Supplementary Files

Table S1. Search terms and retrieval records

Table S2. Summary of diagnostic performance of fecal occult blood test according to anatomical location of colorectal cancer

Table S3. Summary of diagnostic performance of fecal occult blood test according to anatomical location of advanced adenomas

Table S4. Summary of diagnostic performance of fecal occult blood test according to anatomical location of advanced neoplasms

Table S1. Search terms and retrieval records

Search	Term	PubMed	Embase	Cochrane Library	Wed of Science
1	Colorectal	7844	11229	2254	13102
2	colon	5355	11152	1288	9337
3	rectum	1053	5593	505	1445
4	1 or 2 or 3	11955	21833	3413	19782
5	cancer	103476	150784	18299	126973
6	neoplasm	17297	14308	1419	65159
7	carcinoma	19155	34083	4327	40011
8	adenoma	1482	3054	356	2552
9	malignancy	20060	9521	661	12208
10	5 or 6 or 7 or 8 or 9	111786	159934	20319	159930
11	faecal immunochemical test	36	32	33	41
12	fecal immunochemical testing	31	33	15	123
13	fecal immunochemical test	80	87	33	123
14	faecal immunochemical testing	5	7	15	41
15	faecal occult blood test	41	47	64	57
16	fecal occult blood test	76	149	64	143
17	11or 12or13or14or15or16	186	217	84	270
18	detection	33085	36383	2520	70115
19	screening	79675	35363	8525	46833
20	detecting	6464	6614	614	88455
21	diagnosis	76323	130174	10447	94154
22	18or19or20or21	121219	177860	21813	244822
23	4and10and17and22	160	179	68	224

((((Colorectal) OR colon) OR rectum)) AND ("2018/8/17"[Publication Date] : "3000"[Publication Date])

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Table S2. Summary of diagnostic performance of fecal occult blood test according to anatomical location of colorectal cancer

Ref.	Author, year	Brand[a]	Cut-off	Proximal colorectal cancer		Distal colorectal cancer		Free of neoplasms		*P*-value[b]
				Pos. /N	Sensitivity (95% CI)	Pos. /N	Sensitivity (95% CI)	Neg. /N	Specificity (95% CI)	
(a) gFOBT										
15	Thomas, 1992	3	N.A.	5/10	50.0 (23.7-76.3)	24/40	60.0 (44.6-73.7)	248/261	95.0 (91.7-97.1)	0.83
16	Hope, 1996	4	N.A.	1/1	100 (20.7-100)	2/2	100 (34.2-100)	118/136	86.8 (80.0-91.5)	1
20	Sung, 2003	4	N.A.	1/1	100 (20.7-100)	0/3	0	320/399	80.2 (76.0-83.8)	0.25
26	Bjerregaard,2009	5	N.A.	2/4	50.0 (15.0-85.0)	4/4	100 (51.0-100)	165/206	80.1 (74.1-85.0)	0.43
31	Park, 2010	4	N.A.	3/11	27.3 (9.7-56.6)	1/2	50.0 (9.4-90.6)	444/479	92.7 (90.0-94.7)	1
39	Lee, 2013	5	N.A.	17/21	81.0 (60.0-92.3)	17/18	94.4 (74.2-99.0)	2637/2965	88.9 (87.8-90.0)	0.35
(b) iFOBT										
15	Thomas, 1992	2	N.A.	9/10	90.0 (59.6-98.2)	38/40	95.0 (83.5-98.6)	213/261	81.6 (76.5-85.8)	0.5
16	Hope, 1996	12	N.A.	1/1	100 (20.7-100)	2/2	100 (34.2-100)	131/136	96.3 (91.7-98.4)	1
19	Nakama, 2006	13	N.A.	4/8	50.0 (21.5-78.5)	35/56	62.5 (49.4-74.0)	9023/9569	94.3 (93.8-94.7)	0.77
21	Young, 2003(1)[c]	1	N.A.	6/8	75.0 (40.9-92.9)	23/28	82.1 (64.4-92.1)	262/277	94.6 (91.3-96.7)	1
21	Young, 2003(2)[c]	6	N.A.	6/8	75.0 (40.9-92.9)	21/28	75.0 (56.6-87.3)	262/277	94.6 (91.3-96.7)	1
22	Morikawa, 2005	14	20 ng/ml	13/23	56.5 (36.3-76.8)	39/56	69.6 (57.6-81.7)	16698/17480	95.5 (95.2-95.8)	0.26
23	Nakazato, 2006	N.A.	N.A.	3/7	42.9 (15.8-75.0)	7/12	58.3 (32.0-80.7)	2421/2765	87.6 (86.3-88.7)	0.65
25	Shastri, 2008	11	N.A.	15/21	71.4 (50.0-86.2)	24/34	70.6 (53.8-83.2)	497/516	96.3 (94.3-97.6)	0.95
30	Oono, 2010	7	100 ng/ml	19/28	67.9 (49.3-82.1)	49/63	77.8 (66.1-86.3)	679/758	89.6 (87.2-91.6)	0.32
31	Park, 2010	23	100 ng/ml	10/11	90.9 (62.3-98.4)	1/2	50.0 (9.4-90.6)	444/479	92.7 (90.0-94.7)	0.30
34	De Wijkerslooth, 2012	10	50 ng/ml	2/2	100 (34.2-100)	5/6	83.3 (43.7-97.0)	1061/1135	93.5 (91.9-94.8)	1
36	Chiu, 2013	9	50 ng/ml	8/11	72.7 (39.3-92.7)	14/17	82.3 (55.8-95.3)	13500/14252	94.7 (94.3-95.1)	0.89
37	Kaul, 2013	9	40 ng/ml	9/9	100 (70.1-100)	8/8	100 (67.6-100)	83/96	86.5 (78.2-91.9)	1
38	Koga, 2013	8	50 ng/ml	55/85	64.7 (54.1-74.0)	16/32	50.0 (33.6-66.4)	105/107	98.1 (93.4-99.5)	0.15
39	Lee, 2013	10	100 ng/ml	15/21	71.4 (50.0-86.2)	17/18	94.4 (74.2-99.0)	2900/2965	97.8 (97.2-98.3)	0.10
40	Kim, 2014	10	100 ng/ml	24/46	52.2 (38.1-65.9)	70/129	54.3 (45.7-62.6)	150/151	99.3 (96.3-99.9)	0.81
41	Imperiale, 2014	24	100 ng/ml	20/30	66.7 (48.8-80.8)	28/35	80.0 (64.1-90.0)	6033/6281	96.1(95.5-96.5)	0.35
43	Kim, 2016	10	20 μg/g	11/17	64.7 (38.3-85.8)	40/48	83.3 (69.8-92.5)	3006/3566	84.3 (83.1-85.5)	0.21
44	Brenner, 2017	17	100 ng/ml	5/5	100 (56.6-100)	23/24	95.8 (79.8-99.3)	2245/2397	93.7 (92.6-94.6)	1

