

Cover page

Title: The relationship between rosacea and inflammatory bowel disease: A systematic review and meta-analysis

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Search strategy

Search strategies for Ovid MEDLINE, Embase, and Cochrane Library were described.

Ovid MEDLINE: 242 studies

	Search word	Number of result
#1	exp Alopecia/	3,233
#2	"Alopecia".ab,ti.	3,435
#3	1 or 2	4,353
#4	exp Gastrointestinal Diseases/	993,666
#5	"Cholera Infantum*".ab,ti.	11
#6	(gastro* adj5 (disease* or disorder* or comorbid* or prevalen* or incident* or associ* or relation* or risk*)).ab,ti.	72,586
#7	"inflammatory bowel disease*".ab,ti.	51,692
#8	"ulcerative colit*".ab,ti.	41,088
#9	"crohn*".ab,ti.	49,297
#10	"Enterocoliti*".ab,ti.	18,320
#11	"proctit*".ab,ti.	2,612
#12	"Ileit*".ab,ti.	2,239
#13	"Gluten Enteropath*".ab,ti.	162
#14	"Gluten Sensitive Enteropath*".ab,ti.	609
#15	"Sprue*".ab,ti.	2,189
#16	Idiopathic Proctocolitis.ab,ti.	32
#17	"Ulcerative Colit*".ab,ti.	41,088
#18	"Irritable Bowel Syndrome*".ab,ti.	13,745
#19	"Irritable Colon*".ab,ti.	446
#20	"Mucous Coliti*".ab,ti.	23
#21	exp Helicobacter pylori/	35,765
#22	"Helicobacter*".ab,ti.	44,172
#23	"Campylobacter pylori*".ab,ti.	1,083
#24	exp Gastrointestinal Neoplasms/	397,930
#25	(Gastro* adj5 (Neoplasm* or Tumor* or Cancer* or Carcinoma*)).ab,ti.	33,533
#26	(Colo* adj5 (Neoplasm* or Tumor* or Cancer* or Carcinoma*)).ab,ti.	210,877

#27	Alactasia.ab,ti.	9
#28	Hypolactasia.ab,ti.	270
#29	Lactose Malabsorption.ab,ti.	594
#30	lactose intolerance.ab,ti.	1,429
#31	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30	1,165,532
#32	3 and 31	242

Embase: 383 studies

	Search word	Number of result
#1	'rosacea'/exp	6,845
#2	rosacea:ab,ti	4,992
#3	#1 OR #2	7,495
#4	'gastrointestinal disease'/exp	99,258
#5	'cholera infantum*':ab,ti	8
#6	(gastro* NEAR/5 (disease* OR disorder* OR comorbid* OR prevalen* OR incident* OR associ* OR relation* OR risk*)):ab,ti	109,546
#7	'inflammatory bowel disease*':ab,ti	86,193
#8	'ulcerative colit*':ab,ti	68,337
#9	crohn*:ab,ti	85,592
#10	enterocoliti*:ab,ti	23,589
#11	proctit*:ab,ti	4,767
#12	ileit*:ab,ti	3,483
#13	'gluten enteropath*':ab,ti	244
#14	'gluten sensitive enteropath*':ab,ti	793
#15	sprue*:ab,ti	2,514
#16	'idiopathic proctocolitis':ab,ti	43
#17	'ulcerative colit*':ab,ti	68,337
#18	'irritable bowel syndrome*':ab,ti	22,093
#19	'irritable colon*':ab,ti	583
#20	'mucous coliti*':ab,ti	17
#21	'helicobacter pylori'/exp	56,468
#22	helicobacter*:ab,ti	59,224
#23	'campylobacter pylori*':ab,ti	1,379

#24	'gastrointestinal tumor'/exp	30,299
#25	(gastro* NEAR/5 (neoplasm* OR tumor* OR cancer* OR carcinoma*)):ab,ti	50,861
#26	(colo* NEAR/5 (neoplasm* OR tumor* OR cancer* OR carcinoma*)):ab,ti	308,144
#27	alactasia:ab,ti	12
#28	hypolactasia:ab,ti	370
#29	'lactose malabsorption':ab,ti	770
#30	'lactose intolerance':ab,ti	2,152
#31	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30	788,892
#32	#3 AND #31	383

