

Supplementary figures

Metabolic Syndrome Components Correlation with Colorectal Neoplasms: A Systematic Review and a Meta-analysis (Supplementary figures)

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Hiah FBG Normal FBG Risk Ratio Risk Ratio M-H, Random, 95% Cl (a) Study or Subgroup 4.1.1 Cohort ents Total Events Total Weight M-H, Random, 95% Cl 4.1.1 Cohort Kabat 2012 CC / NCEP-ATP III Kabat 2012 CC / NCEP-ATP III Kim 2012 CC / NCEP-ATP III Kim 2012 CC / NCEP-ATP III Lin 2014 CCC / NCEP-ATP III Lin 2014 CCC / NCEP-ATP III 43 46 1169 133 129 29 22 1682 3204 0.97 [0.59, 1.62] 2.4% 1695 420 310 246 221 4574 3207 5539 4503 230 3.2% 9.6% 2.1% 9.7% 1.44 (0.93, 2.23) 1.39 (1.19, 1.62) 1.42 (0.81, 2.48) 1.07 (0.91, 1.24) 35 123 13 147 141 Lin 2014 CRC / NCEP-ATP III (W) Subtotal (95% CI) 118 16801 4.7% 31.6% 2.60 [1.86, 3.62] 1.41 [1.08, 1.84] 481 1549 < 0.0001); I² = 81% Total events Heterogeneity: Tau² = 0.08; Chi² = 26.39, df Test for overall effect: Z = 2.49 (P = 0.01) 4.1.2 Non-Cohort 4.1.2 Mon-Cohort Aleksandrova 2011 CC / NCEP-ATP III (M) Aleksandrova 2011 CC / NCEP-ATP III (M) Aleksandrova 2011 RC / NCEP-ATP III (M) Aleksandrova 2011 RC / NCEP-ATP III (M) Jeon 2014 CC / Other Jeon 2014 RC / Other 1.29 [1.10, 1.51] 1.33 [1.16, 1.53] 1.14 [0.94, 1.37] 1.39 [1.14, 1.70] 1.44 [1.19, 1.74] 1.48 [1.17, 1.89] 317 303 218 148 315 270 248 82 1901 9.5% 10.2% 8.5% 8.1% 6.8% 10.7% 6.3% 68.4% 178 178 116 89 149 104 147 39 134 199 103 96 115 82 360 174 307 451 220 222 349 316 766 540 3171 Shen 2010 CRC / Othe 1.26 [1 .43 Stocks 2008 CRC / Other Subtotal (95% CI) Subtotal (95% CI) Total events Heterogeneity: Tau² = 0.00; Chi² = 5.72, df = 7 (F Test for overall effect: Z = 8.83 (P < 0.00001) 1000 P = 0.57); I² = 0% 1263 Total (95% CI) 1.35 [1.23, 1.47] 6475 19972 100.0% 1004 (95% L) 0475 Total events 1481 2812 Heterogeneity: Tau[#] = 0.01; Chi[#] = 31.66, df = 13 (P = 0.003); I[#] = 59% Test for overall effect: Z = 8.61 (P < 0.00001) Test for subaroup differences: Chi[#] = 0.21, df = 1 (P = 0.64), I[#] = 0% 0.5 0.7 1 1.5 2 Decrease CRC risk Increase CRC risk SE(log[RR]) n. (b) ° 0.1 8 0 0.2 0 0 0 0.3 0.4 RR 0.5 0.5 0.7 1.5 2 O Cohort On-Cohor (a) 0

Supplementary Figure 1.1 Association between FBG and CRC incidence: (a) Forest plot; (b) Funnel plot.

CC colon cancer, CI confidence interval, CRC colorectal cancer, FBG fasting blood glucose, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, RC rectal cancer, RR risk ratio, W women.









(a)

Supplementary Figure 2.1 Association between BP and CRA formation: (a) Forest plot; (b) Funnel plot. AA advanced adenomas, CI confidence interval, CRA colorectal adenoma, df degree of freedom, IDF International Diabetes Foundation, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, W women.







Supplementary Figure 2.3 Association between BP and CRC incidence: (a) Forest plot; (b) Funnel plot. CC colon cancer, Cl confidence interval, CRC colorectal cancer, df degree of freedom, IDF International Diabetes Foundation, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment

Panel III, RC rectal cancer, W women.