45	Jung, 2018	10	100 ng/ml	2/3	67.7 (20.8-93.9)	5/8	62.5 (30.6-86.3)	9314/9575	97.3 (96.9-97.6)	1

[a] 1= FlexSure OBT; 2= HemeSelect; 3= Hemoccult blood; 4= Hemoccult blood II; 5= Hemoccult blood Sensa; 6= InSure; 7= Hemo Techt NS-Plus; 8= OC-Hemocatch; 9= OC-Light; 10= OC-Sensor; 11= PreventID-CC; 12= Monohaem; 13= Imdia-HemSp; 14= Magstream 1000/Hem SP automated system; 15= RIDASCREEN haemoglobin; 16= Hemoccult blood ICT; 17=Sentinel Diagnostics; 18= Bionexia FOBplus; 19= Bionexia Hb/Hp Complex; 20= ImmoCARE-C; 21= FOB advanced; 22= QuickVue iFOB; 23=OC-SENSA MICRO; 24=OC FIT-CHEK.

[b] *P*-values were calculated by chi-square test to compare the sensitivities for detecting proximal vs. distal colorectal cancers.

Abbreviation: CI, confidence intervals; Pos. , positive; Neg. , negative.

[c] Ordinal numbers were applied to mark the studies which contain variable FOBT brands

Table S3. Summary of diagnostic performance of fecal occult blood test according to anatomical location of advanced adenomas

Ref.	Author	Brand[a]	Cut-off	Proximal advanced adenomas		Distal advanced adenomas		Free of neoplasms		*P*-value[b]
				Pos. /N	Sensitivity (95%CI)	Pos./N	Sensitivity (95%CI)	Neg./N	specificity (95%CI)	
(a) gFOBT										
16	Hope, 1996	4	N.A.	3/11	27.3 (9.7-56.6)	3/10	30.0 (10.8-60.3)	118/136	86.8 (80.0-91.5)	1
20	Sung, 2003	4	N.A.	10/51	19.6 (11.0-32.5)	17/75	22.7 (14.7-33.3)	320/399	80.2 (76.0-83.8)	0.68
28	Hundt, 2009	3	N.A.	15/248	6.1 (2.8-11.3)	6/140	4.2 (1.7-8.4)	851/887	95.9 (94.4-97.1)	0.46
31	Park, 2010	4	N.A.	7/33	21.2 (10.7-37.8)	1/26	3.8 (0.7-18.9)	444/479	92.7 (90.0-94.7)	0.12
(b) iFOBT										
16	Hope, 1996	12	N.A.	6/11	54.5 (28.0-78.7)	5/10	50.0 (23.7-76.3)	131/136	96.3 (91.7-98.4)	1
22	Morikawa, 2005	14	20 ng/ml	29/204	14.2 (10.1-19.7)	116/444	26.1 (22.3-30.4)	16698/17480	95.5 (95.2-95.8)	<0.01
23	Nakazato, 2006	N.A.	N.A.	6/34	17.6 (8.3-33.5)	7/19	36.8 (19.1-59.0)	2421/2765	87.6 (86.3-88.7)	0.22
25	Shastri, 2008	11	N.A.	6/12	50.0 (25.4-74.6)	4/9	44.4 (18.9-73.3)	497/516	96.3 (94.3-97.6)	1
28[c]	Hundt, 2009 (1)[d]	18	40ng/ml	45/156	28.9 (21.9-36.6)	61/174	35.1 (28.0-42.6)	749/914	81.9 (79.3-84.4)	0.23
28[c]	Hundt, 2009 (2)[d]	19	25ng/ml	79/156	50.6 (42.5-58.7)	104/174	59.8 (52.2-67.1)	537/914	58.8 (55.5-62.0)	0.01
28[c]	Hundt, 2009 (3)[d]	11	10ng/ml	32/156	20.5 (14.5-27.7)	55/174	31.6 (24.8-39.1)	748/914	81.8 (79.2-84.3)	0.02
28[c]	Hundt, 2009 (4)[d]	20	50ng/ml	8/156	5.1 (2.2-9.9)	22/174	12.6 (8.1-18.5)	884/914	96.7 (95.4-97.7)	0.02
28[c]	Hundt, 2009 (5)[d]	21	40ng/ml	17/156	10.9 (6.5-16.9)	33/174	19.0 (13.4-25.6)	849/914	92.9 (91.0-94.5)	0.04
28[c]	Hundt, 2009 (6)[d]	22	50ng/ml	67/156	43.0 (35.1-51.1)	74/174	42.5 (35.1-50.2)	642/914	70.2 (67.2-73.2)	0.94
29	Haug, 2010	15	2 μg/g	30/156	19.1 (13.3-26.1)	47/174	27.0 (20.6-34.3)	819/914	89.6 (87.4-91.5)	0.10
31	Park, 2010	23	100 ng/ml	18/33	56.3 (38.0-70.2)	2/26	7.7 (2.1-24.1)	444/479	92.7 (90.0-94.7)	<0.01
33	Khalid-de Bakker, 2011	10	50 ng/ml	0/10	0	6/28	21.4 (8.3-41.0)	235/243	96.7 (93.6-98.6)	0.29
36	Chiu, 2013	9	50 ng/ml	65/289	22.5 (17.9-27.8)	97/307	31.6 (26.5-37.2)	13500/14252	94.7 (94.3-95.1)	0.01
43	Kim, 2016	10	20 μg/g	48/151	31.6 (24.5-39.5)	70/162	43.1 (35.6-50.8)	3006/3566	84.3 (83.1-85.5)	0.04
44	Brenner, 2017	17	100 ng/ml	17/118	14.4 (9.2-21.9)	93/214	43.5 (37.0-50.2)	2245/2397	93.7 (92.6-94.6)	<0.01
45	Jung, 2018	10	100 ng/ml	13/111	11.7 (7.0-19.0)	35/180	19.4 (14.3-25.8)	9314/9575	97.3 (96.9-97.6)	0.12

[a] 1= FlexSure OBT; 2= HemeSelect; 3= Hemoccult blood; 4= Hemoccult blood II; 5= Hemoccult blood Sensa; 6= InSure; 7= Hemo Techt NS-Plus; 8= OC-Hemocatch; 9= OC-Light; 10= OC-Sensor; 11= PreventID-CC; 12= Monohaem; 13= Imdia-HemSp; 14= Magstream 1000/Hem SP automated system; 15= RIDASCREEN haemoglobin; 16= Hemoccult blood ICT; 17=Sentinel Diagnostics; 18= Bionexia FOBplus; 19= Bionexia Hb/Hp Complex; 20= ImmoCARE-C; 21= FOB advanced; 22= QuickVue iFOB;

23=OC-SENSA MICRO; 24=OC FIT-CHEK.

