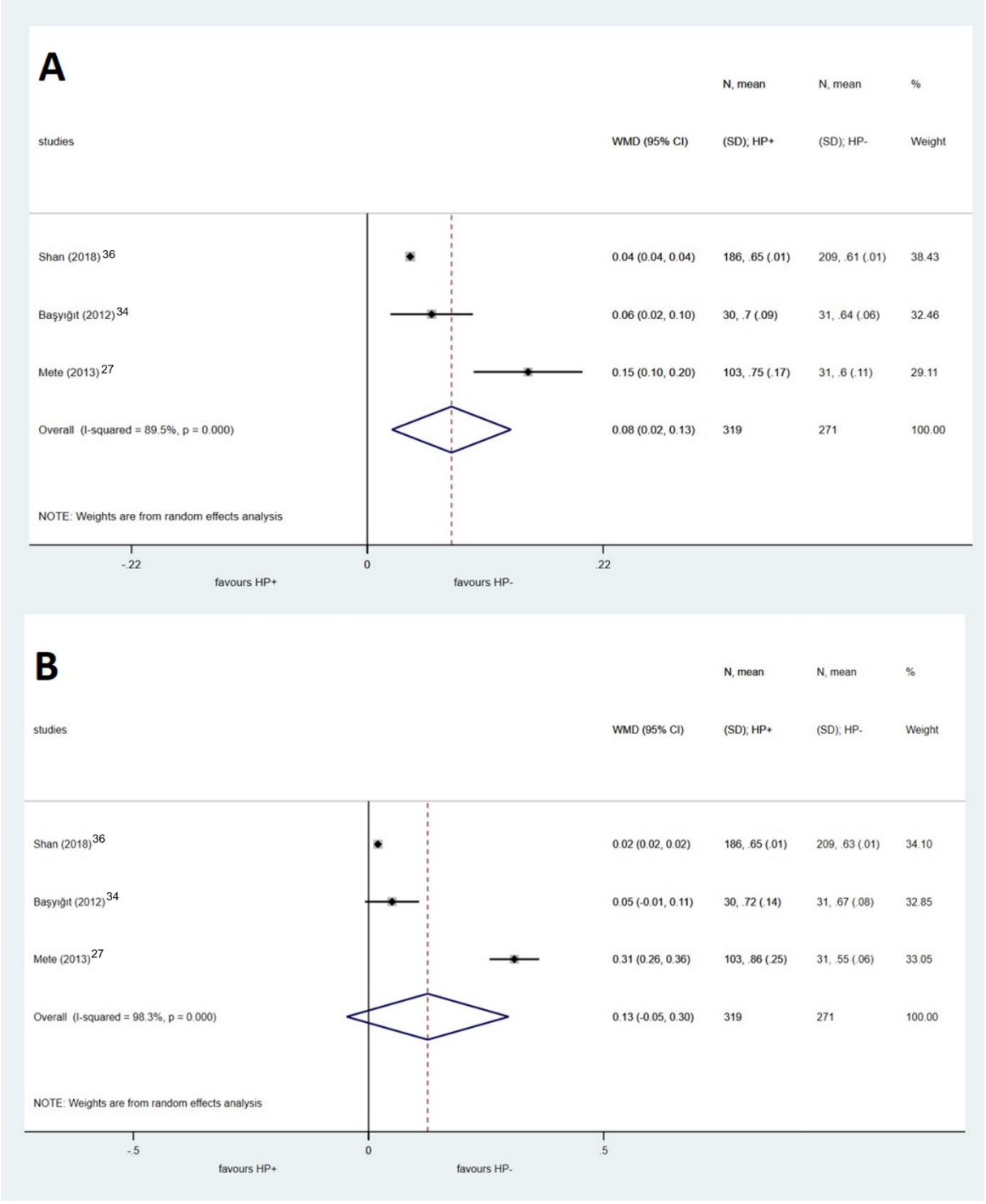


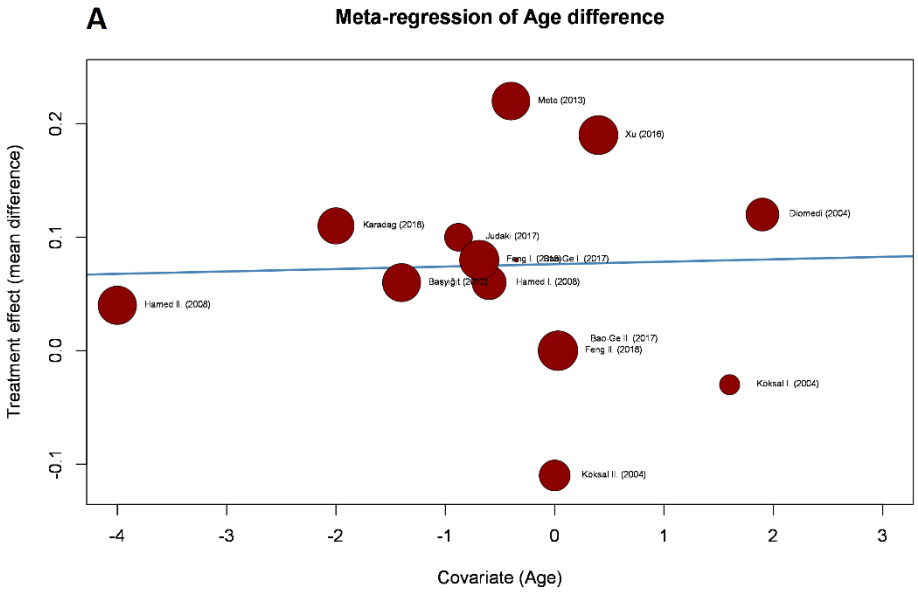
**Figure S4. Forest plot of studies comparing right (A) and left (B) carotid intima-media thickness between *Helicobacter pylori* positive and negative individuals without the study published by El Hadidy *et al.***

