SUPPLEMENTARY DIGITAL CONTENT

List of Supplementary Digital Content

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Appendix 1: Search String

Number	Search Terms	Medline (PubMed)	OVID Medline	Embase	Web of Science	Cochrane
1	((myocardial ischemia[MeSH Terms]) OR (myocardial ischemia[Title/Abstract]) OR (acute coronary syndrome[MeSH Terms]) OR (acute coronary syndrome*[Title/Abstract]) OR (myocardial infarction[MeSH Terms]) OR (myocardial infarction[Title/Abstract]) OR (coronary artery disease[MeSH Terms]) OR (coronary artery disease[Title/Abstract]) OR (heart attack[Title/Abstract]) OR (percutaneous coronary intervention[MeSH Terms]) OR (percutaneous coronary intervention[Title/Abstract]) OR (drug-eluting stents[MeSH Terms]) OR (drug-eluting stent*[Title/Abstract]) OR (drug eluting stent*[Title/Abstract]))	**484,438**	**582,176**	**894,761**	**667, 555**	**59377**
2	((inflammatory bowel diseases[MeSH Terms]) OR (inflammatory bowel disease*[Title/Abstract]) OR (crohn disease[MeSH Terms]) OR (colitis, ulcerative[MeSH Terms]) OR (ulcerative colitis[Title/Abstract]))	**108,905**	**123173**	**221,773**	**140, 394**	**8888**
3	1 AND 2	**508**	**514**	**2,556**	**664**	**46**

Total = 3328 (960 duplicates excluded manually)

Appendix 2: Justification of Exclusions at Full-Text Review

Studies included after full-text review (n=12)

1. Aniwan S, Roger V, Pardi DS, Tremaine WJ, Loftus EV. Risk of myocardial infarction and congestive heart failure in inflammatory bowel disease: A population-based inception cohort study. Gastroenterology. 2017;152(5):S76-S7.
2. Card TR, Zittan E, Nguyen GC, Grainge MJ. Disease Activity in Inflammatory Bowel Disease Is Associated with Arterial Vascular Disease. Inflammatory Bowel Diseases. 2021;27(5):629-38.
3. Kristensen SL, Ahlehoff O, Lindhardsen J, Erichsen R, Jensen GV, Torp-Pedersen C, et al. Disease Activity in Inflammatory Bowel Disease Is Associated with Increased Risk of Myocardial Infarction, Stroke and Cardiovascular Death - A Danish Nationwide Cohort Study. PLoS ONE. 2013;8(2).
4. Rungoe C, Basit S, Ranthe MF, Wohlfahrt J, Langholz E, Jess T. Risk of ischaemic heart disease in patients with inflammatory bowel disease: A nationwide Danish cohort study. Gut. 2013;62(5):689-94.
5. Osterman MT, Yang YX, Brensinger C, Forde KA, Lichtenstein GR, Lewis JD. No increased risk of myocardial infarction among patients with ulcerative colitis or Crohn's disease. Clin Gastroenterol Hepatol. 2011;9(10):875-80.
6. Setyawan J, Mu F, Zichlin ML, Billmyer E, Downes N, Yang HB, et al. Risk of Thromboembolic Events and Associated Healthcare Costs in Patients with Inflammatory Bowel Disease. ADVANCES IN THERAPY. 2022;39(1):738-53.
7. Sinha A, Rivera AS, Chadha SA, Prasada S, Pawlowski AE, Thorp E, et al. Comparative Risk of Incident Coronary Heart Disease Across Chronic Inflammatory Diseases. Frontiers in cardiovascular medicine. 2021;8:757738.
8. Tsai M-S, Lin C-L, Chen H-P, Lee P-H, Sung F-C, Kao C-H. Long-term risk of acute coronary syndrome in patients with inflammatory bowel disease: a 13-year nationwide cohort study in an Asian population. Inflammatory bowel diseases. 2014;20(3):502-7.
9. Yarur AJ, Deshp, e AR, Pechman DM, Tamariz L, Abreu MT, et al. Inflammatory bowel disease is associated with an increased incidence of cardiovascular events. American Journal of Gastroenterology. 2011;106(4):741-7.
10. Choi YJ, Lee DH, Shin DW, Han K-D, Yoon H, Shin CM, et al. Patients with inflammatory bowel disease have an increased risk of myocardial infarction: a nationwide study. Alimentary pharmacology & therapeutics. 2019;50(7):769-79.
11. Ha C, Magowan S, Accortt NA, Chen J, Stone CD. Risk of arterial thrombotic events in inflammatory bowel disease. American Journal of Gastroenterology. 2009;104(6):1445-51.
12. Gill GS, Fern, ez SJ, Malhotra N, Mete M, Garcia-Garcia HM. Major acute cardiovascular events in patients with inflammatory bowel disease. Coronary Artery Disease. 2020:73-7.

