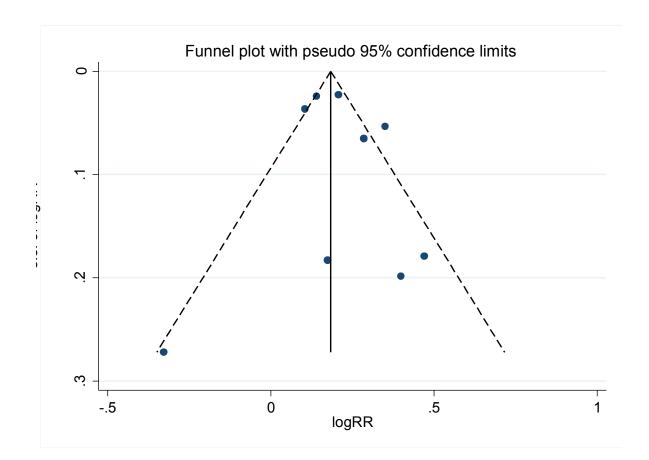
SUPPLEMENTAL MATERIAL

Supplemental Figure I. Funnel Plots Assessing for Publication Bias in Publications on Gallstone Disease and Risk of Coronary Heart Disease.



Citation (y)	Study population	Sample size, n	Baseline age (y)	Follow-up (y)	Participants with gallstone disease	CHD cases	Adjustment for potential confounders	Relative risk (95% Cl)
Bortnichak *, 1984 ¹	Framingham Heart Study original cohort	4,647 (males: 2171, females: 2476)	28-62	Up to 26	421 (diagnosed cholesterol gallstone disease)	699 (myocardial infarction, sudden death, coronary insufficiency, and angina pectoris)	Age, gender, overweight, left ventricular hypertrophy, smoking, systolic blood pressure, diabetes, serum cholesterol, and length of follow—up	Males: 1.60 (1.13–2.28) Females: 0.72 (0.42–1.22)
Olaiya, 2013	The Taiwan National Health Insurance Research Database	34,905	18-80	6	6,981 (diagnosed)	Not known (3,693 including stroke, CHD and heart failure cases)	Age, gender, peripheral vascular disease, chronic obstructive pulmonary disease, hypertension, diabetes, hyperlipidemia, alcoholism, chronic liver disease, and anemia	1.42 (1.28–1.58) (this estimate was for CHD only)
Wirth, 2013 ³	EPIC-Potsdam	24,422	35-65	On average 8.2	3,178 (self–reported)	243 (myocardial infarction)	Age, gender, education, physical activity, smoking, alcohol intake, BMI, waist circumference, hypertension and hyperlipidemia	1.19 (0.83-1.70)
	EPIC-Heidelberg	22,064			1,650 (self–reported)	264 (myocardial infarction)		1.49 (1.01–2.20)
Lv, 2015 ⁴	China Kadoorie Biobank study	487,373	30-79	7.2 (median)	28,345 (self–reported)	24,959 (ischemic heart disease)	Age, gender, education, level of education; marital status; alcohol consumption; smoking; physical activity; intake of red meat, fresh fruits, and vegetables; prevalent hypertension and	1.23 (1.17–1.28)

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							diabetes; family history of heart attack; menopausal status (for women only), and BMI	
Zheng, (present study)	Nurses' Health Study	112,520	30-55	Up to 30	8,796 (self–reported with high validity) ⁵	10,923 (myocardial infarction, and revascularization)	Age, BMI, myocardial infarction family history, smoking, alcohol intake, daily cholesterol intake,	1.15 (1.10–1.21)
Zheng, (present study)	Nurses' Health Study II	112,919	25-42	Up to 22	5,227 (self–reported with high validity) ⁵	1,397 (myocardial infarction, and revascularization)	daily energy intake, physical activity, race, marital status, post-menopausal	1.33 (1.17–1.51)
Zheng, (present study)	Health Professionals Follow-up Study	43,703	40-75	Up to 24	1,449 (self–reported with high validity) ⁵	8,945 (myocardial infarction, and revascularization)	hormone replacement, Alternative Health Eating Index Score, hypercholesterolemia, hypertension, diabetes, and regular aspirin use	1.11 (1.04–1.20)

^{*:} this study excluded the participants with baseline prevalent gallstone disease, this study presented odds ratio as the final result, and we used a statistical method to convert odds ratio to relative risk approximately.^{6, 7}

Supplemental References:

- 1. Bortnichak EA, Freeman DH, Jr., Ostfeld AM, Castelli WP, Kannel WB, Feinleib M, McNamara PM. The association between cholesterol cholelithiasis and coronary heart disease in framingham, massachusetts. *Am J Epidemiol*. 1985;121:19-30
- 2. Olaiya MT, Chiou HY, Jeng JS, Lien LM, Hsieh FI. Significantly increased risk of cardiovascular disease among patients with gallstone disease: A population-based cohort study. *PLoS One*. 2013;8
- 3. Wirth J, Giuseppe RD, Wientzek A, Katzke VA, Kloss M, Kaaks R, Boeing H, Weikert C. Presence of gallstones and the risk of cardiovascular diseases: The epic-germany cohort study. *Eur J Prev Cardiol*. 2015;22:326-334
- 4. Lv J, Qi L, Yu C, Guo Y, Bian Z, Chen Y, Yang L, Shen J, Wang S, Li M, Liu Y, Zhang L, Chen J, Chen Z, Li L. Gallstone disease and the risk of ischemic heart disease. *Arterioscler Thromb Vasc Biol*. 2015;35:2232-2237
- 5. Leitzmann MF WW, Rimm EB, Stampfer MJ, Spiegelman D, Colditz GA, Giovannucci E. A prospective study of coffee consumption and the risk of symptomatic gallstone disease in men. *JAMA*. 1999;281:2106-2112
- 6. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998;280:1690-1691
- 7. Wang Z. Converting odds ratio to relative risk in cohort studies with partial data information. J Stat Softw. 2013;55