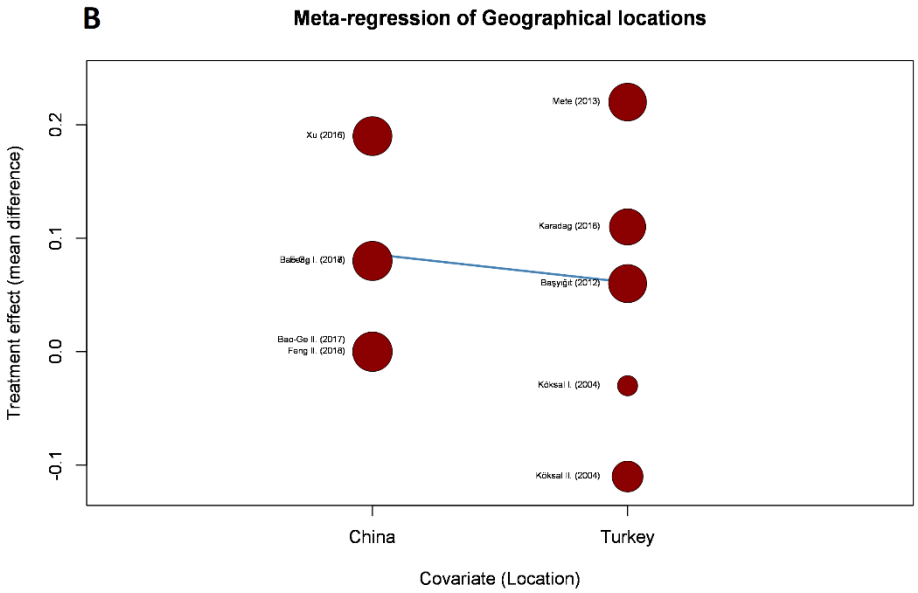


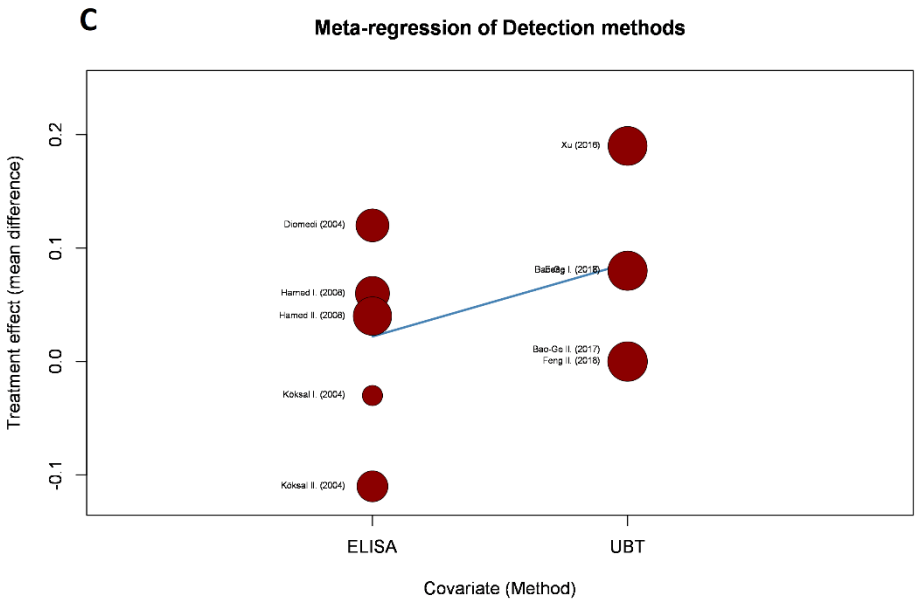

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey

squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S5. A, Meta-regression of age difference. X-axis represents age. The estimate predicts the increase of the effect size, if one was added to the predictor (age, continuous variable) B, Meta-regression of geographical location. X-axis represents the geographical locations, China and Turkey. The estimate predicts the decrease of the effect size, if Turkey was compared to China. C, Meta-regression of detection method. X-axis represents the detection methods, enzyme-linked immunosorbent assay and urea breath test. The estimate predicts the increase of the effect size, if urea breath test was compared to enzyme-linked immunosorbent assay.**

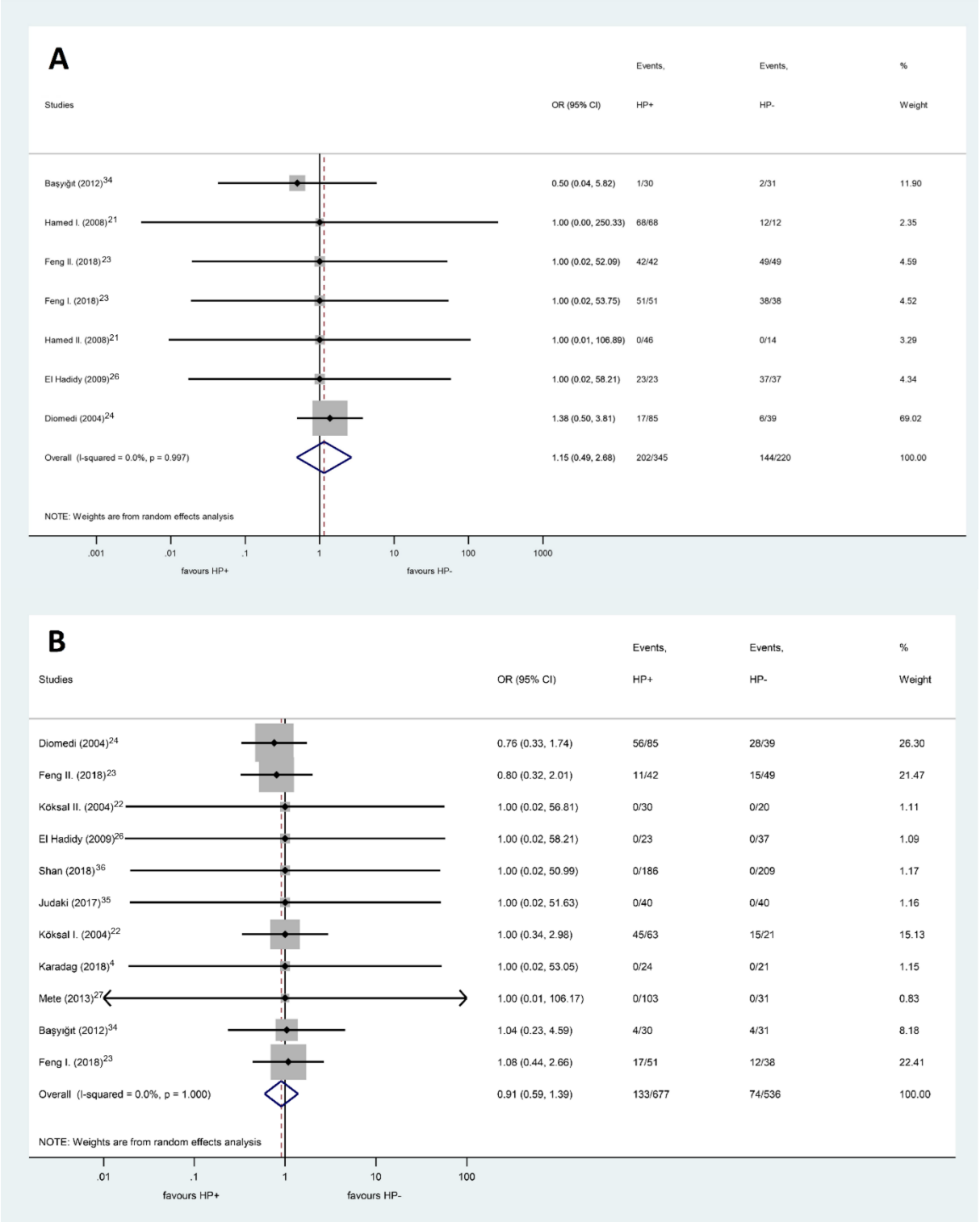

A
Meta-regression of Age difference
Mete (2013)
Xu (2016)
Diomedi (2004)
Karadag (2016)
Judaki (2017)
Hamed I. (2008)
Hamed II. (2008)
Bao-Ge II. (2017)
Feng II. (2016)
Köksal I. (2004)
Köksal II. (2004)
Treatment effect (mean difference)
Covariate (Age)