Studies excluded after full-text review (n=23)

Wrong population

Prior Myocardial Infarction

1. Aggarwal A, Atreja A, Kapadia S, Lopez R, Achkar J-P. Conventional risk factors and cardiovascular outcomes of patients with inflammatory bowel disease with confirmed coronary artery disease. Inflammatory bowel diseases. 2014;20(9):1593-601.
2. Close H, Mason JM, Wilson DW, Hungin APS, Jones R, Rubin G. Risk of ischaemic heart disease in patients with inflammatory bowel disease: Cohort study using the general practice research database. PLoS ONE. 2015;10(10).
3. Kristensen SL, Ahlehoff O, Lindhardsen J, Erichsen R, Lamberts M, Khalid U, et al. Prognosis after first-time myocardial infarction in patients with inflammatory bowel disease according to disease activity: Nationwide cohort study. Circulation: Cardiovascular Quality and Outcomes. 2014;7(6):857-62.
4. Popovic B, Varlot J, Hennequin J, Metzdorf PA, Jay N, Camenzind E, et al. Outcomes after acute coronary syndrome in patients with inflammatory bowel disease. Heart and Vessels. 2022;37(9):1604-10.

Wrong exposure

1. Kwon OC, Han K, Chun J, Kim R, Hong SW, Kim JH, et al. Effects of immune-mediated inflammatory diseases on cardiovascular diseases in patients with type 2 diabetes: a nationwide population-based study. Scientific reports. 2022;12(1):11548.
2. Marcusohn E, Zukermann R, Kerner A, Roguin A, Kobo O. Long-term outcomes of patients with chronic inflammatory diseases after percutaneous coronary intervention. Catheterization and Cardiovascular Interventions. 2021;98(5):E655-E60.

ACS population not specified

1. Bernstein CN, Wajda A, Blanchard JF. The incidence of arterial thromboembolic diseases in inflammatory bowel disease: a population-based study. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2008;6(1):41-5.
2. Dregan A, Charlton J, Chowienczyk P, Gulliford MC. Chronic inflammatory disorders and risk of type 2 diabetes mellitus, coronary heart disease, and stroke: a population-based cohort study. Circulation. 2014;130(10):837-44.
3. Dregan A, Chowienczyk P, Molokhia M. Cardiovascular and type 2 diabetes morbidity and all-cause mortality among diverse chronic inflammatory disorders. Heart. 2017;103(23):1867-73.
4. Kirchgesner J, Beaugerie L, Carrat F, Andersen NN, Jess T, Schwarzinger M. Increased risk of acute arterial events in young patients and severely active IBD: a nationwide French cohort study. Gut. 2018;67(7):1261-8.
5. Lee MT, Mahtta D, Chen L, Hussain A, Al Rifai M, Sinh P, et al. Premature Atherosclerotic Cardiovascular Disease Risk Among Patients with Inflammatory Bowel Disease. American Journal of Medicine. 2021;134(8):1047-51.e2.

6. Nasir K, Acquah I, Dey AK, Agrawal T, Hassan SZ, Glassner K, et al. Inflammatory bowel disease and atherosclerotic cardiovascular disease in U.S. adults-A population-level analysis in the national health interview survey. American journal of preventive cardiology. 2022;9:100316.
7. Thapa SD, Hadid H, Imam W, Hassan A, Usman M, Jafri SM, et al. Persistent Reactive Thrombocytosis May Increase the Risk of Coronary Artery Disease Among Inflammatory Bowel Disease Patients. Digestive Diseases and Sciences. 2015;60(10):3062-8
8. Fang LL, Gao H, Gao X, Wu W, Miao YL, Zhang HJ, et al. Risks of Cardiovascular Events in Patients With Inflammatory Bowel Disease in China: A Retrospective Multicenter Cohort Study. INFLAMMATORY BOWEL DISEASES. 2022;28:S52-S8.