[b] *P*-values were calculated by chi-sqaure test to compare the sensitivities for detecting proximal vs. distal advanced adenomas.

[c] all cases of adenomas were calculated.

Abbreviation: CI, confidence intervals; Pos. , positive; Neg. , negative.

[d] Ordinal numbers were applied to mark the studies which contain variable FOBT brands

Table S4. Summary of diagnostic performance of fecal occult blood test according to anatomical location of advanced neoplasms

Ref	Author, year	Brand[a]	Cut-off	Proximal advanced neoplasms		Distal advanced neoplasms		Free of neoplasms		*P*-value[b]
				Pos./N	Sensitivity (95%CI)	Pos./N	Sensitivity (95%CI)	Neg./N	Specificity (95%CI)	
(a) gFOBT										
16	Hope, 1996	4	N.A.	4/12	33.3 (13.8-60.9)	5/12	41.7 (19.3-68.0)	100/118	84.7 (77.1-90.1)	1
18	Lieberman, 2010	4	N.A.	32/137	23.4 (17.1-31.1)	41/169	24.3 (18.4-31.2)	1680/1791	93.8 (92.6-94.8)	0.85
20	Sung, 2001	4	N.A.	11/52	21.1 (12.2-34.0)	17/78	21.8 (14.1-32.2)	320/399	80.2 (76.0-83.8)	0.93
24	Ahlquist, 2008(1)[c]	3	N.A.	4/56	7.1 (2.8-17.0)	13/101	12.9 (7.7-20.8)	1838/1871	98.2 (97.5-98.7)	0.27
24	Ahlquist, 2008(2)	5	N.A.	6/56	10.7 (5.0-21.5)	27/101	26.7 (19.1-36.1)	1810/1871	96.7 (95.8-97.5)	0.02
27	Graser, 2009	N.A.	N.A.	1/4	25.0 (4.6-69.9)	4/19	21.1 (8.5-43.3)	166/177	93.8 (89.2-96.5)	1
31	Park, 2009	4	N.A.	10/44	22.7 (12.8-37.0)	2/28	7.1 (2.0-22.7)	444/479	92.7 (90.0-94.7)	0.08
35	Wong, 2012	4	N.A.	0/17	0	5/51	9.8 (1.6-18.0)	994/1006	98.8 (98.1-99.5)	0.42
(b) iFOBT										
16	Hope, 1996	12	N.A.	7/12	58.3 (32.0-80.7)	7/12	58.3 (32.0-80.7)	131/136	96.3 (91.7-98.4)	1
17	Greenberg, 2000	1	N.A.	5/18	27.8 (12.5-50.9)	20/34	58.8 (42.2-73.6)	341/390	87.4 (83.8-90.4)	0.03
22	Morikawa, 2005	14	20 ng/ml	29/178	16.3 (11.3-21.3)	169/549	30.7 (26.7-34.8)	16698/17480	95.5 (95.2-95.8)	<0.01
23	Nakazato, 2006	N.A.	N.A.	9/41	22.0 (12.0-36.7)	14/31	45.2 (29.2-62.2)	2421/2765	87.6 (86.2-88.7)	0.04
25	Shastri, 2008	11	N.A.	21/33	63.6 (46.6-77.8)	28/43	65.1 (50.2-77.6)	497/516	96.3 (94.3-97.6)	0.89
27	Graser, 2009	17	14 ng/ml	1/4	25.0 (4.6-69.9)	6/18	33.3 (16.3-56.3)	163/183	89.1 (83.7-92.8)	1
31	Park, 2010	23	100 ng/ml	28/44	63.6 (48.9-76.2)	3/28	10.7 (3.7-27.2)	444/479	92.7 (90.0-94.7)	<0.01
32	Haug, 2011	15	2 μg/g	21/71	29.5 (20.2-41.0)	69/157	43.9 (36.4-51.8)	1832/2082	88.0 (86.6-89.4)	0.04
34	De Wijkerslooth, 2012	10	50 ng/ml	9/24	37.5 (21.2-57.3)	31/83	37.3 (27.7-48.1)	1061/1135	93.5 (91.9-94.1)	0.99
35	Wong, 2012(1)[c]	14	20 ng/ml	3/17	17.6 (6.2-41.0)	22/51	43.1 (29.5-56.7)	938/1006	93.2 (91.7-94.8)	0.06
35	Wong, 2012(2)[c]	16	N.A.	2/17	11.8 (3.3-27.1)	14/51	27.5 (15.2-39.7)	964/1006	95.8 (94.6-97.1)	0.32
36	Chiu, 2013	9	50 ng/ml	72/299	24.1 (19.4-29.4)	111/324	34.3 (29.2-39.7)	13500/14252	94.7 (94.3-95.1)	<0.01
42	Castro, 2013	10	20 μg/g	8/47	17.0 (8.1-31.3)	49/115	42.6 (34.0-51.7)	1096/1129	97.1 (95.9-97.9)	<0.01
43	Kim, 2016	10	20 μg/g	55/168	32.7 (25.7-40.4)	103/210	49.0 (42.1-56.0)	3006/3566	84.3 (83.1-85.5)	<0.01
44	Brenner, 2017	17	100 ng/ml	22/123	17.9 (12.1-25.6)	116/238	48.7 (42.5-55.1)	2245/2397	93.7 (92.6-94.6)	<0.01
45	Jung, 2018	10	100 ng/ml	15/114	13.2 (8.1-20.6)	40/188	21.3 (16.0-27.7)	9314/9575	97.3 (96.9-97.6)	0.08

[a] 1= FlexSure OBT; 2= HemeSelect; 3= Hemoccult blood; 4= Hemoccult blood II; 5= Hemoccult blood Sensa; 6= InSure; 7= Hemo Techt NS-Plus; 8= OC-Hemocatch;

9= OC-Light; 10= OC-Sensor; 11= PreventID-CC; 12= Monohaem; 13= Imdia-HemSp; 14= Magstream 1000/Hem SP automated system; 15= RIDASCREEN haemoglobin; 16= Hemoccult blood ICT; 17=Sentinel Diagnostics; 18= Bionexia FOBplus; 19= Bionexia Hb/Hp Complex; 20= ImmoCARE-C; 21= FOB advanced; 22= QuickVue iFOB; 23=OC-SENSA MICRO; 24=OC FIT-CHEK.