B
Meta-regression of Geographical locations
Mete (2013)
Xu (2016)
Karadag (2016)
Başyiğit (2012)
Bao-Ge II. (2017)
Feng II. (2016)
Köksal I. (2004)
Köksal II. (2004)
China
Turkey
Treatment effect (mean difference)
Covariate (Location)


C
Meta-regression of Detection methods
Xu (2016)
Diomedi (2004)
Hamed I. (2008)
Hamed II. (2008)
Bao-Ge II. (2017)
Feng II. (2016)
Köksal I. (2004)
Köksal II. (2004)
ELISA
UBT
Treatment effect (mean difference)
Covariate (Method)

In all cases, Y-axis represents the weighted mean differences of overall carotid intima-media thickness in articles reporting these results. Each red dot represents one of these articles.

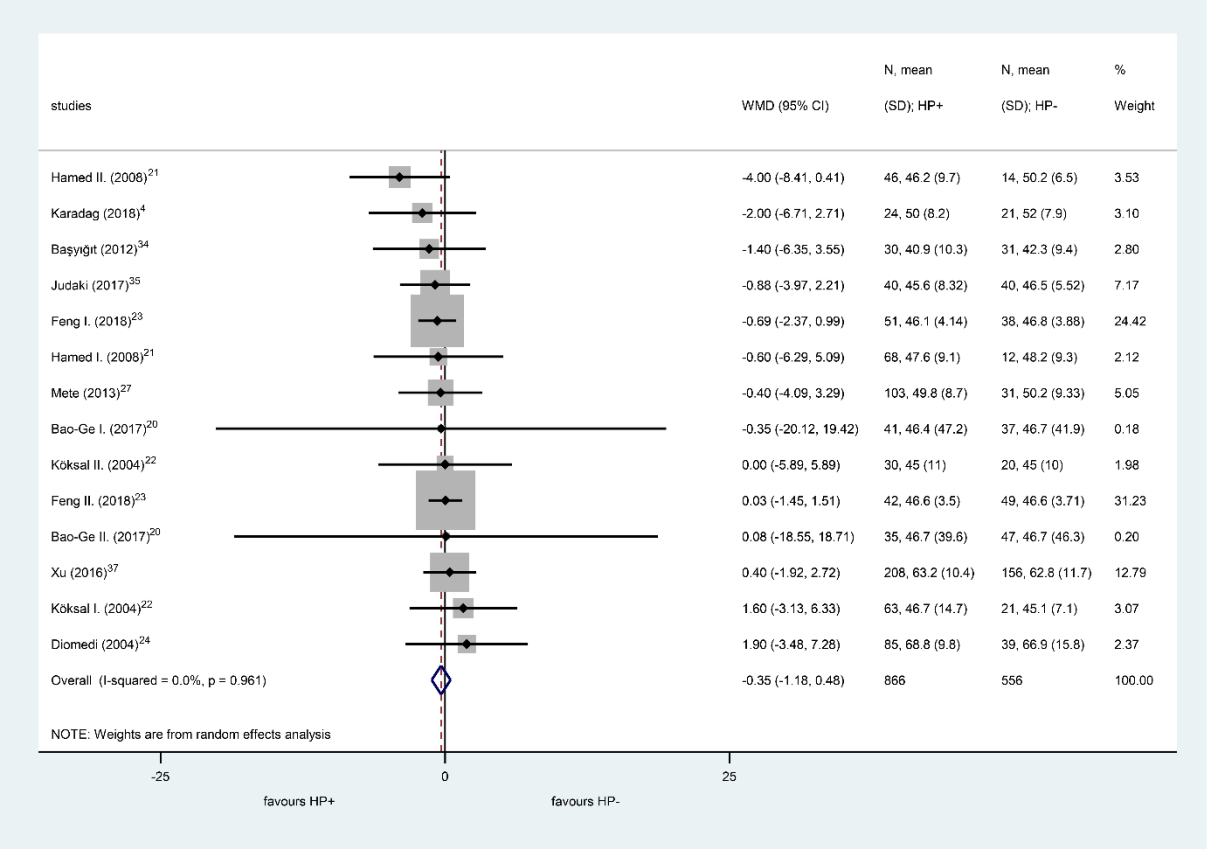
**Figure S6. Forest plot of studies comparing the prevalence of diabetes mellitus (A) and hypertension (B) between *Helicobacter pylori* positive and negative individuals.**




Black diamonds represent the odds ratios and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The

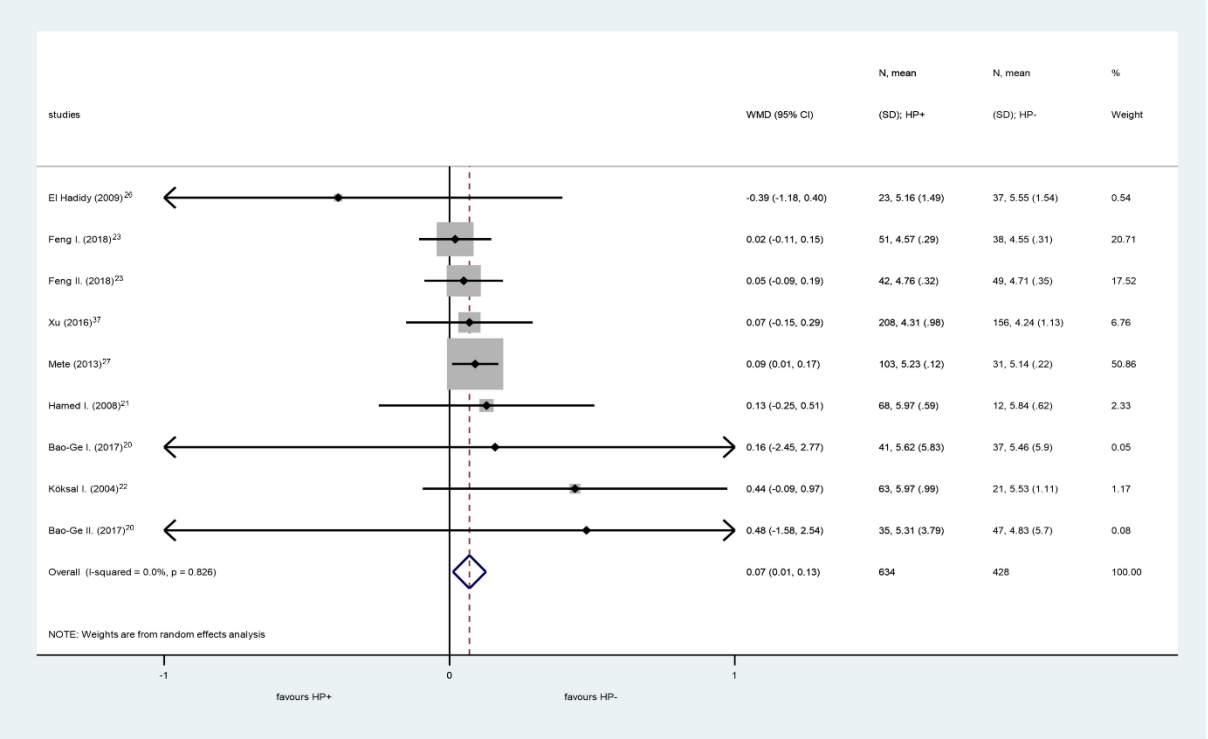
blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S7. Forest plot of studies comparing the mean age between *Helicobacter pylori* positive and negative individuals.**



