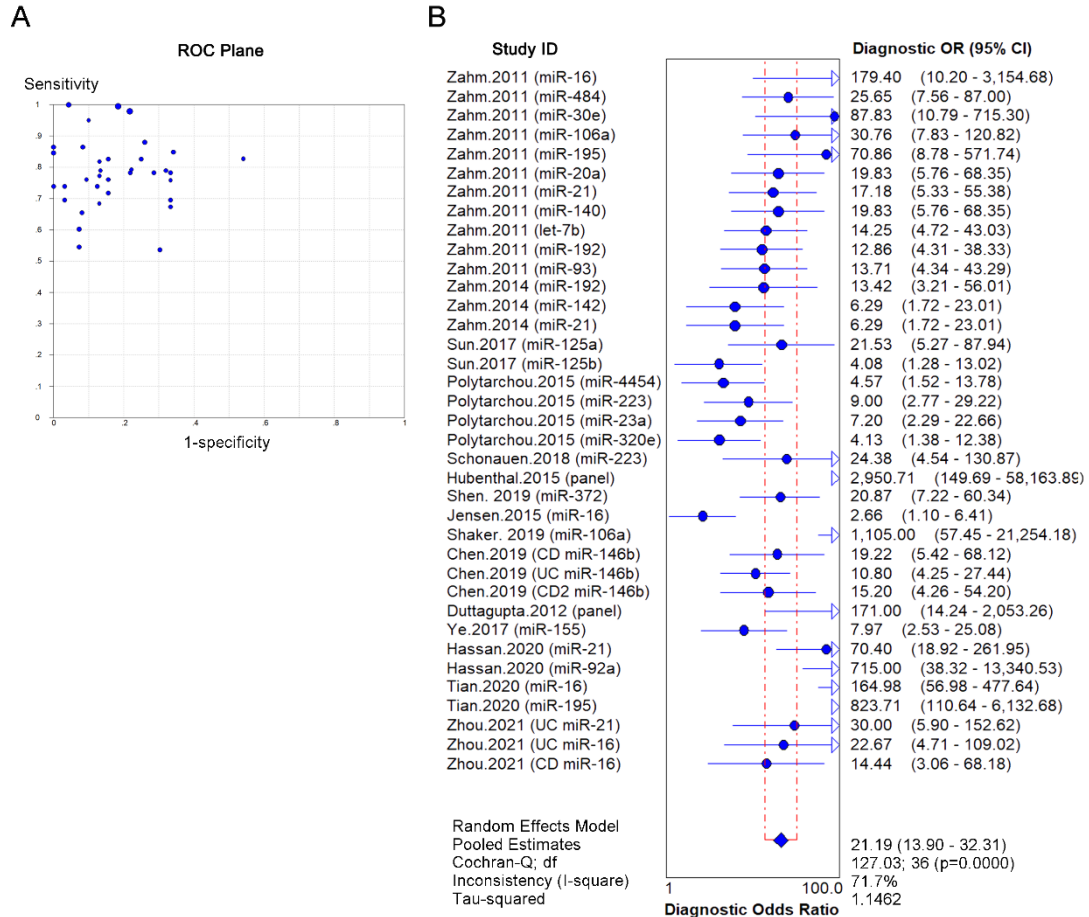


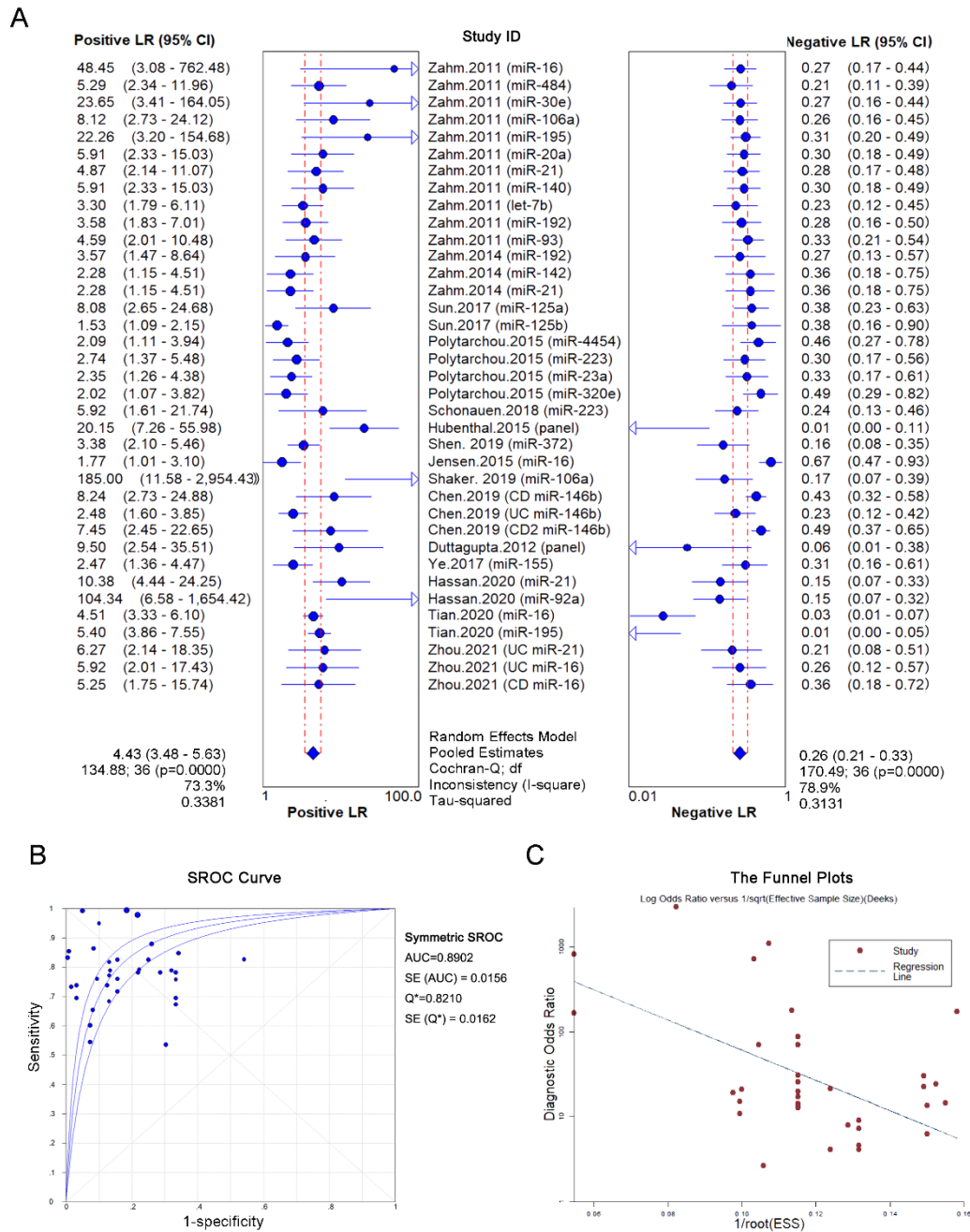
## Supplementary Figures

### Supplementary Figure 1



**Figure S1 Heterogeneity analysis by the ROC plane and by the diagnostic odds ratio. A, Heterogeneity analysis by the ROC plane. B, Diagnostic odds ratio of altered miRNA expression in IBD diagnosis of in all studies. ROC: receiver operating characteristic.**