[b] *P*-values were calculated by chi-square test to compare the sensitivities for detecting proximal vs. distal advanced adenomas.

Abbreviation: CI, confidence intervals; Pos. , positive; Neg. , negative

[c] Ordinal numbers were applied to mark the studies which contain variable FOBT brands

Legends of supplementary Figures

Figure S1a. Subgroup analysis of pooled sensitivities of immunochemical fecal occult blood test (iFOBT) on detection of proximal and distal colorectal cancer, according to type of iFOBT brand, a) for detecting proximal colorectal cancer in studies with qualitative iFOBT; b) for detecting distal colorectal cancer in studies with qualitative iFOBT; c) for detecting proximal colorectal cancer in studies with quantitative iFOBT; d) for detecting distal colorectal cancer in studies with quantitative iFOBT. **Note:** [a] Ordinal numbers were applied to mark the studies which contain variable FOBT brands. **Abbreviation:** iFOBT, immunochemical fecal occult blood testing.

Figure S2a. Subgroup analysis of pooled sensitivities of immunochemical fecal occult blood test (iFOBT) on detection of proximal and distal advanced adenoma, according to type of iFOBT brand, a) for detecting proximal advanced adenoma in studies with qualitative iFOBT; b) for detecting distal advanced adenoma in studies with qualitative iFOBT; c) for detecting proximal advanced adenoma in studies with quantitative iFOBT; d) for detecting distal advanced adenoma in studies with quantitative iFOBT. **Note:** [a] Ordinal numbers were applied to mark the studies which contain variable FOBT brands. **Abbreviation:** iFOBT, immunochemical fecal occult blood testing.

Figure S3a. Subgroup analysis of pooled sensitivities of immunochemical fecal occult blood test (iFOBT) on detection of proximal and distal advanced neoplasia, according to type of iFOBT brand, a) for detecting proximal advanced neoplasia in studies with qualitative iFOBT; b) for detecting distal advanced neoplasia in studies with qualitative iFOBT; c) for detecting proximal advanced neoplasia in studies with quantitative iFOBT; d) for detecting distal advanced neoplasia in studies with quantitative iFOBT. **Note:** [a] Ordinal numbers were applied to mark the studies which contain variable FOBT brands. **Abbreviation:** iFOBT, immunochemical fecal occult blood testing.

Figure S1b. Subgroup analysis of pooled sensitivities of immunochemical fecal occult blood test (iFOBT) on detection of proximal and distal colorectal cancer, according to type of study setting, a) for detecting proximal colorectal cancer in studies with clinical setting; b) for detecting distal colorectal cancer in studies with clinical setting; c) for detecting proximal colorectal cancer in studies with screening setting; d) for detecting distal colorectal cancer in studies with screening setting. **Note:** [a] Ordinal numbers were applied to mark the studies which contain variable FOBT brands. **Abbreviation:** iFOBT, immunochemical fecal occult blood testing.

Figure S2b. Subgroup analysis of pooled sensitivities of immunochemical fecal

occult blood test (iFOBT) on detection of proximal and distal colorectal cancer, according to type of study setting, a) for detecting proximal advanced adenomas in studies with screening setting; b) for detecting distal advanced adenomas in studies with screening setting. **Note:** [a] Ordinal numbers were applied to mark the studies which contain variable FOBT brands. **Abbreviation:** iFOBT, immunochemical fecal occult blood testing.

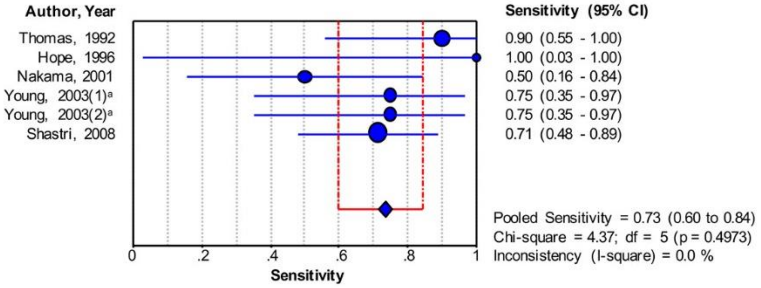
Figure S3b. Subgroup analysis of pooled sensitivities of immunochemical fecal occult blood test (iFOBT) on detection of proximal and distal advanced neoplasia, according to type of study setting, a) for detecting proximal advanced neoplasia in studies with clinical setting; b) for detecting distal advanced neoplasia in studies with clinical setting; c) for detecting proximal advanced neoplasia in studies with screening setting; d) for detecting distal advanced neoplasia in studies with screening setting. **Note:** [a] Ordinal numbers were applied to mark the studies which contain variable FOBT brands. **Abbreviation:** iFOBT, immunochemical fecal occult blood testing.

Figure S4. Funnel plots by detection methods and outcomes, a) for testing publication bias of detecting colorectal cancer by using guaiac-fecal occult blood test; b) for testing publication bias of detecting colorectal cancer by using immunochemical fecal occult blood test; c) for testing publication bias of detecting advanced adenoma by using guaiac-fecal occult blood test; d) for testing publication bias of detecting advanced adenoma by using immunochemical fecal occult blood test; e) for testing publication bias of detecting advanced neoplasia by using guaiac-occult blood test; f) for testing publication bias of detecting advanced neoplasia by using immunochemical fecal occult blood test.