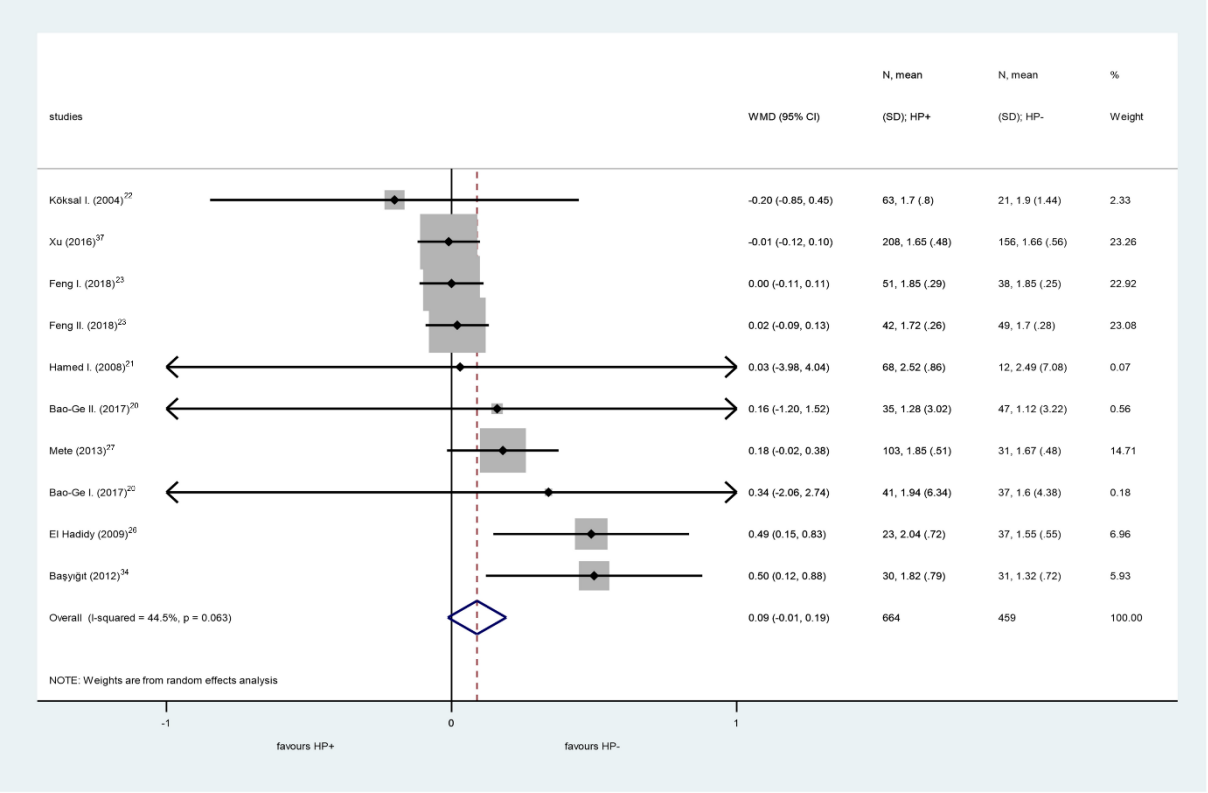

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S8. Forest plot of studies comparing total cholesterol levels between *Helicobacter pylori* positive and negative individuals.**