Supplementary Figure 2



**Figure S2 Forest plot of meta-analysis of aberrant expression of microRNAs and its diagnostic value index in IBD, and publication bias assessment by Deeks' funnel plot. A, Positive likelihood ratio and negative likelihood ratio of altered miRNA expression in IBD diagnosis in all studies. B, sROC of altered miRNA expression in IBD diagnosis in all studies. C, Publication bias assessment by Deeks' funnel plot. IBD: inflammatory bowel diseases; miRNA: microRNAs; sROC: summary receiver operating characteristic.**

## Supplementary Tables

**Table S1 Text-words terms used in searching literature.**

No.	MeSH terms/text words used
#1	"Inflammatory Bowel Diseases"[Mesh]
#2	"Crohn Disease"[Mesh]
#3	"Colitis, Ulcerative"[Mesh]
#4	"Enterocolitis"[Mesh]
#5	"Proctitis"[Mesh]
#6	"Ileitis"[Mesh]
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6
#8	"inflammatory bowel disease*"[All Fields]
#9	crohn*[All Fields]
#10	"ulcerative colitis"[All Fields]
#11	#8 OR #9 OR #10
#12	#7 OR #11
#13	"MicroRNAs"[Mesh]
#14	miR*[All Fields]
#15	miRNA*[All Fields]
#16	MicroRNA*[All Fields]
#17	#13 OR #14 OR #15 OR #16
#18	#12 AND #17

**Table S2 Systematic review of included studies that detected altered miRNA expression in patients with IBD using miRNA microarray analysis.**

Study ID	Platform of miRNA microarray	miRNA probes	Expression validation	Sample from disease/control (N or pairs)	Cut off	Patients with IBD				Controls				Sample type	The most frequently altered miRNAs ( $\geq 4$ -fold)		Related clinical/pathological factors	
						Disease	Gender % (Male/Female)	Age (y) mean $\pm$ SD/mean(range)/mean	Case number	Control	Gender % (Male/Female)	Age (y) mean $\pm$ SD/mean(range)/mean	Case number		Over-expressed miRNAs	Down-regulated miRNAs		
Lu Yi Wu 2017	miRCURY LNA microRNA Array	36,333	qPCR	7 CD with inflammation, 7 CD without inflammation and 7 healthy controls	2 folds	Active CD	NA	NA	14	Healthy controls	NA	NA	7	Mucosa	miR-451, miR-31, miR-144, miR-142-5p, miR-142-3p, miRPlus-A1087, miR-374a, miR-338-3p, miR-223, miR-21, miR-126, let-7a	miRPlus-E1186, miRPlus-E1028, miR-1937	NA	
Zhen Guo 2015	miRCURY LNA microRNA Array	3100	qPCR	6 pairs CD and 6 healthy controls	2 folds	Active CD	NA	NA	6	Healthy controls	NA	NA	6	Mucosa	miR-4644, miR-4709-3p, miR-5187-3p, miR-4445-5p	let-7g-5p, miR-101-3p, miR-141-3p, miR-145-5p, miR-192-5p, miR-200c-3p, miR-21-5p, miR-22-3p, miR-23b-3p, miR-24-3p, miR-29a-3p, miR-4286, miR-4454, miR-5701, miR-767-5p, let-7b-5p, miR-142-3p, miR-191-5p, miR-200b-3p, miR-		NA

																30c-5p, miR-31-5p, miR-4284	
<b>Ayilia Mohammedi 2018</b>	Nanostring technology platform	NA	NA	35 CD, 46 UC and 39 healthy controls	NA	IBD	49.38/50.62	CD: 33±13, UC: 36±10	81	Healthy controls	41.03/58.97	56±9	39	PBMC	Non	Non	IBD type
<b>Yahong Ji 2018</b>	miRCURY LNA microRNA Array	345	qPCR	51 CD, 66 UC and 66 healthy controls	4 folds	IBD	NA	45.19	117	Healthy controls	NA	49.5	66	Feces	miR-199a-5p, miR-223-3p	miR-1226, miR-548ab, miR-515-5p	IBD type, disease severity
<b>Angelos Oikonomopoulos 2016</b>	Nanostring technology platform	NA	NA	45 CD and 21 healthy controls	2 folds	CD	51/49	42±14	45	Healthy controls	38/62	33±8	21	Serum	miR-30e-5p	miR-1183, miR-1286, miR-504	Disease severity, disease location
<b>Feng Wu 2010</b>	Ncode Multi-Species miRNA Microarrays	467	qPCR	11 CD and 13 healthy controls	2 folds	Active CD	72.73/27.27	36.8 (23-64)	11	Healthy controls	46.15/53.85	54.6 (38-68)	13	Mucosa	miR-21, miR-223	Non	IBD type, location
<b>Magali Fasseu 2010</b>	qPCR	321	NA	16 CD and 10 healthy controls	5 folds	IBD	56.25/43.75	41.75 (20-58)	16	Healthy controls	NA	NA	10	Mucosa	miR-126*, miR-29a, miR-29b, miR-324-3p, miR-127-3p, miR-196a, miR-26a, miR-34c-5p, miR-133b, miR-30b, miR-155, miR-106a, miR-22, miR-29c, miR-31, miR-150, miR-21,	miR-320a, miR-215, miR-346, miR-188-5p	IBD type, disease severity