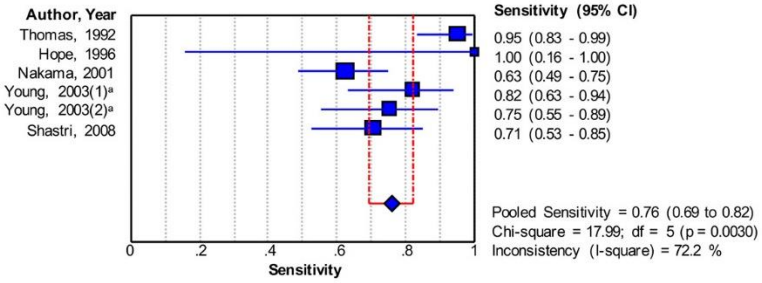
Figure S5. Methodological quality graph of risk of bias and applicability concerns

Figure S6. Risk of bias and applicability concerns summary

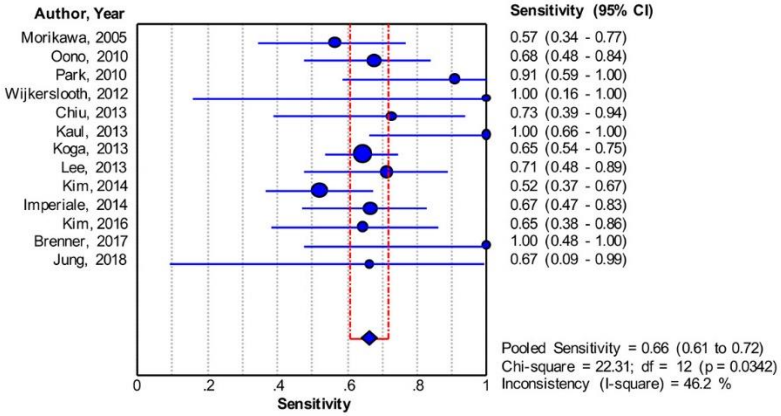
(A) qualitative iFOBT for colorectal cancer of proximal colon



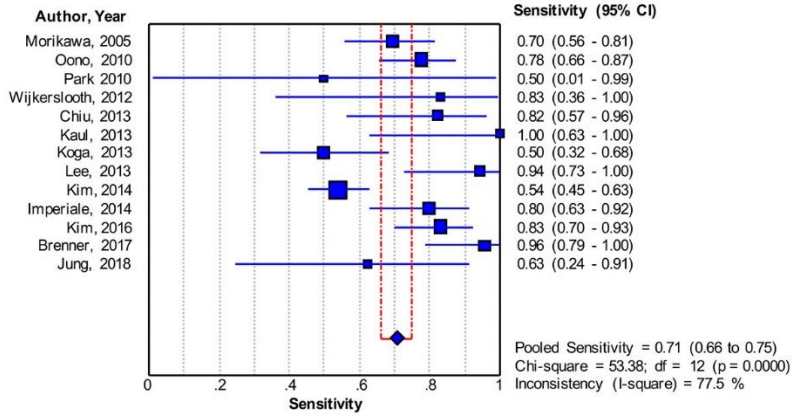
(B) qualitative iFOBT for colorectal cancer of distal colon/rectum



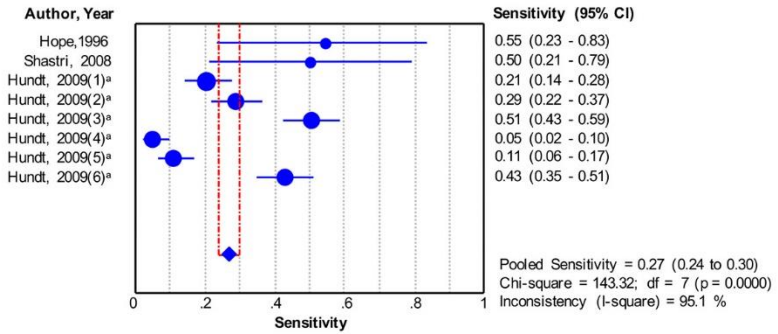
(C) quantitative iFOBT for colorectal cancer of proximal colon



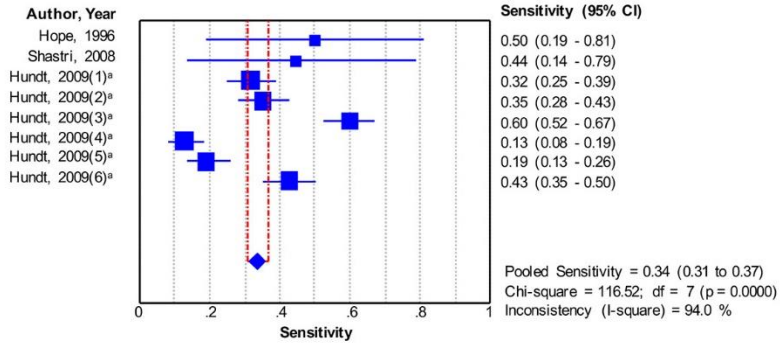
(D) quantitative iFOBT for colorectal cancer of distal colon/rectum



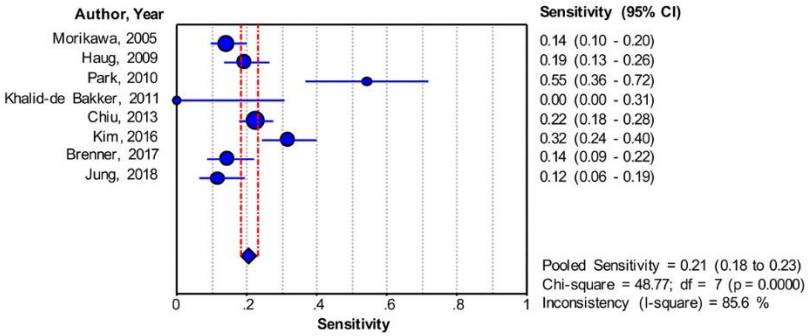
(A) qualitative iFOBT for advanced adenomas of proximal colon



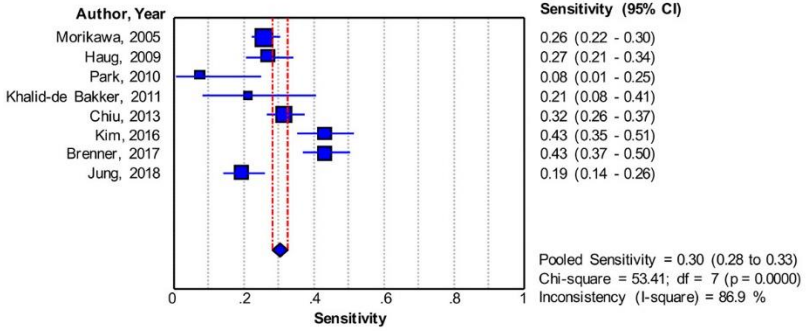
(B) qualitative iFOBT for advanced adenomas of distal colon/rectum