Wrong Study Design

Case Control or Cross-Sectional Studies

1. Barnes EL, Beery RM, Schulman AR, McCarthy EP, Korzenik JR, Winter RW. Hospitalizations for Acute Myocardial Infarction Are Decreased among Patients with Inflammatory Bowel Disease Using a Nationwide Inpatient Database. Inflammatory Bowel Diseases. 2016;22(9):2229-37.
2. Ehrenpreis ED, Zhou Y, Alexoff A, Melitas C. Effect of the diagnosis of inflammatory bowel disease on risk-adjusted mortality in hospitalized patients with acute myocardial infarction, congestive heart failure and pneumonia. PLoS ONE. 2016;11(7).
3. Golovics PA, Verdon C, Wetwittayakhlang P, Filliter C, Gonczi L, Hahn GD, et al. Increased Prevalence of Myocardial Infarction and Stable Stroke Proportions in Patients with Inflammatory Bowel Diseases in Quebec in 1996–2015. Journal of Clinical Medicine. 2022;11(3).
4. Le Gall G, Kirchgesner J, Bejaoui M, man C, Nion-Larmurier I, Bourrier A, et al. Clinical activity is an independent risk factor of ischemic heart and cerebrovascular arterial disease in patients with inflammatory bowel disease. PLoS ONE. 2018;13(8).
5. Panhwar MS, Mansoor E, Al-Kindi SG, Sinh P, Katz J, Oliveira GH, et al. Risk of Myocardial Infarction in Inflammatory Bowel Disease: A Population-based National Study. Inflammatory Bowel Diseases. 2019;25(6):1080-7.
6. Pemmasani G, Elgendy I, Mamas MA, Leighton JA, Aronow WS, Tremaine WJ. Epidemiology and Clinical Outcomes of Patients with Inflammatory Bowel Disease Presenting with Acute Coronary Syndrome. Inflammatory Bowel Diseases. 2021;27(7):1017-25.
7. Sinh P, Tabibian JH, Biyani PS, Mehta K, Mansoor E, Loftus EV, et al. Inflammatory Bowel Disease Does Not Impact Mortality but Increases Length of Hospitalization in Patients with Acute Myocardial Infarction. Digestive Diseases and Sciences. 2021;66(12):4169-77.
8. Zakroysky P, Thai W-E, Deaño RC, Basnet S, eep, On, et al. Steroid exposure, acute coronary syndrome, and inflammatory bowel disease: insights into the inflammatory milieu. The American journal of medicine. 2015;128(3):303-11.

Insufficient Data

Unable to extract data for meta-analysis

1. Kobo O, Mohamed MO, Farmer AD, Alraies CM, Patel T, Sharma K, et al. Outcomes of Percutaneous Coronary Intervention in Patients With Crohn's Disease and Ulcerative Colitis (from a Nationwide Cohort). American Journal of Cardiology. 2020;130:30-6

Appendix 3: Risk of bias assessment for included studies using the Downs and Black checklist

Study	Reporting average (/11)	External validity average (/3)	Internal Validity - Bias average (/7)	Internal Validity - Confounding average (/5)	Power average (/1)	Total Score	Rating
Aniwan	8	2	4	1	0	15	Fair
Card	8	2	4	1	0	15	Fair
Ha	8	2	4	1	0	15	Fair
Kristensen	8	2	4	3	0	17	Fair
Rungoe	8	2	4	1	0	15	Fair
Setyawan	8	2	4	2	0	16	Fair
Sinha	8	2	4	1	0	15	Fair
Tsai	8	2	4	3	0	17	Fair
Yarur	8	2	4	3	0	17	Fair
Choi	8	2	4	1	0	15	Fair
Gill	8	2	4	1	0	15	Fair

Appendix 4: Complete Data

6.1 - For complete data, see attached excel sheet.