															miR-146b-5p, miR-146a		
<b>M. Iborra 2013</b>	TaqMan® human miRNA array	700	qPCR	18 CD, 18 UC and 33 healthy controls	2 folds	IBD	58.33/41.67	43.08	36	Healthy controls	54.55/45.45	47.3±9.6	33	Serum and Mucosa	miR-27a*, miR-760, miR-423-5p, miR-128, miR-196b, miR-103, miR-221, miR-532-5p, miR-15b, miR-27a	Non	IBD type, disease severity
<b>Tomohisa Takagi 2010</b>	Ncode human miRNA microarrays	710	qPCR	2 active UC and 2 healthy controls	P < 0.05	Active UC	50/50	35±11	2	Healthy controls	50/50	48±11	2	Mucosa	let-7a, let-7c, let-7d, let-7g, miR-21, miR-155, miR-923	Non	NA
<b>Jan Van der Goten 2014</b>	Affymetrix GeneChip microRNA arrays	4560	qPCR	10 active UC, 7 inactive UC and 10 healthy controls	Top 20	UC	58.82/41.18	Active UC: 55.0 (45.3-61.3), inactive UC: 51.1 (36.1-60.4)	17	Edge biopsies of the ulcers from CDC patients and infectious or ischemic colitis patients	30/70	Active UC: 45.9 (36.1-60.1), inactive UC: 69.1 (68.2-78.4)	10	Mucosa	miR-1971, miR-665, miR-27a-5p, miR-885-3p, miR-3162-5p, miR-31-5p, miR-650, miR-140-5p, miR-223-3p, miR-708-5p, miR-3201, miR-133a, miR-1973, miR-429, miR-196b-3p, miR-147b	miR-422a, miR-141-3p, miR-192-3p, miR-148a-3p	Disease severity
<b>Amy Lewis 2015</b>	miScript miRNA PCR 384HC array	NA	qPCR	6 stricturing CD, 11 nonstricturing CD and 5 healthy controls	NA	CD	NA	NA	17	Healthy controls	NA	NA	5	Serum	Non	Non	NA

<b>Min Min 2014</b>	Human v2.0 miRNA Expression BeadChip	1146	qPCR	20 active UC and 16 healthy controls	1 fold	Active UC	75/25	42.6±12.4	20	Healthy controls	62.5/37.5	52.2±10.0	16	Mucosa	miR-658	Non	NA
<b>Swati Valmiki 2017</b>	GeneChip © miRNA 4.0 Array	NA	qPCR	8 UC and 8 non-IBD controls	1.5 folds	UC	37.5/62.5	39.75±10.29	8	NIBD-related illnesses	25/75	40.75±11.86	8	Mucosa	miR-138-5p, miR-708-5p, miR-212-3p, miR-4538, miR-4521, miR-4417, miR-17-3p, miR-424-3p, miR-874-3p, miR-25-5p, miR-223-3p, miR-1271-5p, miR-148b-3p, miR-501-5p, miR-4486, miR-224-3p, miR-21-3p, miR-146b-5p, miR-149-5p, miR-31-5p	miR-552-3p, miR-196b-5p, miR-378d-5p	NA
<b>Jeremy S Schaefer 2015</b>	miRCURY LNA microRNA Array	over 600	qPCR	2 CD, 2 UC and 1 healthy control	3 folds	IBD	NA	NA	4	Healthy controls	NA	NA	1	Mucosa	miR-31, miR-494	Non	NA
<b>Bailey C. E. Peck 2015</b>	Illumina HiSeq 2500 platform	NA	qPCR	21 CD, 6 UC and 14 healthy controls	2 folds	Inactive CD	33/67	36.6 (15-76)	21	NIBD-related illnesses	57/43	56.4 (41-82)	14	FFPE	NA	NA	Disease subclass (about stricturing and penetrating)
<b>Mehmet Cosk</b>	NA	NA	qPCR	4 CD, 4 UC and 2	NA	IBD	50/50	37 (25-73)	8	Healthy controls	50/50	39 (37-41)	2	Mucosa	miR-15a, miR-199b-3p, miR-20b, miR-20a, miR-106b, miR-	Non	IBD type, diseases

<b>un 2013</b>				healthy controls											27b, miR-99a, miR-222, miR-151-5p, miR-203, miR-30a, miR-25, miR-26b, miR-646, miR-125b, miR-98, miR-768-3p, miR-195, miR-99b, miR-23a, miR-18a, miR-17, miR-155, miR-23b, miR-1201, miR-130a, miR-199a-3p, miR-16, miR-126, miR-106a, miR-1248, miR-27a, miR-222*, miR-506, miR-125b-1*, let-7e*, miR-512-5p, miR-1288, miR-330-3p, miR-623, miR-34b		e severit y
<b>María Rojas -Feria 2018</b>	NA	88	qPCR	NA	1.5 folds	Active CD	NA	NA	17	Paired adjacent normal colon tissues	NA	NA	18	Mucosa	miR-144, miR-519	Non	Gut microbi ota
<b>Zhen Guo 2016</b>	miRCURY LNA microRNA Array	NA	qPCR	6 pairs CD and 6 healthy controls	2 folds	Active CD	NA	NA	6	Healthy controls	NA	NA	6	Mucosa	Non	miR-192-5p	NA
<b>Jingm ei Lin 2016</b>	Illumina next generation sequencin g of small RNA	NA	qPCR	9 CD, 10 UC and 18 healthy controls	2 folds	IBD	NA	NA	19	Healthy controls	NA	NA	18	Mucosa	miR-194-2, miR-383, miR-615	Non	Diseas e severit y



<b>Geoffrey W. Krissansen 2015</b>	NA	289	qPCR	57 CD, 62 UC and 58 healthy controls	2 folds	IBD	50.42/49.58	40 (16-74)	119	Healthy controls	44.83/55.17	43.7 (19-67)	58	Serum	miR-595, miR-143, miR-1246	Non	IBD type, disease severity
<b>Feng Wu 2011</b>	miRCURY LNA microRNA Array	1300	qPCR	19 CD, 23 UC and 13 healthy controls	miRNA signal > mean $\pm$ 2 SD of the controls	IBD	47.62/52.38	46.5 (21-81)	42	Healthy controls	46.2/53.8	56.3 (43-75)	13	Blood	miR-362-3p	miR-505*	IBD type, disease severity
<b>Raju Ranjha 2015</b>	miRCURY LNA microRNA Array	NA	qPCR	30 UC and 20 non-IBD controls	1.7 folds	UC	56.7/43.3	34.84 $\pm$ 13.75	30	NIBD-related illnesses	65/35	34.23 $\pm$ 13.1	20	Mucosa	miR-141-3p	Non	Location
<b>Georgios Koukos 2015</b>	miRCURY LNA microRNA Array	NA	qPCR	5 pairs UC	NA	UC	40/60	15.2 $\pm$ 1.83	5	Paired adjacent normal colon tissues	40/60	15.2 $\pm$ 1.83	5	Mucosa	miR-223, miR-1973, miR-3611, miR-21	miR-4284, miR-378a/c/d, miR-378a, miR-138-1, miR-4286	Age
<b>Jing Han 2018</b>	miRCURY LNA microRNA Array	NA	qPCR	3 UC and 3 healthy controls	NA	Active UC	NA	NA	3	Healthy controls	NA	NA	3	Mucosa	Non	Non	NA
<b>Karen Dubois-Cama</b>	Affymetrix GeneChip microRNA arrays	more than 5,000 mature miRNAs	qPCR	8 pairs UC	1.5 folds	Active UC	37.5/62.5	34 (18-44)	8	Paired adjacent normal colon tissues	37.5/62.5	34 (18-44)	8	Mucosa	miR-223-3p, miR-708-5p	miR-147b, hsa-miR-196b-3p	Disease severity