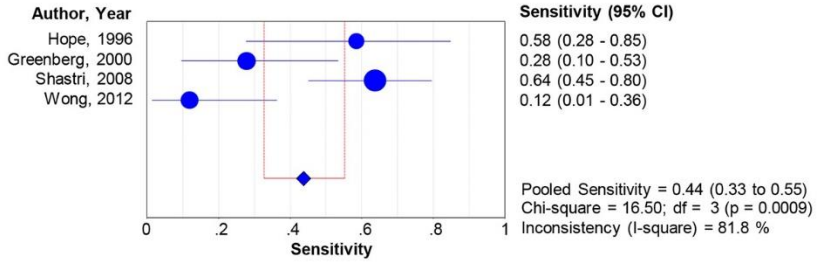
(C) quantitative iFOBT for advanced adenomas of proximal colon



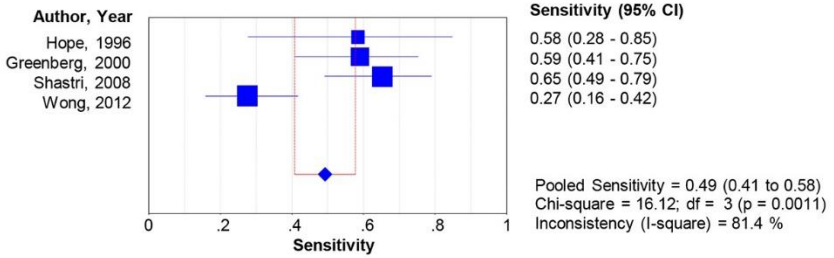
(D) quantitative iFOBT for advanced adenomas of distal colon/rectum



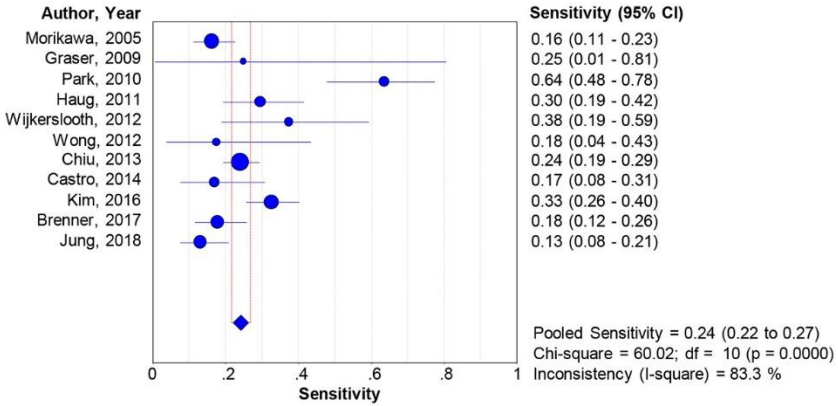
(A) qualitative iFOBT for advanced neoplasia of proximal colon



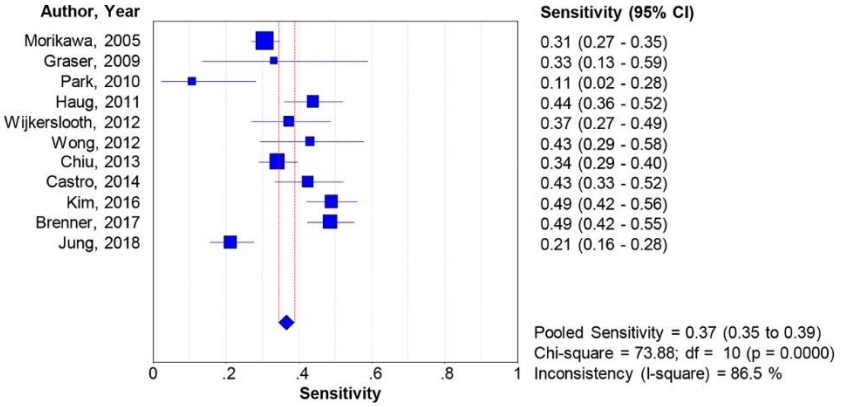
(B) qualitative iFOBT for advanced neoplasia of distal colon/rectum



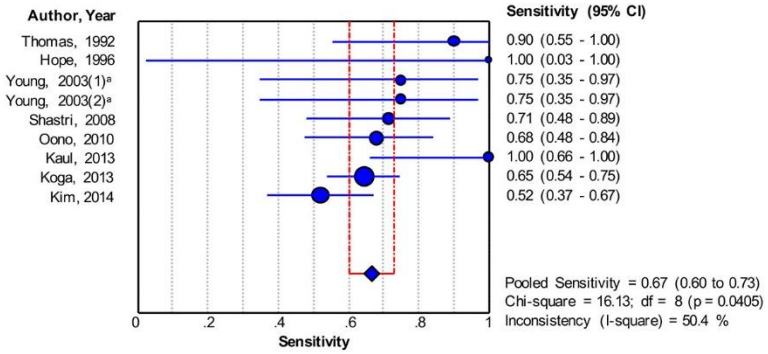
(C) quantitative iFOBT for advanced neoplasia of proximal colon



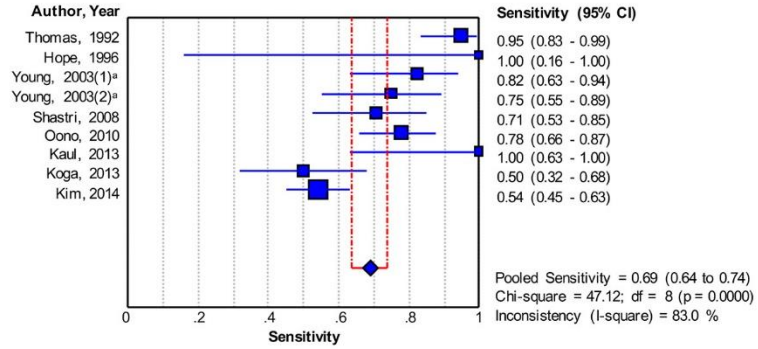
(D) quantitative iFOBT for advanced neoplasia of distal colon/rectum