Appendix 5: Extra Figures

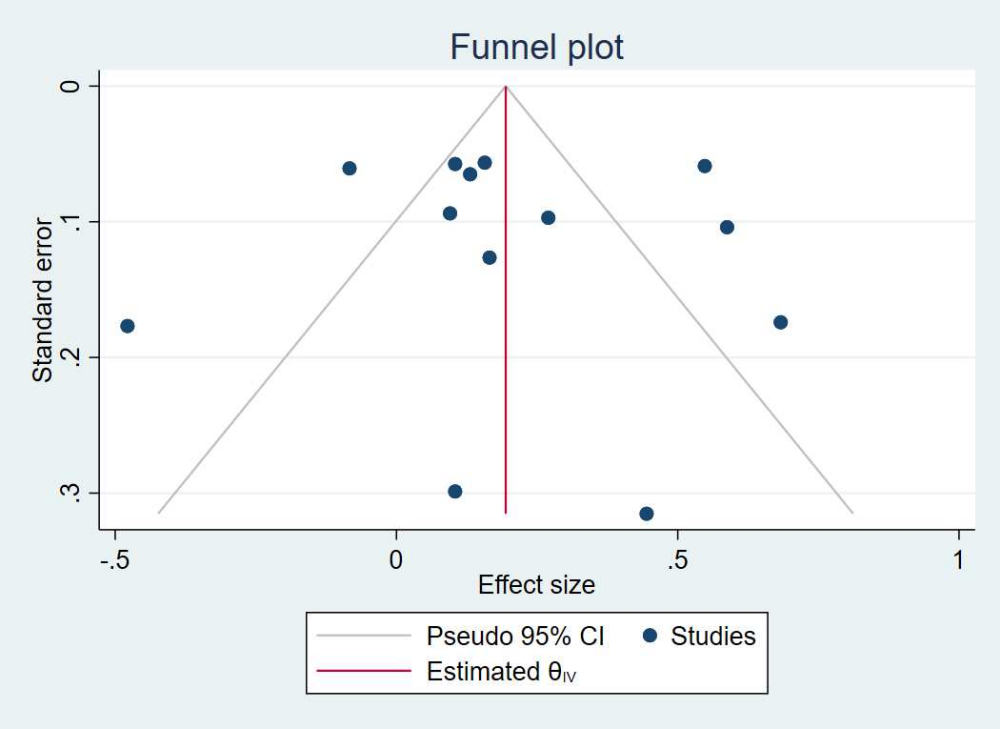

Figure 5: Funnel plot of the adjusted association between IBD and ACS

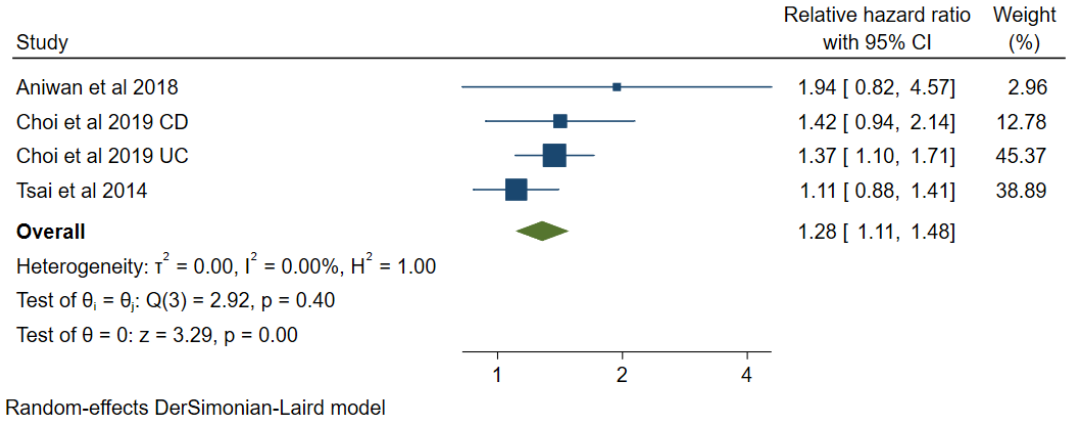

Figure 6: Meta-analysis of the relative association between IBD and ACS for females vs males