Cochrane Library: 19 studies

	Search word	Number of result
#1	MeSH descriptor: [Rosacea] explode all trees	279
#2	(rosacea):ti,ab,kw	618
#3	#1 OR #2	619
#4	MeSH descriptor: [Gastrointestinal Diseases] explode all trees	35,677
#5	(Cholera Infantum*):ti,ab,kw	-
#6	((gastro* NEAR/5 (disease* OR disorder* OR comorbid* OR prevalen* OR incident* OR associ* OR relation* OR risk*))) :ti,ab,kw	13,974
#7	(inflammatory bowel disease*):ti,ab,kw	3,766
#8	(ulcerative colit*):ti,ab,kw	5,188
#9	(crohn*):ti,ab,kw	5,071
#10	(enterocoliti*):ti,ab,kw	1,993
#11	(proctit*):ti,ab,kw	530
#12	(ileit*):ti,ab,kw	164
#13	(gluten enteropath*):ti,ab,kw	31
#14	(gluten sensitive enteropath*):ti,ab,kw	5
#15	(sprue*):ti,ab,kw	27
#16	(idiopathic proctocolitis):ti,ab,kw	4
#17	(ulcerative colit*):ti,ab,kw	5,188
#18	(irritable bowel syndrome*):ti,ab,kw	3,897
#19	(irritable colon*):ti,ab,kw	2,170

#20	(mucous coliti*):ti,ab,kw	22
#21	(helicobacter pylori):ti,ab,kw	5,368
#22	(helicobacter*):ti,ab,kw	5,468
#23	(campylobacter pylori*):ti,ab,kw	107
#24	MeSH descriptor: [Gastrointestinal Neoplasms] explode all trees	13,272
#25	((gastro* NEAR/5 (neoplasm* OR tumor* OR cancer* OR carcinoma*))) :ti,ab,kw	3,929
#26	((colo* NEAR/5 (neoplasm* OR tumor* OR cancer* OR carcinoma*))) :ti,ab,kw	20,245
#27	(alactasia):ti,ab,kw	-
#28	(hypolactasia):ti,ab,kw	22
#29	(lactose malabsorption):ti,ab,kw	122
#30	(lactose intolerance):ti,ab,kw	405
#31	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30	73,842
#32	#3 AND #31	19

Table S1. Newcastle-Ottawa quality assessment scale

Quality assessment of included case-control studies by the Newcastle-Ottawa scale

	Selection				Comparability	Exposure		
	Is the case definition adequate?	Representativeness of the cases	Selection of controls	Definition of controls	Comparability of cases and cohorts on the basis of the design or analysis	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-Response rate
Spoendlin <i>et al.</i> , 2016	★	★	-	★	★	★	★	-

Quality assessment of included cross-sectional studies by the modified Newcastle-Ottawa scale

	Selection				Comparability	Outcome	
	Representativeness of the cases	Sample size	non-respondents	Ascertainment of exposure	Comparability of groups on the basis of the design or analysis	Assessment of outcome	Statistical test
Jo <i>et al.</i> , 2021	★	★	-	-	★	★★	★
Kim <i>et al.</i> , 2017	★	★	-	-	★	★★	★

Quality assessment of included cohort studies by the Newcastle-Ottawa scale

	Selection				Comparability	Outcome		
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts
Egeberg <i>et al.</i> , 2017	★	★	★	★	★	★	★	-
Hung <i>et al.</i> , 2021	★	★	★	★	★	★	★	-
Li <i>et al.</i> , 2016	-	-	★	★	★	★	★	-
Lo <i>et al.</i> , 2021	-	-	★	★	★	★	★	-
Wu <i>et al.</i> , 2017	★	★	★	★	★	★	★	-

Figure S1. Funnel plot of studies examining the prevalence of rosacea in IBD, CD, and UC group. IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis.