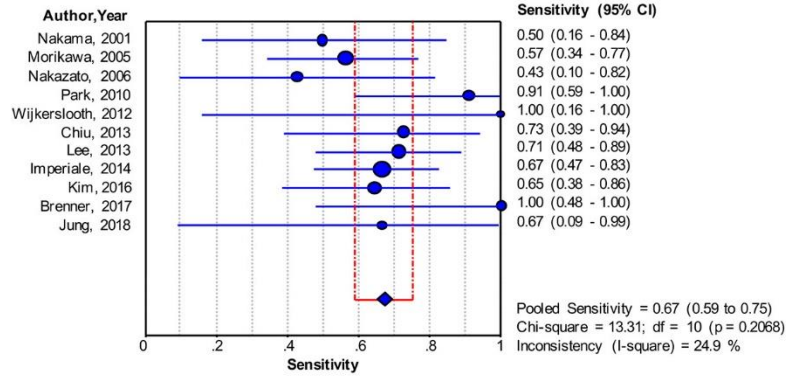
(A) iFOBT for detecting proximal colorectal cancer in clinical setting



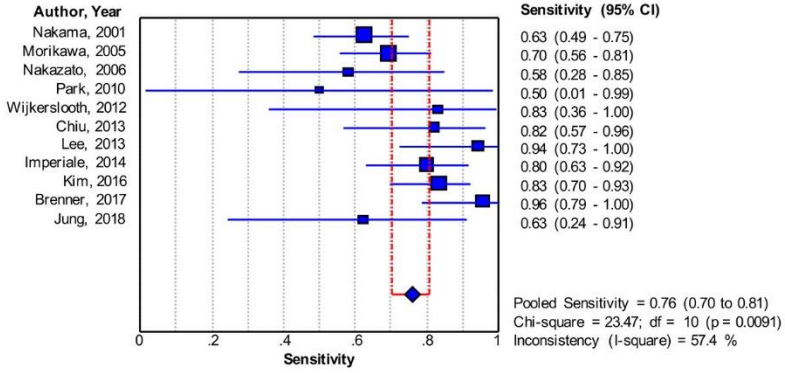
(B) iFOBT for detecting distal colorectal cancer in clinical setting



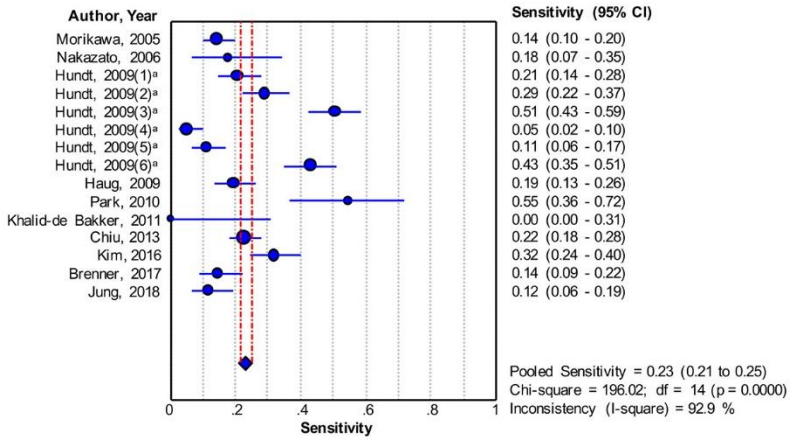
(C) iFOBT for detecting proximal colorectal cancer in screening setting



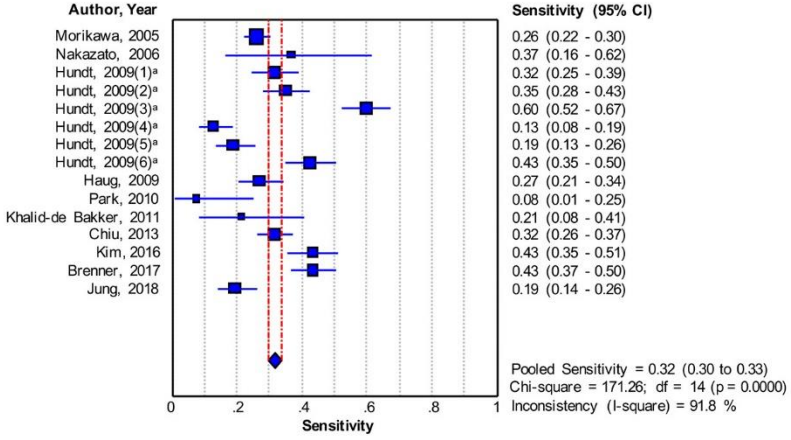
(D) iFOBT for detecting distal colorectal cancer in screening setting



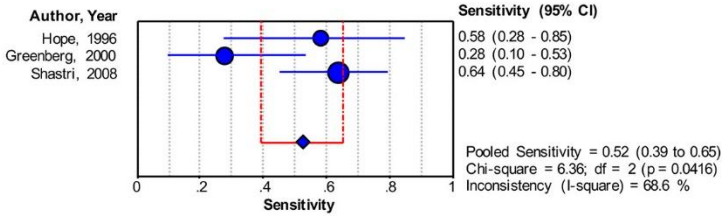
(A) iFOBT for detecting proximal advanced adenomas in screening setting



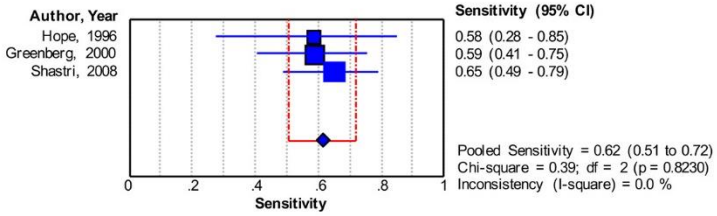
(B) iFOBT for detecting distal advanced adenomas in screening setting



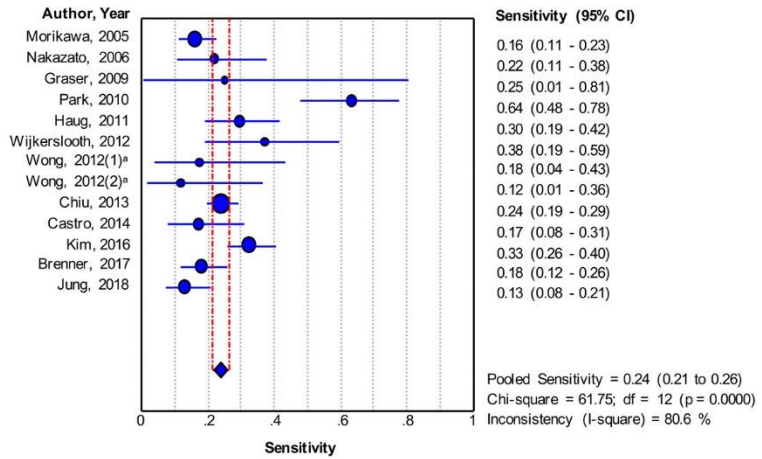
(A) iFOBT for detecting proximal advanced neoplasia in clinical setting