<b>cho 2019</b>																	
<b>Ayilia Mohammedi 2019</b>	Nanostring technology platform	798	Non	23 quiescent CD and 38 healthy controls	P < 0.05	Inactive CD	34.78/64.22	34±13	23	Healthy controls	57.89/42.11	55±9	38	Mucosa	Non	Non	Location
<b>Julien Verrier 2020</b>	nCounter human v2 miRNA Expression Assay	800	qPCR	6 CD and 6 healthy controls	P < 0.05	Active CD	83/17	37.6 (27-69)	6	Healthy controls	83/17	36.8 (25-73)	6	Feces	miR-223, miR-1246, miR-451, miR-21, miR-15a, miR-15b	Non	Disease severity
<b>Filip Ambrózkiwicz 2020</b>	Nanostring technology platform	800	Non	15 CD and 9 healthy controls	1.5 folds	CD	66.7/33.3	32 (20-62)	15	Healthy controls	NA	NA	9	Feces	miR-223-3p	miR-577, miR-642a-3p, miR-26b-5p	Disease severity
<b>Christian T. Wohnhaas 2020</b>	Nanostring technology platform	555	qPCR	52 CD and 15 healthy controls	3.0 folds	CD	25/75	38 (19-74)	52	Healthy controls	53.3/46.7	38 (23-65)	15	Feces	miR-16-5p, miR-142-5p, miR-223-3p	miR-10b-5p, miR-192-5p, miR-10a-5p, miR-375	Disease severity
<b>Jie Zhao 2020</b>	Agilent Human miRNA Microarray	NA	qPCR	3 CD and 3 healthy controls	4.0 folds	CD	NA	54.3±4.8	3	Healthy controls	NA	54.1±5.1	3	Mucosa	miR-130a-3p, miR-106b-5p, miR-30b-5p	Non	NA
<b>Kalla R 2021</b>	miRCURY LNA microRNA Array	340	qPCR	9 CD, 14 UC, 1 IBDU and 8 healthy controls	NA	IBD	66.67/33.33	34 (18-68)	24	Healthy controls	50/50	43 (20-59)	8	Leucocytes (CD4+, CD8+ and CD14+ cells)	CD4+ cells: miR-4792, miR-921, CD8+ cells: miR-4792, CD14+ cells: non	CD4+ cells: non, CD8+ cells: miR-200b-3p, CD14+ cells: non	NA

miRNA: microRNAs; IBD: Inflammatory bowel disease; UC: Ulcerative colitis; CD: Crohn's disease; y: years; SD: Standard deviation; PBMC: Peripheral blood mononuclear cell; FFPE: Formalin-fixed paraffin-embedded; qPCR: Quantitative real-time polymerase chain reaction; NA: Not available; Non: None of valid data.

**Table S3 Systematic review of included studies that detected altered miRNA expression in patients with IBD using validated methods.**

Study ID	Patients with IBD				Controls				Sample type	miRNA assay	Normalization controls	No. of miRNAs	Up or down	miRNA studied	Target	Related clinicopathological factors
	Disease	Gender % (Male/Female)	Age (y) mean±SD/mean(range)/mean	Case number	Control	Gender % (Male/Female)	Age (y) mean±SD/mean(range)/mean	Case number								
<b>Benjamin P. Keith 2018</b>	CD	50.22/49.78	26.85±20.27	229	Non-IBD	NA	NA	187	Mucosa	qPCR	RNU48	1	Up	miR-31	NA	Disease location, ileal stricturing
<b>Georgios Koukos 2013</b>	IBD	NA	Adult and children	33	Non-IBD	NA	NA	12	Mucosa	qPCR	U6	1	Down	miR-124	STAT3	Age, IBD type, disease severity
<b>Hye-Youn Kim 2016</b>	Active UC and CD	NA	NA	10	Healthy controls	NA	NA	5	Mucosa	qPCR	U6	2	Up	miR-132, miR-223	FOXO3a	IBD type
<b>Mao Cai 2017</b>	Active UC	66.67/33.33	50.4±13.8	15	Healthy controls	69.23/30.78	43.1±11.2	13	Mucosa	qPCR	U6	1	Down	miR-141	CXCL5	NA
<b>Jing Han 2018</b>	Active UC	NA	NA	NA	Healthy controls	NA	NA	NA	Mucosa	qPCR	NA	1	Up	miR-142-5p	SOCS1	NA
<b>Zhen Huang 2014</b>	Active CD	NA	NA	15	Paired adjacent normal colon tissues	NA	NA	15	Mucosa	qPCR	U6	1	Down	miR-141	CXCL12β	Histological score
<b>Guodong Chen 2015</b>	Active UC	42.86/57.14	42.5	35	Healthy controls	50/50	34±8.9	10	Mucosa and serum	qPCR	U6	1	Down	miR-195	Smad7	Steroid resistance
<b>Nina Zidar 2016</b>	Active UC and CD	UC: 40/60, CD: 40/60	UC: 50.6±18.2, CD: 41.7±13.1	UC: 10, CD: 10	Paired macroscopically normal mucosa	40/60	UC: 50.6±18.2, CD: 41.7±13.1	UC: 10, CD: 10	Surgery tissue	qPCR	U6	5	Down	miR-141, miR-200a, miR-200b, miR-200c and miR-429	NA	IBD type
<b>Ye Zhao 2016</b>	Active CD	65/35	32.05±10.59	20	Healthy controls	75/25	35.1±15.68	20	Mucosa	qPCR	U6	4	Up or down	Up: miR-124, miR-9, down: miR-145, miR-143	AHR (miR-124)	NA