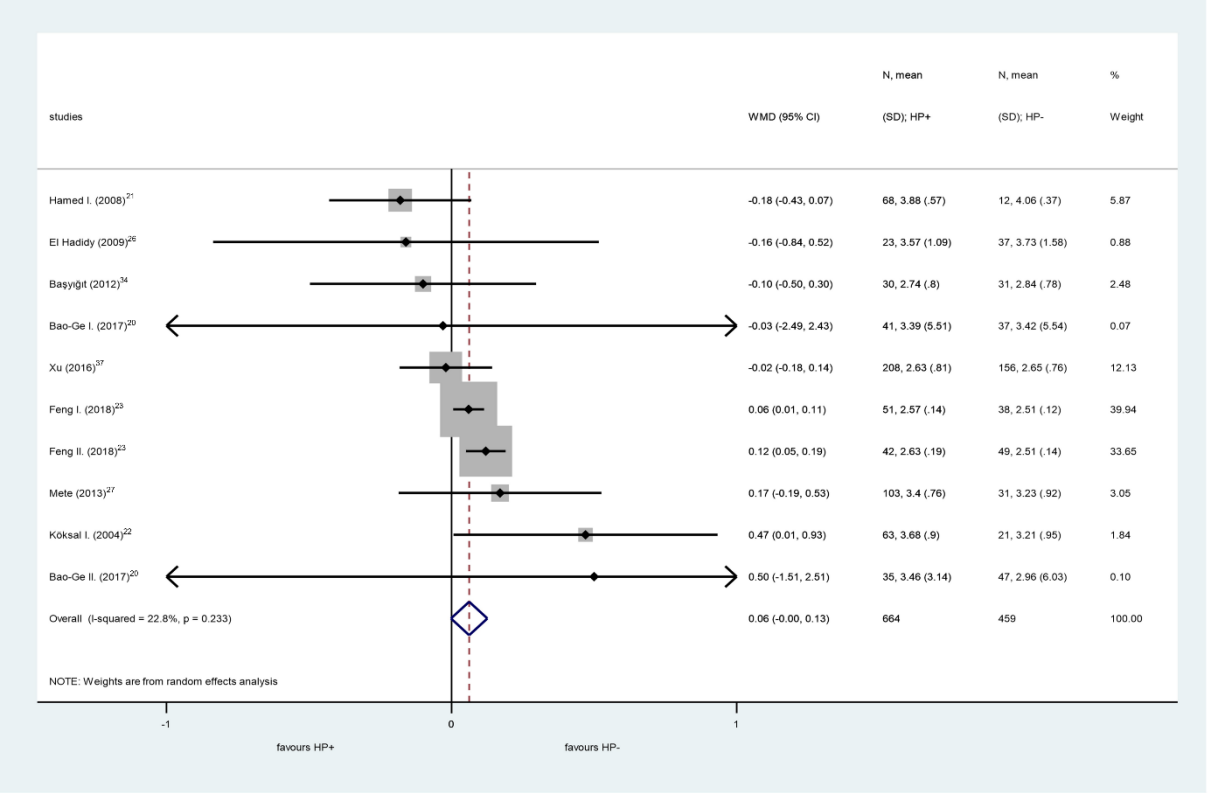

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S9. Forest plot of studies comparing triglyceride levels between *Helicobacter pylori* positive and negative individuals.**



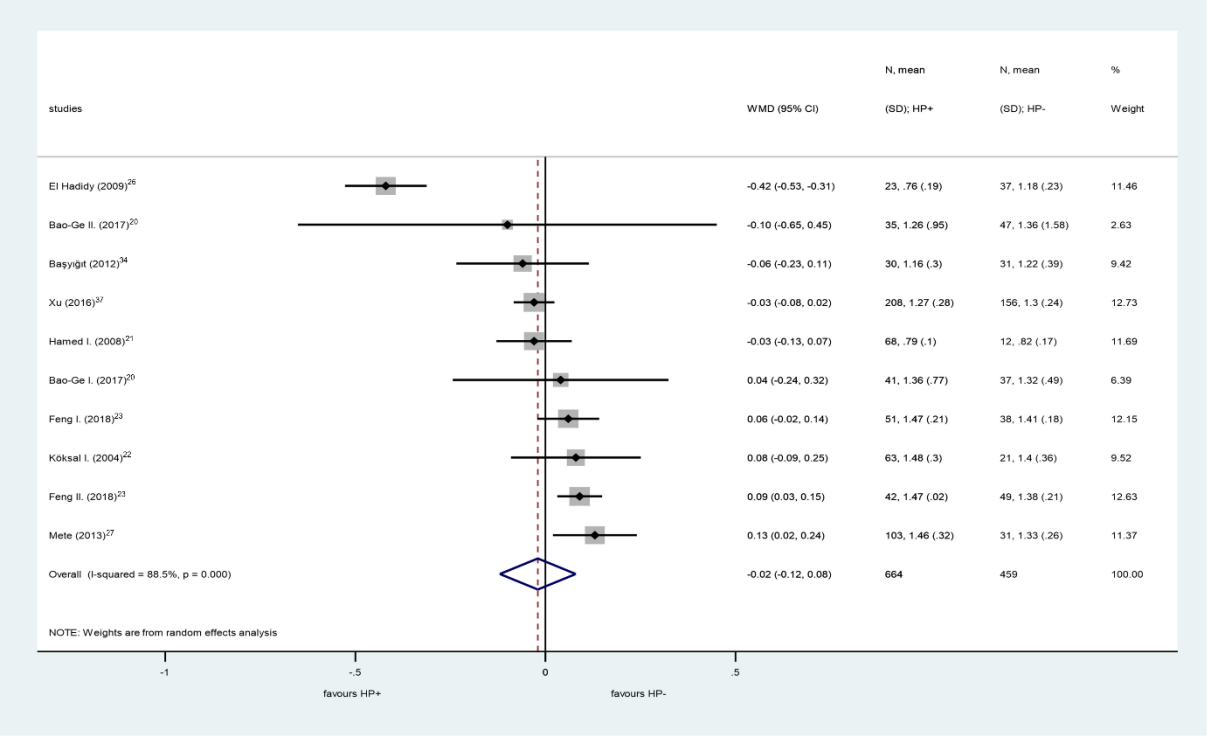

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S10. Forest plot of studies comparing low-density lipoprotein levels between *Helicobacter pylori* positive and negative individuals.**



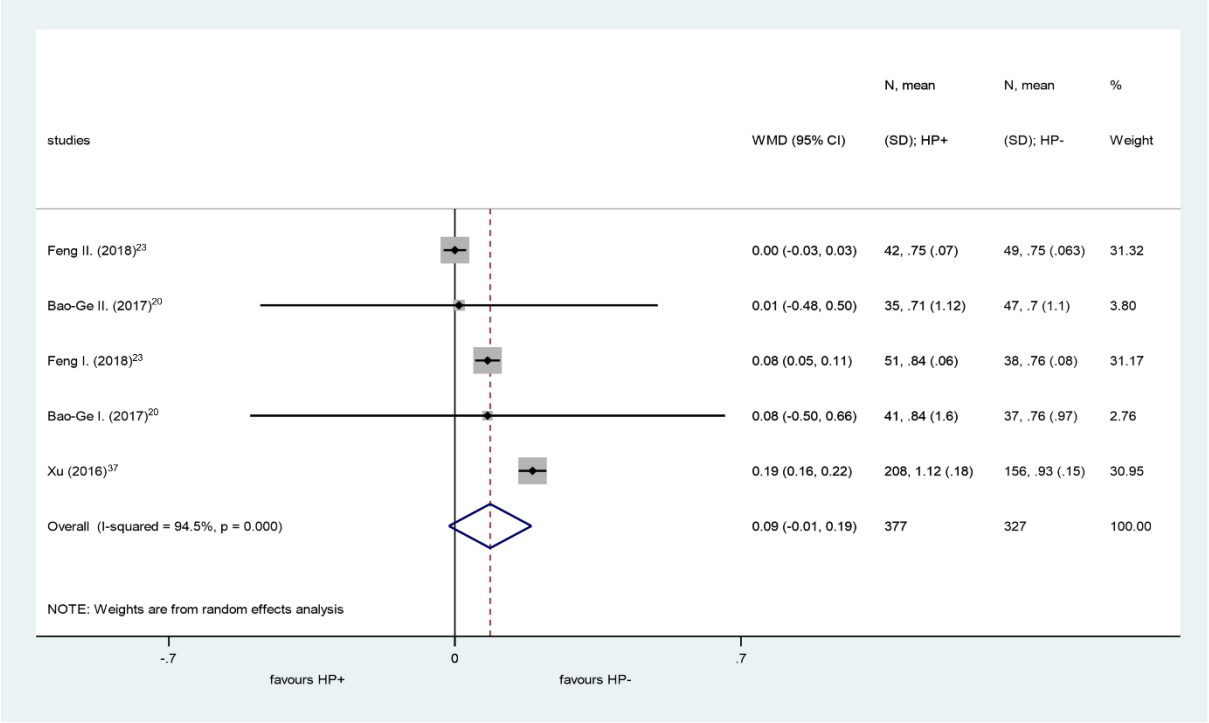

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals. Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S11. Forest plot of studies comparing high-density lipoprotein levels between *Helicobacter pylori* positive and negative individuals.**