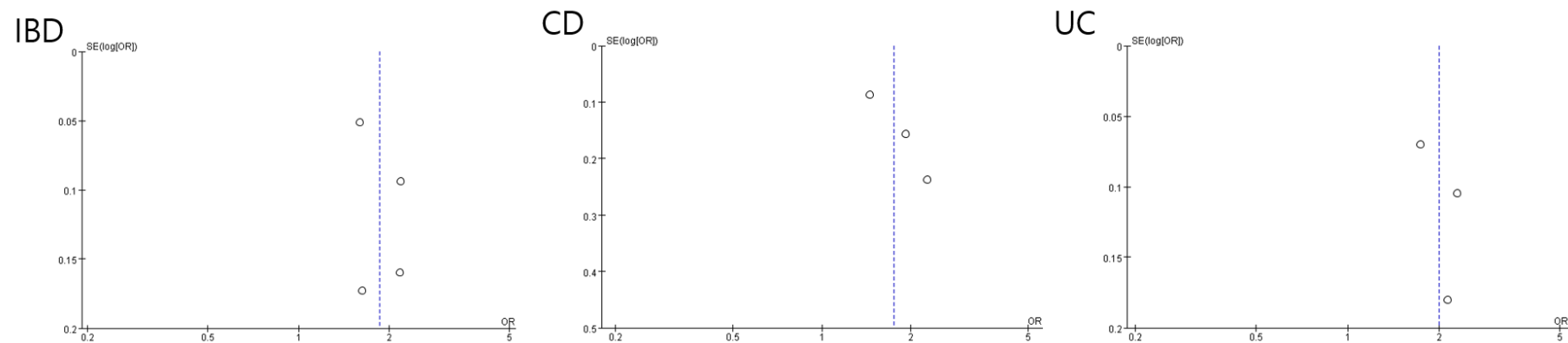
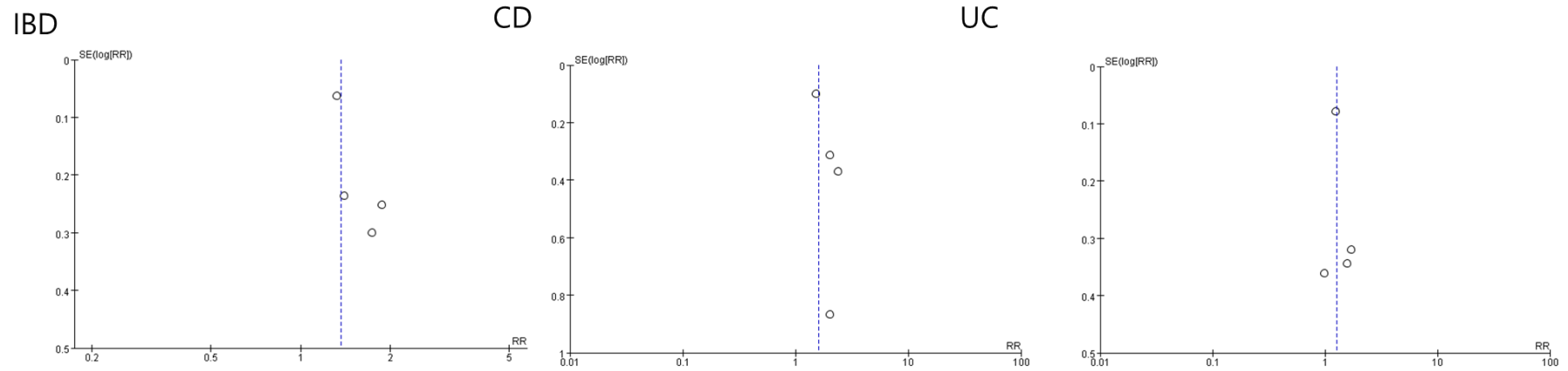


Figure S2. Funnel plot of studies examining the relative risk of IBD, CD, and UC in rosacea group. IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis.



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Manuscript Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Supplementary file
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Manuscript Page 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Manuscript Page 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Manuscript Page 4
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.	Manuscript Page 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supplementary file
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.	Manuscript Page 4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Manuscript Page 4
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.	Manuscript Page 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding	Manuscript

Section and Topic	Item #	Checklist item	Location where item is reported
		sources). Describe any assumptions made about any missing or unclear information.	Page 4
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.	Supplementary file
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.	Manuscript Page 5
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)).	Manuscript Page 4-5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Manuscript Page 4-5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Manuscript Page 4-5
	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.	Manuscript Page 5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	-
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	-
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Supplementary file
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Manuscript Page 4-5
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.	Manuscript Page 5
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	-
Study characteristics	17	Cite each included study and present its characteristics.	Manuscript Page 5, Table 1

Section and Topic	Item #	Checklist item	Location where item is reported
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary file
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Manuscript Page 5-6
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Manuscript Page 6 Supplementary file
	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.	Manuscript Page 5-6
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	-
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	-
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Manuscript Page 6 Supplementary file
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Manuscript Page 5-6
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Manuscript Page 6
	23b	Discuss any limitations of the evidence included in the review.	Manuscript Page 9
	23c	Discuss any limitations of the review processes used.	Manuscript Page 9
	23d	Discuss implications of the results for practice, policy, and future research.	Manuscript Page 9
OTHER INFORMATION			

Section and Topic	Item #	Checklist item	Location where item is reported
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Manuscript Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	-
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	-
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Manuscript Page 10
Competing interests	26	Declare any competing interests of review authors.	Title page
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.	Supplementary file

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

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