<b>Huixia Zhang 2018</b>	Active UC	NA	NA	23	Healthy controls, IBS	NA	NA	20	Mucosa	qPCR	U6	1	Up	miR-15	A2aAR	NA
<b>Chen Zhang 2014</b>	Active UC and CD	UC: 72.2/27.8, CD: 61.5/38.5	UC: 46 (19-74), CD: 41 (16-68)	UC: 36, CD: 26	Diverticular disease	73.7/26.3	50 (23-87)	38	FFPE	qPCR	U6	1	Up	miR-31	NA	IBD type
<b>Bin Zhang 2017</b>	IBD	NA	NA	NA	Paired adjacent normal colon tissues	NA	NA	NA	Surgery tissue	qPCR	NA	1	Up	miR-122a	EGFR	NA
<b>Yongzhi Yang 2013</b>	UC	46.67/53.33	39.4 (20-65)	15	Healthy controls	53.33/46.67	44.5 (23-67)	15	Mucosa	qPCR, ISH	U6	1	Up	miR-21	RhoB	NA
<b>Xue Yang 2018</b>	Active UC and CD	NA	NA	UC: 32, CD: 35	①Healthy controls, ②inactive IBD and ③paired adjacent normal colon tissues	NA	NA	①43, ②UC: 28, CD: 29 and ③UC: 32, CD: 35	Mucosa, PBMC	qPCR	U6	1	Up	miR-425	Foxo1	Disease severity
<b>Weiyun Wu 2017</b>	Active UC	NA	NA	26	Healthy controls	NA	NA	19	Mucosa	qPCR	U6	1	Up	miR-206	A3AR	NA
<b>Simon R Whiteoak 2018 (Cohort 1)</b>	Active UC	52/48	49 (36-62)	25	①Healthy controls, ②inactive UC patients	④47.62/52.38, ⑤53.33/46.67	⑥59 (49-66), ⑦55 (49-66)	⑧21, ⑨19	Mucosa	qPCR	RNU44	1	Up	miR-31	TSLP	Disease severity
<b>Simon R Whiteoak 2018 (Cohort 2)</b>	Active UC	25/75	53 (46-62)	4	Healthy controls	25/75	76 (61-89)	4	Mucosal lymphocytes	qPCR	RNU44	1	Up	miR-31	TSLP	NA
<b>Simon R Whiteoak 2018 (Cohort 3)</b>	Active UC	80/20	50 (31-66)	5	Healthy controls	66.67/33.33	64 (35-71)	6	Blood (CD4 <sup>+</sup> C D25 <sup>intermediate</sup> T cells)	qPCR	RNU44	1	Up	miR-31	TSLP	NA

<b>Gorm Thorlacius-Ussing 2017</b>	Active UC and CD	UC: 40/60, CD: 87.5/12.5	UC: 46.1 (32-67), CD: 54 (29-77)	UC: 10, CD: 8	Healthy controls	55.56/44.44	54.2 (26-83)	9	FFPE	⓪qPCR, ⓪Quantitative ISH	⓪U6, hsa-let-7a-5p, hsa-miR-103a-3p, and hsa-miR-191-5p, ⓪scramble probe	⓪3, ⓪2	Up	⓪miR-21, miR-126, miR-223, ⓪miR-21, miR-126	NA	IBD type
<b>Wen-Juan Tang 2018</b>	Active UC and CD	UC: 57.14/42.86, CD: 52.63/47.37	UC: 9.74±2.96, CD: 10.76±3.25	UC: 7, CD: 19	⓪Juvenile polyps, ⓪Inactive CD patients	⓪57.14/42.86⓪57.14/42.86	⓪9.57±3.51, ⓪11.86±3.25	⓪21, ⓪7	Mucosa	qPCR	U6	1	Up	miR-15a	Cdc42	IBD type, disease severity
<b>Dániel Szűcs 2016</b>	Active CD	80/20	12.11±1.63	10	⓪Non-IBD, ⓪inactive CD patients	⓪80/20, ⓪50/50	⓪8.75±2.36, ⓪12.4±1.52	⓪10, ⓪10	Mucosa	qPCR	U6	3	Up	miR-146a, miR-155, miR-122	NA	Disease severity
<b>Magali Svrcek 2013</b>	IBD	50/50	37 (19-78)	18 (24 samples)	Healthy mucosa from patients with diverticulitis	30/70	58.6 (24-81)	20	Mucosa	qPCR	RNU48	3	Up	miR-155, miR-21, miR-423-5p	NA	CRC
<b>Xu-Feng Pei 2018</b>	IBD	UC: 46.30/53.70, CD: 53.33/46.67	UC: 36.51±8.14, CD: 33.58 ± 7.36	UC: 54, CD: 45	Healthy mucosa from patients with diverticulitis; peripheral venous blood was taken from healthy examinees	53.33/46.67; NA	35.14±6.45, NA	Mucosa: 15, peripheral venous blood: 20	Mucosa and blood (CD4+ T cells)	qPCR	U6	1	Up	miR-22	HDAC 4	IBD type, disease severity
<b>Surajit Pathak 2015</b>	Active UC and CD	UC: 37.5/62.	UC: 42 (24-71),	UC: 8, CD: 8	Healthy controls	50/50	55 (27-69)	8	Mucosa (intestinal)	qPCR	U6	1	Up	miR-155	SOCS 1	NA

		5, CD: 50/50	CD:39 (28-64)						fibroblasts and myofibroblasts)							
<b>Archanioti Paraskevi 2012</b>	Active UC and CD	UC: 47.73/52 .27, CD: 44.53/55 .47	UC: 33.36±11.23, CD: 30.72±10.61	UC: 88, CD: 128	Healthy controls	46.92/53 .08	44.52±8.64	162	Blood	qPCR	U6	19	Up	UC: miR-16, miR-21, miR-28-5p, miR-143, miR-151-5p, miR-155, miR-199a-5p, CD: miR-16, miR-23a, miR-28-5p, miR-29a, miR-106a, miR-107, miR-126, miR-191, miR-199a-5p, miR-200c, miR-362-3p, miR-532-3p	NA	IBD type
<b>Ameneh Omidbakhsh 2018</b>	IBD	UC: 53.12/46 .88, CD: 53.12/46 .88	UC: 31.53±12.28, CD: 32.45±11.3	UC: 32, CD: 32	Healthy controls	53.12/46 .88	33.47±10.92	32	Blood	qPCR	U6	2	Up	miR-106a, miR-362-3p	NA	IBD type, disease severity
<b>Alexandru V. Olaru 2011</b>	IBD	68.57/34 .43	46.2	35	Normal mucosa from patients without IBD or colorectal cancer history	85.71/14 .29	60.6	14	Mucosa	qPCR	U6	1	Up	miR-31	FIH-1	Disease severity, neoplasia, CRC
<b>Viola Neudecker 2017</b>	Active UC and CD	NA	UC:51.5, CD: 36.7	UC: 6, CD: 6	①Healthy controls, ②inactive	NA	①51.4, ② UC: 47.8, CD: 47.5	①10, ② UC: 6, CD: 4	Mucosa	qPCR	U6	1	Up	miR-223	NA	IBD type, disease severity