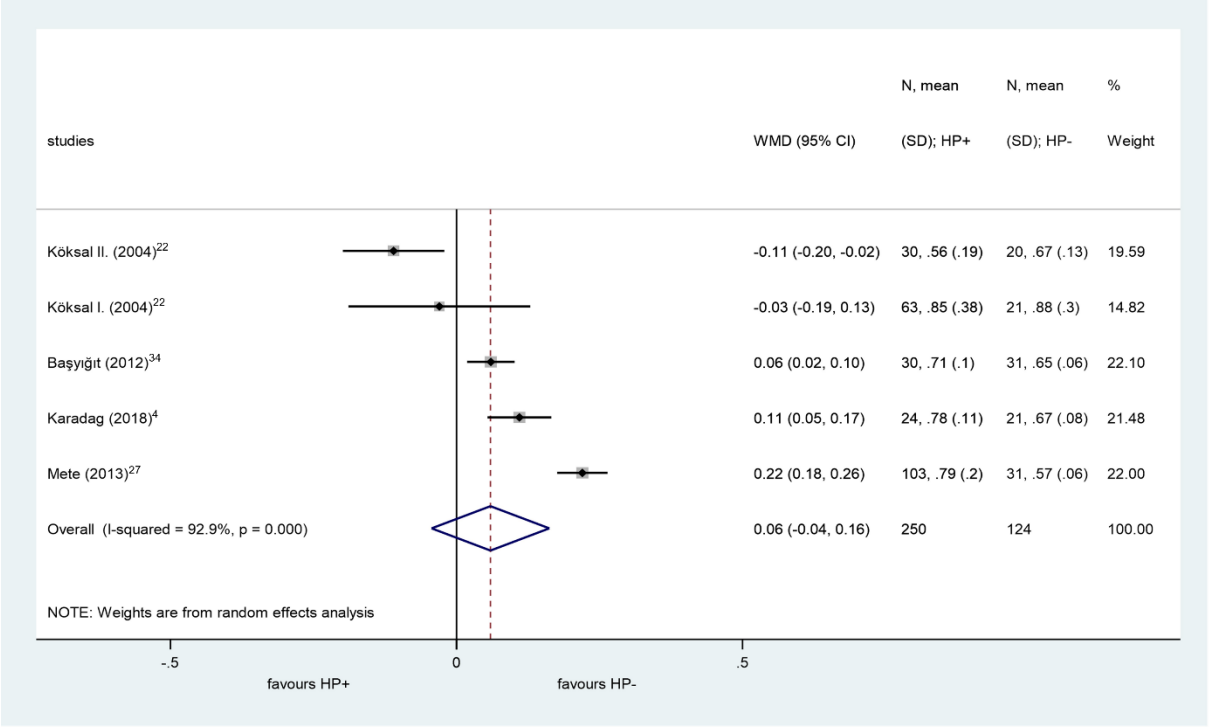

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S12. Forest plot of studies comparing overall carotid intima-media thickness between *Helicobacter pylori* positive and negative Chinese individuals.**



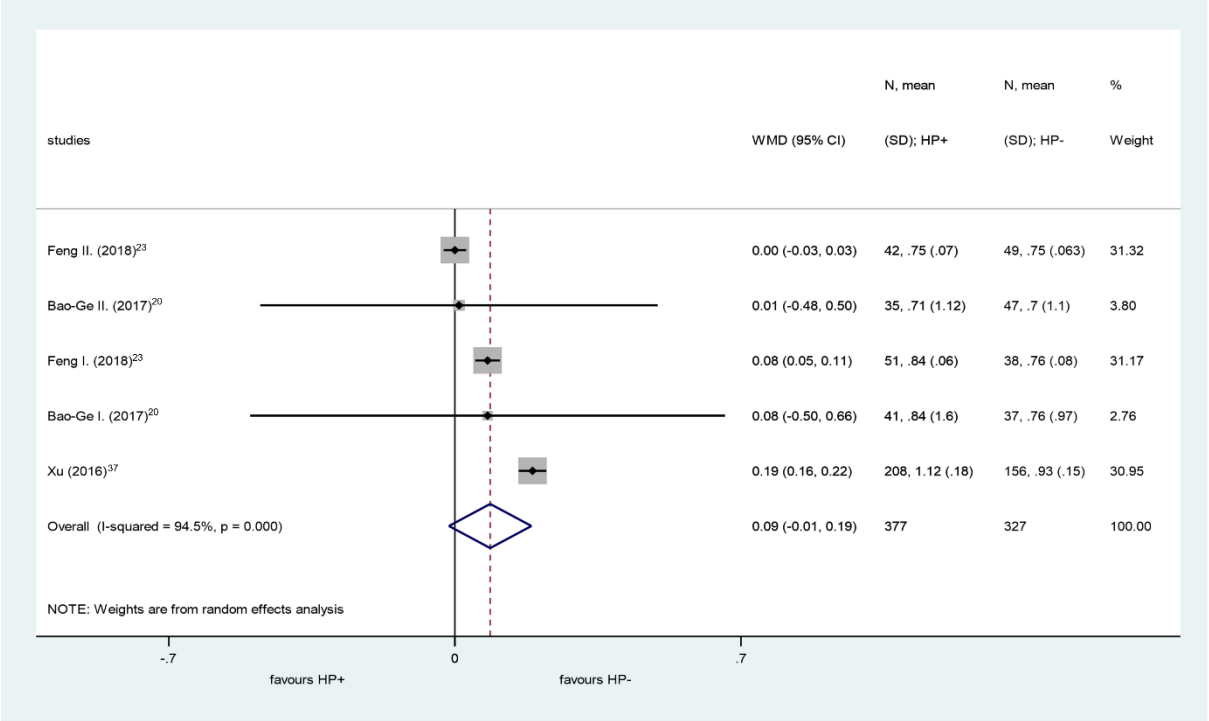

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S13. Forest plot of studies comparing overall carotid intima-media thickness between *Helicobacter pylori* positive and negative Turkish individuals.**