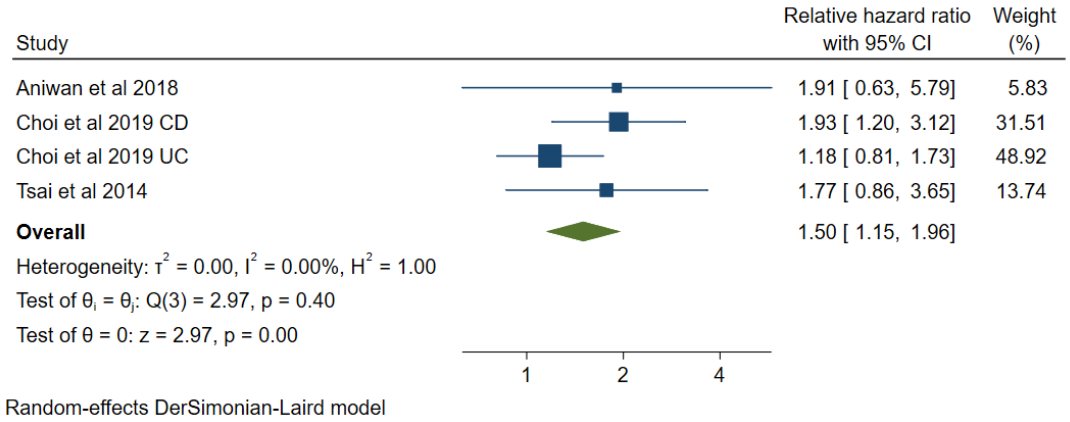

Figure 7: Meta-analysis of the relative association between IBD and ACS for age ≤40 vs >40 years