					patients with IBD											
<b>Hang Thi Thu Nguyen 2014</b>	IBD	NA	NA	UC: 20, CD: 20	Non-IBD	NA	NA	13	Mucosa	qPCR	NA	2	Up	miR-130c, miR-130a	NA	IBD type, disease severity
<b>Mousa Mohammadni a-Afrouzi 2016</b>	UC	46.67/53.33	37.26±9.59	30	Healthy controls	50/50	36.90±10.61	30	Blood (CD4 <sup>+</sup> C D25 <sup>+</sup> CD127 <sup>-</sup> FoxP3 <sup>+</sup> Treg cells)	qPCR	RNU48	8	Up or down	Up: miR-29b, miR-31, miR-181a, down: miR-21, miR-29a, miR-146a, miR-155, miR-181c	NA	NA
<b>Carlos D. Minacapelli 2019</b>	Active UC	53.33/46.67	41.73 (23-64)	15	Healthy controls	60/40	40.8 (42-65)	5	Mucosa	qPCR	β-actin	1	Up	miR-206	NA	Efficacy of 5-aminosalicylic acid
<b>Friederike Cordes 2016</b>	CD	NA	38 (20-55)	15	Healthy controls	NA	30 (18-65)	13	Blood	qPCR	U6	1	Up	miR-320a	PPP2R5B, JAM-A	Disease severity
<b>Weixu Chen 2014</b>	Active CD	NA	NA	10	Healthy controls	NA	NA	10	Mucosa	qPCR	U6	1	Up	miR-124	AHR	NA
<b>Shameer J. Mehta 2018</b>	CD	50/50	36.02	42	Healthy controls	NA	NA	13	Serum	qPCR	U6	4	Down	miR - 141, miR - 200a, miR - 200b and miR - 200c	ZEB1	Strictureing
<b>Nitsan Maharshak 2013</b>	IBD	34/66	13.45±39.9	33	Healthy controls	44/56	7.93±51.2	16	Mucosa	qPCR	SNO135	1	Up	miR-132	AChE	Disease severity
<b>Dan Ma 2019</b>	Active UC and CD	NA	NA	16	Paired adjacent normal colon tissues	NA	NA	11	Mucosa	qPCR	U6	1	Down	miR-185-3p	MLCK	NA
<b>Jin-an Li 2017</b>	UC	NA	NA	24	Healthy controls	NA	NA	20	Mucosa	qPCR	U6	1	Down	miR-214-3p	STAT6	NA

<b>Ying Kang 2016</b>	IBD	UC: 57.14/42 .86, CD: 54.05/45 .95	UC: 41.6±10. 4, CD: 38.3±9.2	UC: 63, CD: 37	Healthy controls	59.52/40 .48	40.5±12.4	42	Mucosa and serum	qPCR	U6	1	Up	miR-595	NCAM 1, FGFR 2	IBD type, disease severity
<b>Chong He 2016</b>	IBD	NA	NA	UC: 66, CD: 72	Healthy controls	NA	NA	32	Mucosa	qPCR	U6	1	Up	miR-301a	SNIP1	Disease severity
<b>Markus Gwiggner 2018</b>	Active UC	54.55/45 .45	47.3 (22- 85)	11	Healthy controls	54.55/45 .45	56.1 (46- 78)	11	Mucosa	qPCR	RNU44	4	Up or down	Up: miR-31-5p, miR-155-5p, miR-183-5p, down: miR-324- 3p	IL13R A	IBD type, disease severity
<b>Jing Guo 2017</b>	IBD	87.50/12 .50	3.5-14	UC: 3, CD: 5	Normal colon tissues from patients who had undergone intestinal surgery for other diseases	62.50/37 .50	2.75-10	8	Mucosa	qPCR	U6	1	Up	miR-7-5p	TFF3	NA
<b>Sezin Günaltay 2014</b>	UC	87.50/12 .50	56.38 (33- 79)	16	Non-IBD	54.55/45 .45	58.6 (29- 88)	11	Mucosa	qPCR	U6, RNU44 and RNU48	3	Up	miR-146a, miR- 155, miR-21	NA	Disease severity
<b>Y Chen 2013</b>	Active UC and CD	NA	NA	UC: 11, CD: 11	Paired adjacent normal colon tissues	NA	NA	UC: 11, CD: 11	Mucosa	qPCR	U6	1	Down	miR-200b	ZEB1	IBD type
<b>Xu-tao Lin 2018</b>	Active CD	NA	NA	18	Paired adjacent normal colon tissues	NA	NA	18	Mucosa	qPCR	U6	1	Up	miR-143	ATG2 B	NA
<b>Tanzhou Chen 2017</b>	IBD	NA	NA	20	Non-IBD	NA	NA	5	Mucosa	qPCR	NA	1	Up	miR-126	S1PR 2	NA



<b>Bin Chen 2013</b>	Active UC	62.5/37.5	36.5 (19-51)	24	Healthy controls	60/40	32.4 (21-48)	10	Mucosa	qPCR	U6	1	Down	miR-19a	TNF-a	NA
<b>Chong He 2017</b>	IBD	NA	NA	UC: 72, CD: 81	Healthy controls	NA	NA	35	Mucosa (intestinal epithelial cells)	qPCR	U6	1	Up	miR-301a	BTG1	IBD type, disease severity
<b>Nóra J. Béres 2016 (Cohort 1)</b>	CD	50/50	14.73±0.58	12	Healthy controls	68.75/31.25	10.56±1.36	16	FFPE	qPCR	U6	3	Up	miR-146, miR-155, miR-122	NA	Disease severity
<b>Nóra J. Béres 2016 (Cohort 2)</b>	Active UC and Active or inactive CD	UC: 60/40, CD: 44.74/55.26	UC: 11.8±1.75, active CD: 12.92±1.13, inactive CD: 12.86±1.6	UC: 10, CD: 38	Healthy controls	69.57/30.43	8.57±1.09	23	Mucosa	qPCR	U6	3	Up	miR-146, miR-155, miR-122	NA	IBD type, disease severity
<b>Nóra Judit Béres 2018</b>	CD	NA	Active: 12.19±1.2, inactive: 10.97±1.29	33	Non-colitis-controls	NA	6.48±1.1	20	Mucosa	qPCR	U6	1	Up	miR-223	NA	Disease severity
<b>Natalya Benderska 2015</b>	UC	40/60	42.5±14.5	10	Healthy controls	46.67/53.33	41.6±31	15	Mucosa	qPCR	U6	1	Up	miR-26b	DIP1	NA
<b>Yugo Ando 2016</b>	IBD	UC: 73.68/26.32, CD: 58.82/41.18	Active UC: 45.6±14.6, inactive UC: 49.7±14.2, active CD: 46.0±19.4, inactive CD: 37.2±15.9	UC: 19, CD: 17	Non-IBD	40/60	54.9±16.1	10	Mucosa (CD3+ T cells)	qPCR	SNORD95	1	Down	miR-21	NA	IBD type, disease severity