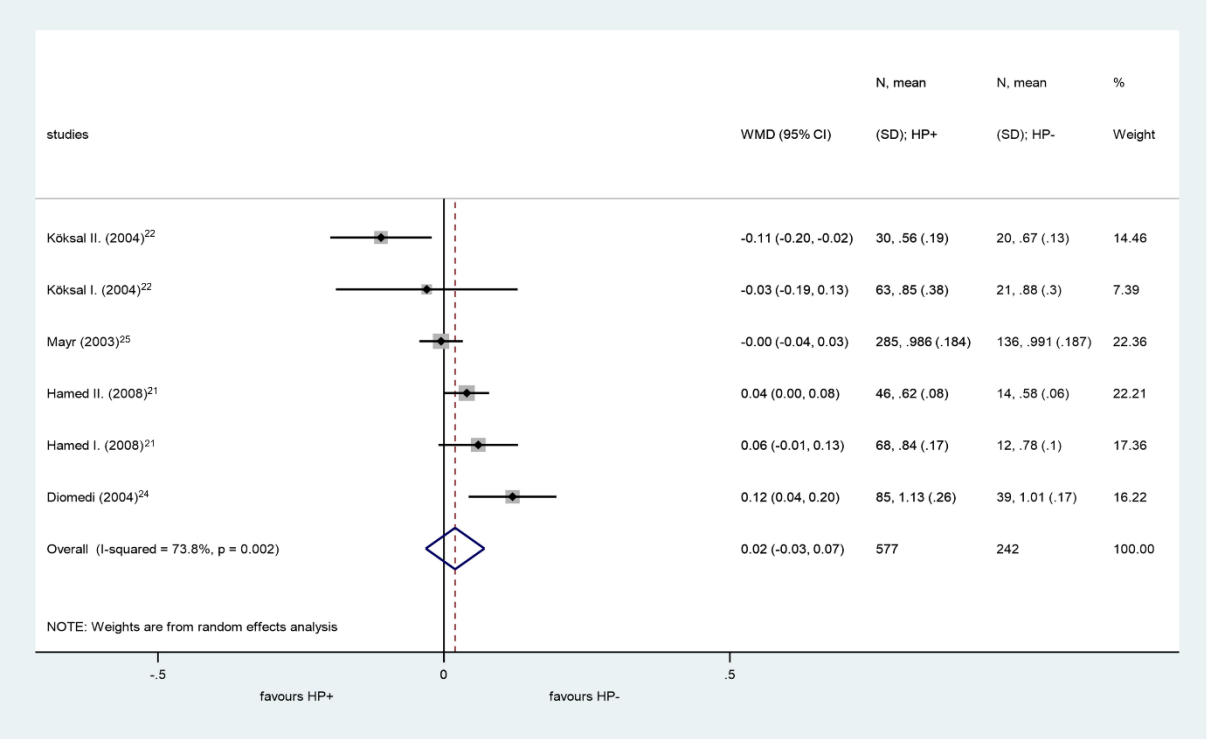

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S14. Forest plot of studies comparing overall carotid intima-media thickness between *Helicobacter pylori* positive and negative individuals if the pathogen was detected by urea breath test.**




Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

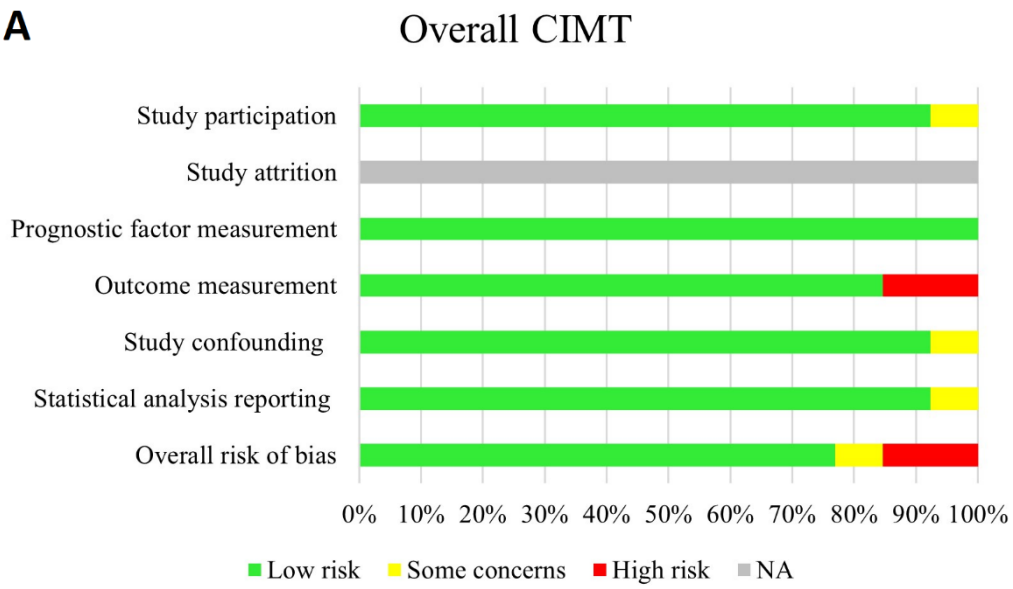
**Figure S15. Forest plot of studies comparing overall carotid intima-media thickness between *Helicobacter pylori* positive and negative individuals if the pathogen was detected by enzyme-linked immunosorbent assay.**



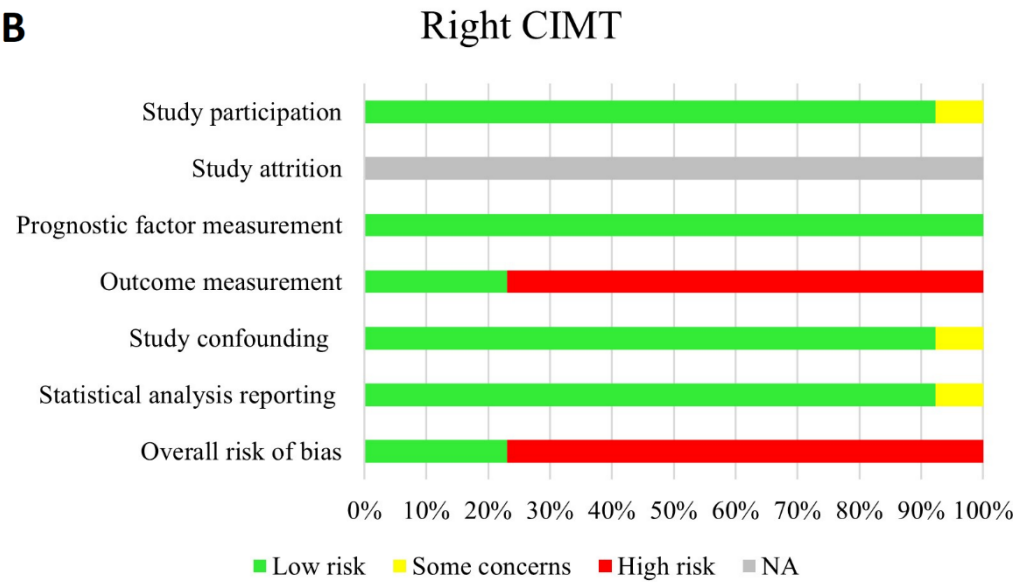

Black diamonds represent the weighted mean difference between the two groups we compared and horizontal lines show the corresponding 95% confidence intervals (CI). Size of the grey squares reflect the weight of a particular study. The blue diamond is the overall or summary effect. The outer edges of the diamonds represent the CIs.