Supplementary Figure 2.4 Additional analyses for the association between BP and CRC incidence: (a) Funnel plot after adjustment to publication bias with the trim and fill method. No studies were estimated missing. (b) Baujat plot: indicates that the 15^{th} dataset (that falls to the top right quadrant of the Baujat plot which corresponds to (Jeon 2014 RC / Other)) has contributed to the overall heterogeneity and result. (c) Influence plot: as there is no marked study, no study has met the criteria as an influential study.



Supplementary Figure 3.1 Association between TG and CRA formation: (a) Forest plot; (b) Funnel plot. AA advanced adenomas, CI confidence interval, CRA colorectal cancer, IDF International Diabetes Foundation, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, TG triglycerides, W women.



Supplementary Figure 3.2 Additional analyses for the association between TG and CRA development: (a) Funnel plot after adjustment to publication bias with the trim and fill method. No studies were estimated missing. (b) Baujat plot: indicates that the 1st and 8th dataset (which corresponds to (Kim 2012 AA / NCEP-ATP III) and (Lee 2014 AA / NCEP-ATP III)) has contributed to the overall heterogeneity, while only the first contributed to the overall result. (c) Influence plot: as there is no marked study, no study has met the criteria as an influential study.



High TG ents T Risk Ratio Risk Ra Normal TG Total Weight M-H Random, 95% CI M-H, Random, 95% Cl (a) <u>Study or Subgroup</u> 6.1.1 Cohort Total 6.1.1 CONDIT Kim 2012 CC / NCEP-ATP III Kim 2012 RC / NCEP-ATP III Lin 2014 CRC / NCEP-ATP III (M) Lin 2014 CRC / NCEP-ATP III (M) Subtotal (95% CI) 382 44 98 54 1335 997 147 99 2578 910 102 178 116 1.45 [1.31, 1.61] 1.65 [1.17, 2.33] 1.23 [1.06, 1.43] 1.13 [0.90, 1.41] 1.33 **[1.15, 1.54]** 4624 10.8% 6.0% 9.9% 8.4% 35.1% 3816 329 240 9009 $\label{eq:2578} \begin{array}{c} 2578 \\ \text{Heterogeneity: Tau"} = 0.01; \ \text{Chi"} = 7.56, \ \text{df} = 3 \ (\text{P} = 0.06); \ \text{P} = 60\% \\ \text{Test for overall effect $Z = 3.91$ ($P < 0.0001$)} \\ \end{array}$ 1306 6.1.2 Non-Cohort 6.1.2 Mon-Cohort Aleksandrova 2011 CC / NCEP-ATP III (M) Aleksandrova 2011 CC / NCEP-ATP III (M) Aleksandrova 2011 RC / NCEP-ATP III (M) Jeon 2014 CC / Other Jeon 2014 RC / Other Jung 2014 RC / Other Shahota (95% CI) Total events 1.11 [0.93, 1.32] 1.17 [0.98, 1.39] 1.12 [0.92, 1.36] 0.91 [0.65, 1.25] 0.78 [0.62, 0.97] 1.63 [1.07, 2.48] 1.19 [1.04, 1.37] 1.04 [0.91, 1.20] 150 123 133 48 202 181 12815 9.4% 9.5% 9.0% 6.3% 8.4% 7.1% 4.9% 10.2% 64.9% 231 307 147 163 197 140 69 382 474 631 305 322 462 405 45004 796 48399 81 70 72 22 67 46 32 125 218 13870 515 1636 P = 0.001); P = 71% Total events Heterogeneity: Tau² = 0.03; Chi² = 23.87, df = Test for overall effect: Z = 0.60 (P = 0.55) Total (95% CI) 16448 57408 100.0% 1.14 [1.01, 1.28] $\label{eq:constraint} \begin{array}{l} \textbf{10} \textbf{448} \\ \textbf{10} \textbf{3} & \textbf{2942} \\ \textbf{Heterogeneity}, \textbf{Tau'} = 0.03, \textbf{Chi}^{\mu} = 4.9, 4, 6, 103 \\ \textbf{10} \textbf{3} & \textbf{2942} \\ \textbf{Test for overall effect } \textbf{Z} = 2.10 (P = 0.04) \\ \textbf{Test for svalue} \quad \textbf{6fect } \textbf{2} = 2.10 (P = 0.04) \\ \textbf{Test for subaroup differences: } \textbf{Chi}^{\mu} = 5.60, \text{ df} = 1 (P = 0.02), P = 82.2\% \\ \end{array}$ 1.5 0.5 0.7 Decrease CRC risk RC risk SE(log[RR]) (b) ⁶ 800 0 **~** 0.1 ٥ 0 0.2 0 0.3 0.4 RR 0.5 n's n': O Cohort ♦ Non-Cohor

(a) _____

Supplementary Figure 3.3 Association between TG and CRC incidence: (a) Forest plot; (b) Funnel plot.