<b>Xiao Feng 2012</b>	UC	40.91/59.09	active: 48.8 (17-80), inactive: 37(25-58)	22	Healthy controls, IBS	Healthy controls: 46.7/53.3. IBS: 60/40	Healthy controls: 47.1±54.61, IBS:40.2±38.3	Healthy control: 15, IBS: 15	Mucosa	qPCR	U6	2	Up	miR-126, miR-21	miR-126: IKBA, PLK2, CRK	Disease severity
<b>Gao Chao 2019</b>	IBD	NA	NA	UC: 31, CD: 37	Healthy controls	NA	NA	24	Blood (CD4 <sup>+</sup> C D25 <sup>+</sup> Fox p3 <sup>+</sup> Treg cells)	qPCR	U6	1	Up	miR-155	CTLA-4	IBD type, disease severity
<b>Min Chen 2019</b>	Active CD	70/30	31-51	10	Normal tissue of anastomosis patients	70/30	31-51	10	Surgery tissue	qPCR	NA	1	Up	miR-16-1	HSP70	NA
<b>Richard K. Felwick 2019</b>	CD	47.83/52.17	active: 32(17-66), inactive: 51(26-80)	23	Healthy controls	30/70	70 (49-86)	10	Mucosa (epithelial cells)	qPCR	RNU44	1	Up	miR-23a	TNFAP3	Disease severity
<b>Yingqi Shi 2019</b>	IBD	UC: 60/40, CD: 52/48	UC: 38.77±9.21, CD: 34.15±7.68	UC: 40, CD: 24	Healthy controls	52.31/47.69	41.62±9.45	65	Mucosa, serum and PBMC	qPCR	NA	1	Down	miR-10a	NA	IBD type
<b>Artin Soroosh 2019</b>	IBD	NA	NA	UC: 57, CD: 22	Healthy controls	NA	NA	26	Mucosa	qPCR	U6	1	Up	miR-24	NA	IBD type, disease severity
<b>CP Wu 2019</b>	IBD	UC: 57.14/42.86, CD: 50/50	UC: 26-66, CD: 23-50	UC: 14, CD12	Healthy controls	NA	NA	30	Mucosa	qPCR	U6	1	Down	miR-375	TLR4	IBD type
<b>Xiaohong Lu 2020</b>	UC	NA	NA	45	Healthy controls	NA	NA	45	Serum	qPCR	U6	1	Up	miR-21-5p	STAT3	NA
<b>Yan Shi 2020 (Cohort1)</b>	IBD	UC: 41.18/58.82, CD:	UC: 47.6±2.92,	UC: 17, CD: 15	Healthy controls	42.86/57.14	29.2±1.01	14	Mucosa	qPCR	sNANA 5s	1	Down	miR-219a-5p	NA	IBD type, disease severity

		66.67/33 .33	CD: 37.5±3.23													
<b>Yan Shi 2020 (Cohort2)</b>	IBD	UC: 55.56/44 .44, CD: 60/40	UC: 46.8±4.31, CD: 38.8±3.25	UC: 18, CD: 15	Healthy controls	56.52/43 .48	29.33±1.1 3	23	Blood	qPCR	sNANA 5s	1	Down	miR-219a-5p	NA	IBD type, disease severity
<b>Swati Valmiki 2020</b>	UC	66.67/33 .33	37.02±11. 87	48	Non-IBD	80/20	38.25±13. 91	30	Mucosa	qPCR	U6	2	Up	miR-125b, miR- 223	miR- 125bT RAF6 and A20, miR- 223: IKKα	NA
<b>Dandan Zhao 2020</b>	IBD	NA	NA	30	Non-IBD	NA	NA	30	Mucosa	qPCR	U6	1	Up	miR-449a	Notch 1	NA
<b>Friederike Cordes 2020</b>	IBD	NA	NA	UC: 37, CD: 40	Healthy controls	NA	NA	19	Blood	qPCR	NA	1	Up	miR-320a	NA	Disease severity and treatment response
<b>Xiaozhi Deng 2020</b>	IBD	50/50	9.4 (7-11)	30	Non-IBD	50/50	8.8 (6-12)	30	Mucosa	qPCR	U6	1	Up	miR-4262	SIRT1	NA
<b>Richard K. Felwick 2020</b>	CD	47.83/52 .17	38 (17-80)	23	Healthy controls	30/70	70 (49-86)	10	Mucosa	qPCR	RNU44	1	Up	miR-23a	TNFAI P3	NA
<b>Malgorzata Guz 2020</b>	IBD	UC: 62.5/38. 5, CD:50/5 0	UC: 49.2 (23-27), CD:45.3 (23-67)	UC: 16, CD: 12	Healthy controls	45.45/54 .55	59.4 (22- 88)	11	Mucosa	qPCR	NA	5	Up	miR-21-3p, miR- 31-3p, miR- 125b-1-3p, miR- 146a-3p, miR- 155-5p	NA	NA
<b>Agnieszka Kempinska-Podhorodecka 2020</b>	UC	20/80	43.5±15	10	Healthy controls	60/40	50±4	10	Mucosa	qPCR	NA	1	Down	miR-346	NA	Primary sclerosing cholangitis
<b>Mohammad Mirzakhani 2020</b>	CD	52.17/47 .83	37.04±10. 45	23	Healthy controls	50/50	36.9±10.6	30	Blood	qPCR	RNU48	2	Up	miR-21, miR- 146a	NA	Disease severity

<b>Mehri Naghdalipour 2020</b>	UC	52.2/47.8	58.09±6.27	23	Non-IBD	38.9/61.1	56.11±9.93	18	Mucosa	qPCR	miR-361-5p	3	Up or down	Up: miR-21, miR-433, down: miR-590	NA	NA
<b>Xiaojuan Shao 2020</b>	IBD	62/38	NA	50	Healthy controls	50/50	NA	24	Blood	qPCR	NA	1	Up	miR-155	GPER 1	Gender
<b>Jun Yao 2020</b>	IBD	UC: 42/58, CD: 54/46	UC: 35.1±6.45, CD: 32.8±7.3	UC: 50, CD:50	Healthy controls	55/45	35±8.1	20	Mucosa and PBMC	qPCR	U6	1	Up	miR-802	SOCS 5	Disease severity
<b>Ting Yu 2020</b>	Active UC	61.29/38.71	38.6±6.2	62	Healthy controls	61.29/38.71	38.7±6.1	62	Plasma	qPCR	NA	1	Up	miR-24	NA	NA
<b>Xiaojing Zhao 2020</b>	CD	NA	NA	10	Healthy controls	NA	NA	8	Mucosa	qPCR	U6	1	Up	miR-124a	AHR	NA

miRNA: microRNAs; IBD: Inflammatory bowel disease; UC: Ulcerative colitis; CD: Crohn's disease; y: years; SD: Standard deviation; PBMC: Peripheral blood mononuclear cell; FFPE: Formalin-fixed paraffin-embedded; qPCR: Quantitative real-time polymerase chain reaction; NA: Not available; Non: None of valid data.

**Table S4 Consistently up-regulated and down-regulated miRNAs that were reported in studies with microarray analysis.**

	miRNA	No. of studies with same direction	Total number of IBD samples tested	
<b>Up-regulated miRNA</b>	miR-223	10	376	
	miR-21	7	60	
	miR-155	3	35	
	miR-708-5p	3	33	
	miR-142	2	66	
	miR-1246	2	64	
	miR-16	2	60	
	miR-27a	3	45	
	miR-15b	2	39	
	miR-144	2	25	
	miR-30b	2	19	
	miR-1973	2	15	
	miR-451	2	13	
	miR-106a	2	12	
	miR-17	2	10	
	miR-126	2	9	
	miR-106b	2	11	
	miR-15a	2	8	
	<b>Down-regulated miRNA</b>	miR-192-5p	3	64
		miR-4286	2	11
miR-4284		2	11	

miRNA: microRNAs; No.: Number.