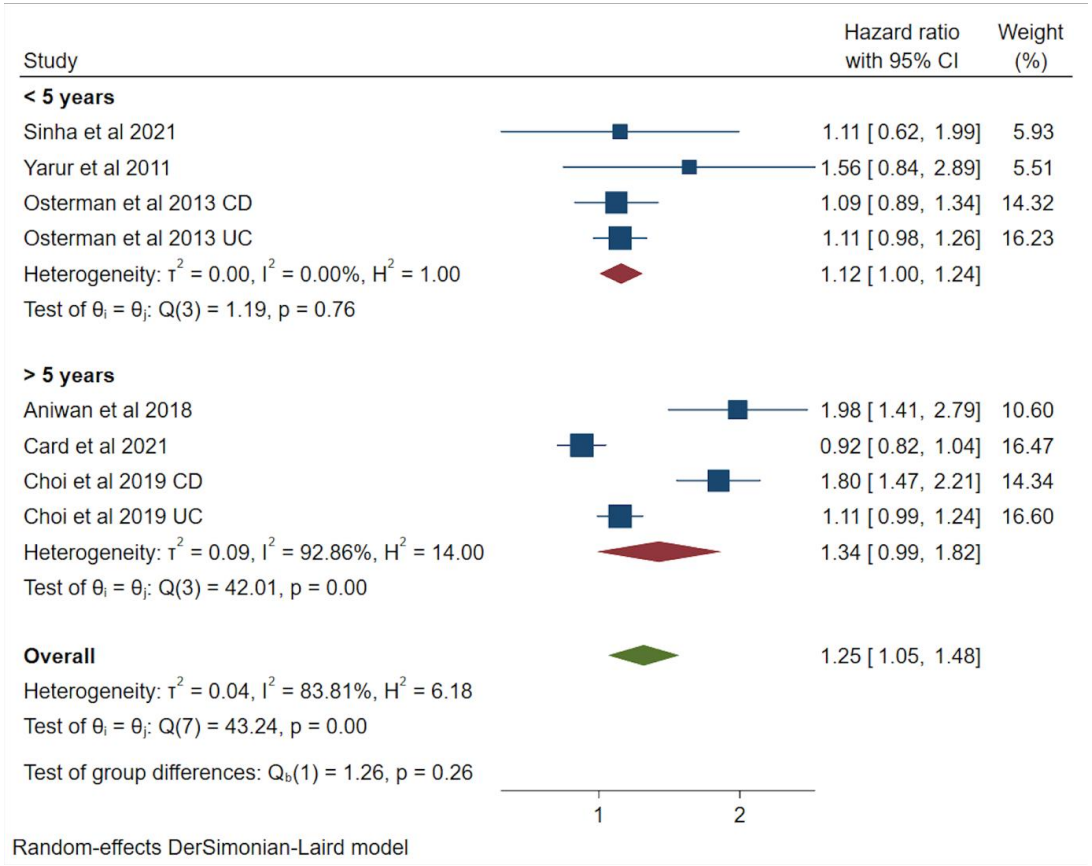

Figure 8 - Subgroup analysis based on follow-up duration

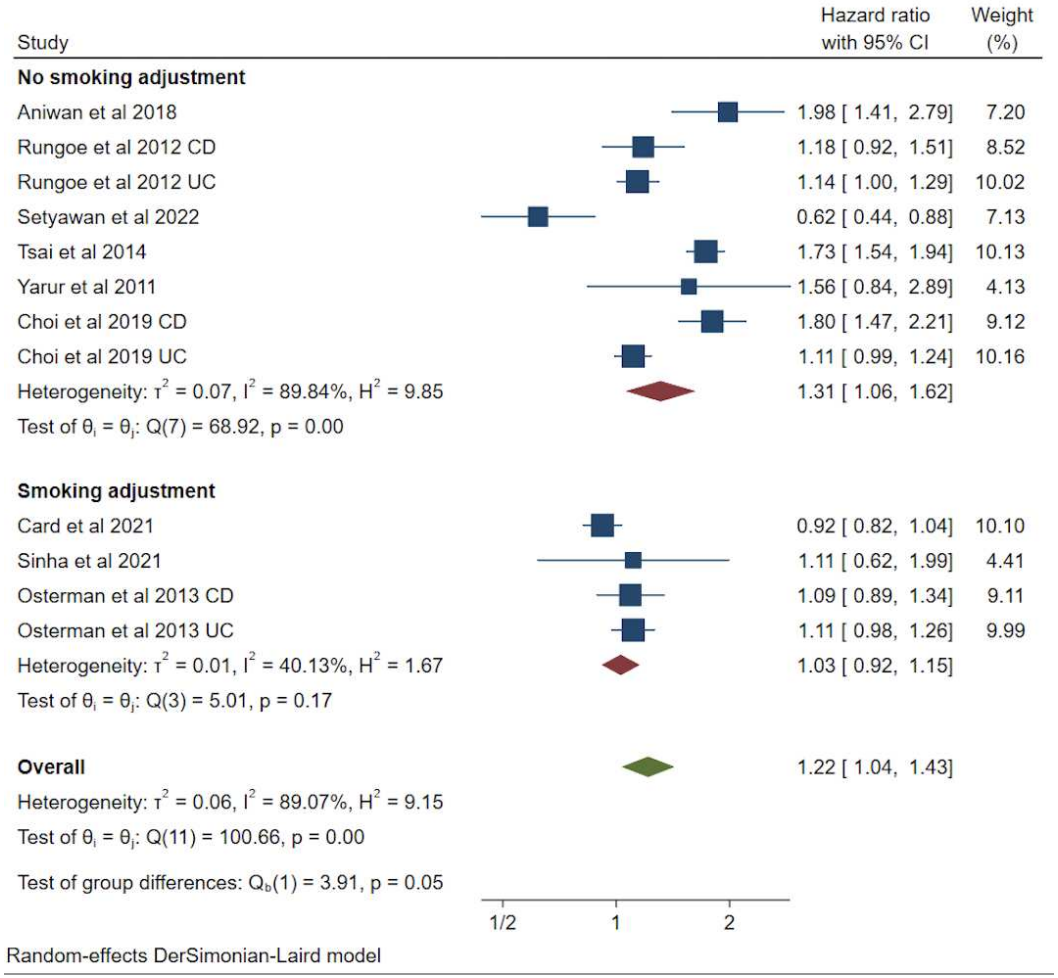

Figure 9 – Subgroup analysis of confounders: smoking

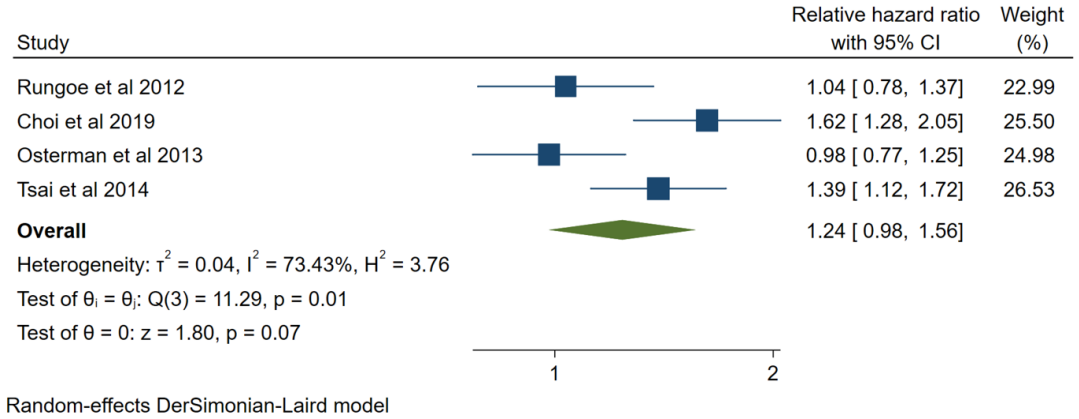

Figure 10 – Crohn Disease versus Ulcerative Colitis