CC colon cancer, CI confidence interval, CRC colorectal cancer, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, RC rectal cancer, RR risk ratio, TG triglycerides, W women.







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0.013 0.018

0.00 0.10

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RR

Supplementary Figure 4.1 Association between WC and CRA formation: (a) Forest plot; (b) Funnel plot. AA advanced adenomas, CI confidence interval, CRA colorectal cancer, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, WC waist circumference.

Supplementary Figure 4.2 Additional analyses for the association between WC and CRA development: (a) Funnel plot after adjustment to publication bias with the trim and fill method. No studies were estimated missing. (b) Baujat plot: indicates that the 9th dataset contributed to the overall heterogeneity, the 3rd and the 13th datasets contributed to the overall result, and the 10th dataset contributed to both overall heterogeneity and result (which corresponds to (Lee et al., 2014), (Fliss-Isakov 2017 CRA / AHA), (Sato 2011 CRA / Harmonized)). (c) Influence plot: as there is no marked study, no study has met the criteria as an influential study.

0.3

0.4

0.5

O Cohort

0.5

ONNON-Cohor

0







Supplementary Figure 4.3 Association between WC and CRC incidence: (a) Forest plot; (b) Funnel plot.

CC colon cancer, Cl confidence interval, CRC colorectal cancer, IDF International Diabetes Foundation, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, RC rectal cancer, RR risk ratio, W women, WC waist circumference.

Supplementary Figure 4.4 Additional analyses for the association between WC and CRC incidence: (a) Funnel plot after adjustment to publication bias with the trim and fill method. Three simulated positive studies were added (hollow circles) to the pooled estimates from the meta-analysis (solid circles). The adjusted RR increased from (1.18; 95% Cl 1.07-1.31) in the initial analysis to (1.25; 95% CI 1.13-1.38) after adjustment. (b) Baujat plot: indicates that the $3^{\mbox{\scriptsize rd}}$ dataset (that falls to the top right quadrant of the Baujat plot which corresponds to (Aleksandrova 2011 CC / IDF (M))) has contributed to the overall heterogeneity and result. (c) Influence plot: as there are one marked datasets (which corresponds to (Aleksandrova 2011 CC / IDF (M))), this dataset has met the criteria as an influential study.





Supplementary Figure 5.1 Association between HDL-C and CRA formation: (a) Forest plot; (b) Funnel plot. AA advanced adenomas, CI confidence interval, CRA colorectal cancer, HDL-C high-density lipoproteincholesterol, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, W women.



Supplementary Figure 5.2 Additional analyses for the association between HDL-C and CRA development: (a) Funnel plot after adjustment to publication bias with the trim and fill method. One simulated negative study was added (hollow circle) to the pooled estimates from the metaanalysis (solid circles). The adjusted RR slightly decreased from (1.02; 95% CI 0.92-1.12) in the initial analysis to (1.00; 95% CI 0.92-1.09) after adjustment. (b) Baujat plot: indicates that the 3rd, 4th, and 5th datasets contributed to the overall heterogeneity and result, and the 8th contributed to the overall heterogeneity (which corresponds to (Lin et al., 2014), (Hu 2011 CRA / NCEP-ATP III), and (Lee 2014 CRA / NCEP-ATP III)). (c) Influence plot: as there are two marked datasets (which corresponds to Lin et al., 2014), this study has met the criteria as an influential study.

Influence on Overall

0.20

0.10

8 - 10





Supplementary Figure 5.3 Association between HDL-C and CRC incidence: (a) Forest plot; (b) Funnel plot. CC colon cancer, CI confidence interval, CRC colorectal cancer, HDL-C high-density lipoprotein-cholesterol, M men, M-H Mantel-Haenszel, NCEP-ATP III National Cholesterol Education Program-Adult Treatment Panel III, RC rectal cancer, RR risk ratio, W women.