**Table S5 Consistently up-regulated and down-regulated miRNAs that were reported in studies with validated methods.**

	miRNA	No. of studies with same direction	Total number of IBD samples tested
<b>Up-regulated miRNA</b>	miR-155	11	493
	miR-31	9	429
	miR-21	9	396
	miR-223	5	121
	miR-126	4	276
	miR-23a	3	262
	miR-122	3	70
	miR-146a	3	49
	miR-301a	2	291
	miR-362	2	280
	miR-106a	2	280
	miR-143	2	234
	miR-16	2	226
	miR-24	2	141
	miR-320a	2	92
	miR-146	2	60
	miR-124	2	30
	miR-132	2	43
	miR-206	2	41
	<b>Down-regulated miRNA</b>	miR-141	4
miR-200b		3	84
miR-200a		2	62
miR-200c		2	62

miRNA: microRNAs; No.: Number.

**Table S6 Results of meta-regression analysis.**

<b>Var</b>	<b>Coeff.</b>	<b>Std. Err.</b>	<b>P value</b>	<b>RDOR</b>	<b>95%CI</b>
<b>Cte.</b>	-0.741	1.0584	0.4895	—	—
<b>S</b>	-0.15	0.145	0.3103	—	—
<b>IBD type</b>	-0.639	0.3007	0.0419	0.53	(0.29 - 0.98)
<b>Age</b>	0.558	0.4115	0.1856	1.75	(0.75 - 4.05)
<b>Sample</b>	1.473	0.6325	0.0268	4.36	(1.20 - 15.88)
<b>miRNAassay</b>	1.861	0.5804	0.0032	6.43	(1.96 - 21.03)
<b>Control</b>	1.587	0.3876	0.0003	4.89	(2.22 - 10.79)

No. studies =37

Filter OFF

Add 1/2 to all cells of the studies with zero

IBD type: UC versus CD, age of participants: pediatric population (<18 years of age) versus adult ( $\geq$ 18 years of age), sample source: blood versus others, method of quantifying miRNA expression (miRNAassay): qPCR versus only microarray and control: healthy controls versus non-IBD controls.

Abbreviations: miRNA = microRNAs; CI = confidence interval; Coeff. = coefficient; Std. Err. = standard error; RDOR = relative diagnostic odds ratios.

Tau-squared estimate = 0.5749 (Convergence is achieved after 9 iterations)

Restricted Maximum Likelihood estimation (REML)

**Table S7 Results of sensitivity analysis.**

<b>StudyID</b>	<b>Sensitivity (95%CI)</b>	<b>Specificity (95%CI)</b>	<b>PLR (95%CI)</b>	<b>NLR (95%CI)</b>	<b>DOR (95%CI)</b>
<b>Adam M. Zahm 2011</b>	0.82 (0.80-0.84)	0.83 (0.80-0.85)	4.03 (3.03-5.37)	0.24 (0.17-0.34)	21.06 (11.80-37.57)
<b>Adam M. Zahm 2014</b>	0.81 (0.79-0.82)	0.84 (0.82-0.86)	4.71 (3.64-6.10)	0.26 (0.21-0.33)	23.45 (14.93-36.84)
<b>Chenming Sun 2017</b>	0.81 (0.79-0.82)	0.85 (0.83-0.87)	4.44 (3.55-5.54)	0.26 (0.21-0.32)	22.43 (14.47-34.77)
<b>Christos Polytarchou 2015</b>	0.81 (0.79-0.83)	0.85 (0.83-0.87)	4.96 (3.80-6.46)	0.25 (0.20-0.32)	25.50 (16.21-40.12)
<b>Katharina Schönauen 2018</b>	0.80 (0.79-0.82)	0.84 (0.82-0.86)	4.41 (3.46-5.63)	0.26 (0.21-0.33)	21.20 (13.77-32.62)
<b>Matthias Hübenthal 2015</b>	0.80 (0.78-0.81)	0.83 (0.81-0.85)	4.20 (3.33-5.30)	0.27 (0.22-0.33)	19.50 (13.02-29.19)
<b>Mengdie Shen 2019</b>	0.80 (0.78-0.82)	0.84 (0.82-0.86)	4.51 (3.51-5.80)	0.27 (0.22-0.33)	21.37 (13.80-33.08)
<b>Michael D. Jensen 2015</b>	0.81 (0.80-0.83)	0.84 (0.82-0.86)	4.58 (3.59-5.84)	0.26 (0.21-0.32)	22.43 (14.88-33.81)
<b>Olfat G. Shaker 2019</b>	0.80 (0.79-0.82)	0.83 (0.81-0.85)	4.28 (3.40-5.40)	0.27 (0.22-0.33)	19.88 (13.16-30.04)
<b>Peng Chen 2019 (training cohort)</b>	0.81 (0.79-0.83)	0.84 (0.82-0.86)	4.49 (3.49-5.77)	0.26 (0.21-0.33)	22.10 (14.07-34.73)
<b>Peng Chen 2019 (validation cohort)</b>	0.81 (0.80-0.83)	0.84 (0.82-0.86)	4.38 (3.43-5.58)	0.26 (0.21-0.32)	21.54 (13.95-33.27)
<b>Radha Duttagupta 2012</b>	0.80 (0.78-0.82)	0.84 (0.82-0.86)	4.36 (3.42-5.56)	0.27 (0.22-0.33)	20.40 (13.37-31.12)
<b>Yulan Ye 2017</b>	0.80 (0.79-0.82)	0.84 (0.82-0.86)	4.54 (3.55-5.81)	0.26 (0.21-0.33)	21.96 (14.24-33.86)
<b>Elham Ahmed Hassan 2020</b>	0.80 (0.78-0.82)	0.83 (0.81-0.85)	4.18 (3.31-5.28)	0.27 (0.22-0.34)	19.23 (12.65-29.24)
<b>Yuanyuan Tian 2020</b>	0.76 (0.74-0.78)	0.85 (0.83-0.87)	4.52 (3.44-5.94)	0.30 (0.26-0.35)	17.08 (11.81-24.71)
<b>Rui Zhou 2021</b>	0.81 (0.79-0.82)	0.84 (0.82-0.86)	4.36 (3.39-5.62)	0.26 (0.21-0.33)	21.46 (13.64-33.76)

95%CI: 95% confidence interval; PLR: Positive likelihood ratio; NLR: Negative likelihood ratio; DOR: Diagnostic odds ratio.