**Figure S16. Bar charts for all domains separately included in risk of bias assessment of overall (A), right (B) and left (C) carotid intima-media thickness.**

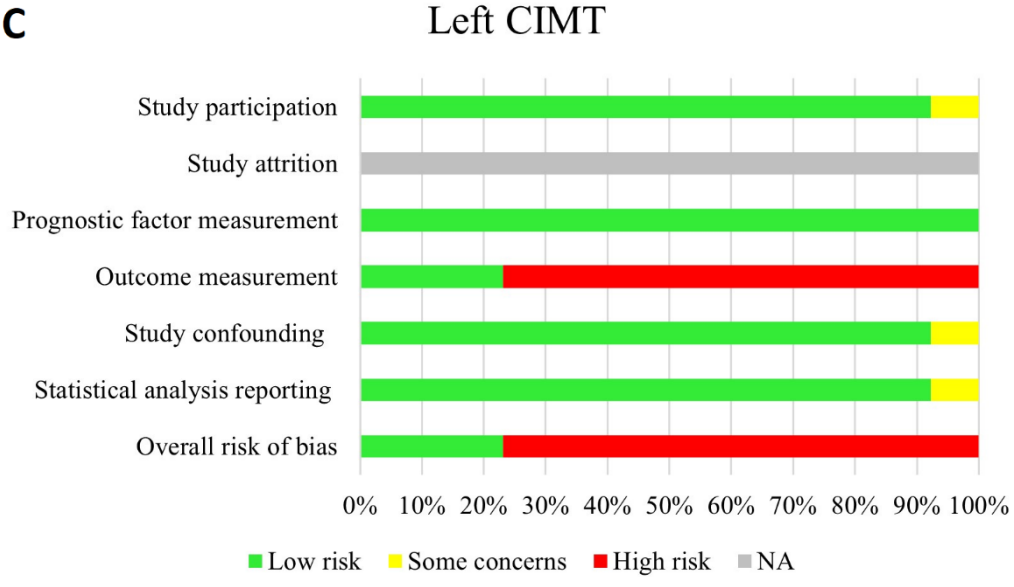
**A**


Overall CIMT
Study participation
Study attrition
Prognostic factor measurement
Outcome measurement
Study confounding
Statistical analysis reporting
Overall risk of bias
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
Low risk
Some concerns
High risk
NA

**B**

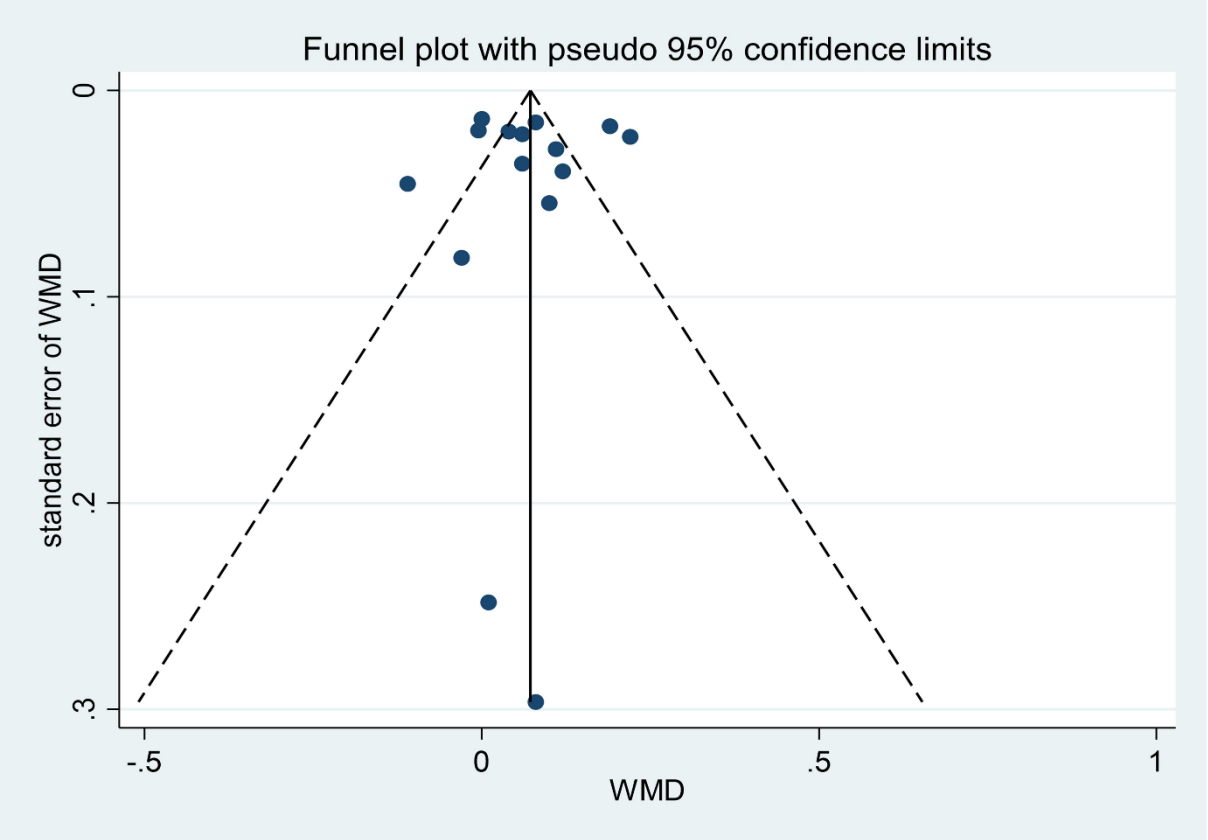

Right CIMT
Study participation
Study attrition
Prognostic factor measurement
Outcome measurement
Study confounding
Statistical analysis reporting
Overall risk of bias
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
Low risk
Some concerns
High risk
NA

**C**


Left CIMT
Study participation
Study attrition
Prognostic factor measurement
Outcome measurement
Study confounding
Statistical analysis reporting
Overall risk of bias
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
Low risk
Some concerns
High risk
NA

Green represents low risk of bias, yellow represents moderate and red represents high risk of bias. Grey represents non-applicability of the subdomain for the study. X-axis represents the percentage of each risk and the domains are represented on Y-axis.

**Figure S17. Funnel plot of studies comparing overall carotid intima-media thickness between *Helicobacter pylori* positive and negative individuals.**




X-axis represents the weighted mean difference between the two groups we compared. Y-axis represents the standard error of weighted mean difference. The vertical is for overall effect. The dashed lines represent the 95% confidence intervals. Each spot represents an included study of the specific analysis.