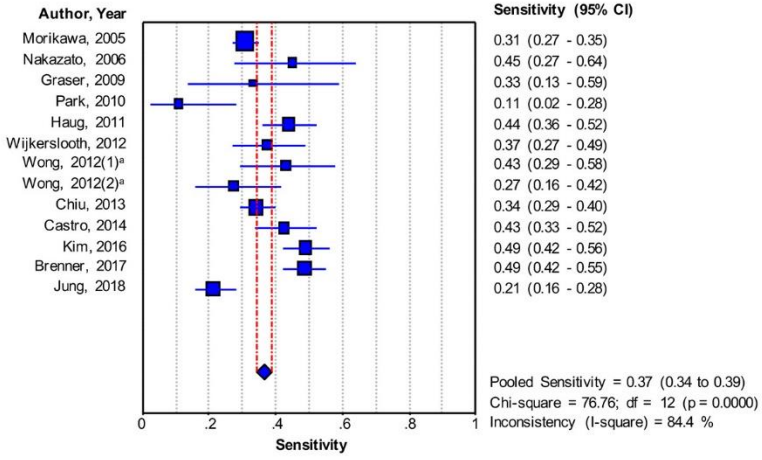
(B) iFOBT for detecting distal advanced neoplasia in clinical setting



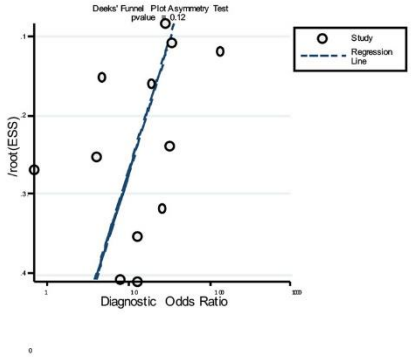
(C) iFOBT for detecting proximal advanced neoplasia in screening setting



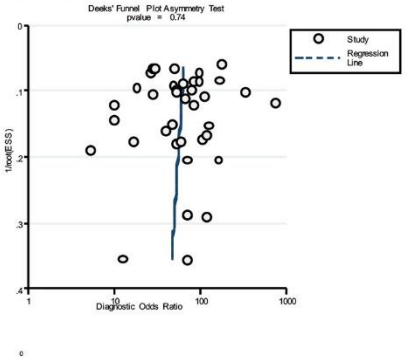
(D) iFOBT for detecting distal advanced neoplasia in screening setting



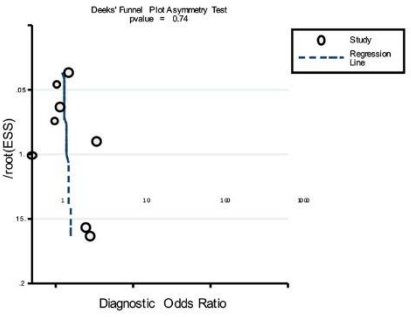
(A) for testing publication bias of detecting colorectal cancer by using guaiac-fecal occult blood test



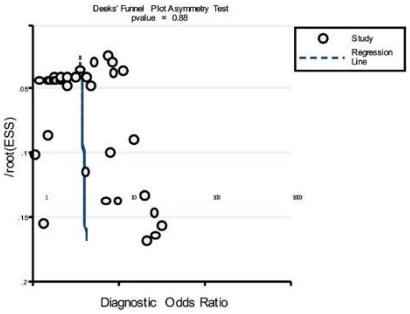
(B) for testing publication bias of detecting colorectal cancer by using immunochemical fecal occult blood test



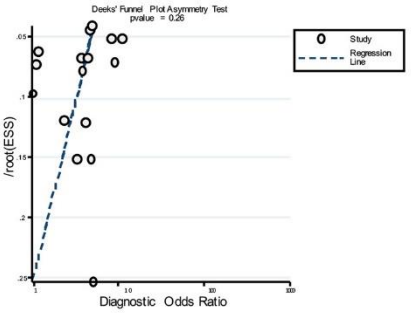
(C) for testing publication bias of detecting advanced adenoma by using guaiac-fecal occult blood test



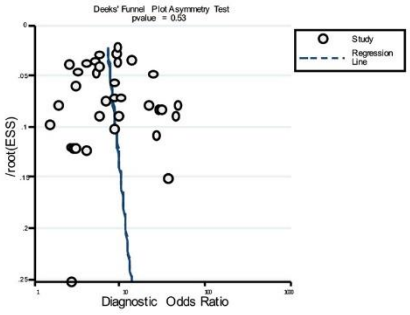
(D) for testing publication bias of detecting advanced adenoma by using immunochemical fecal occult blood test

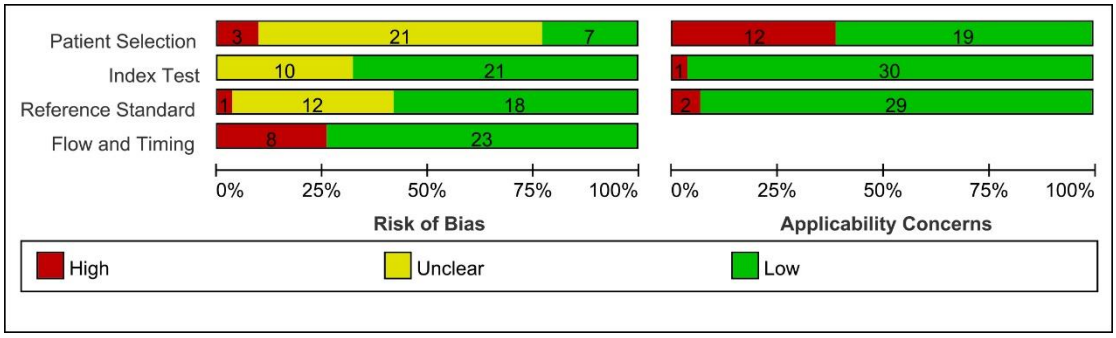


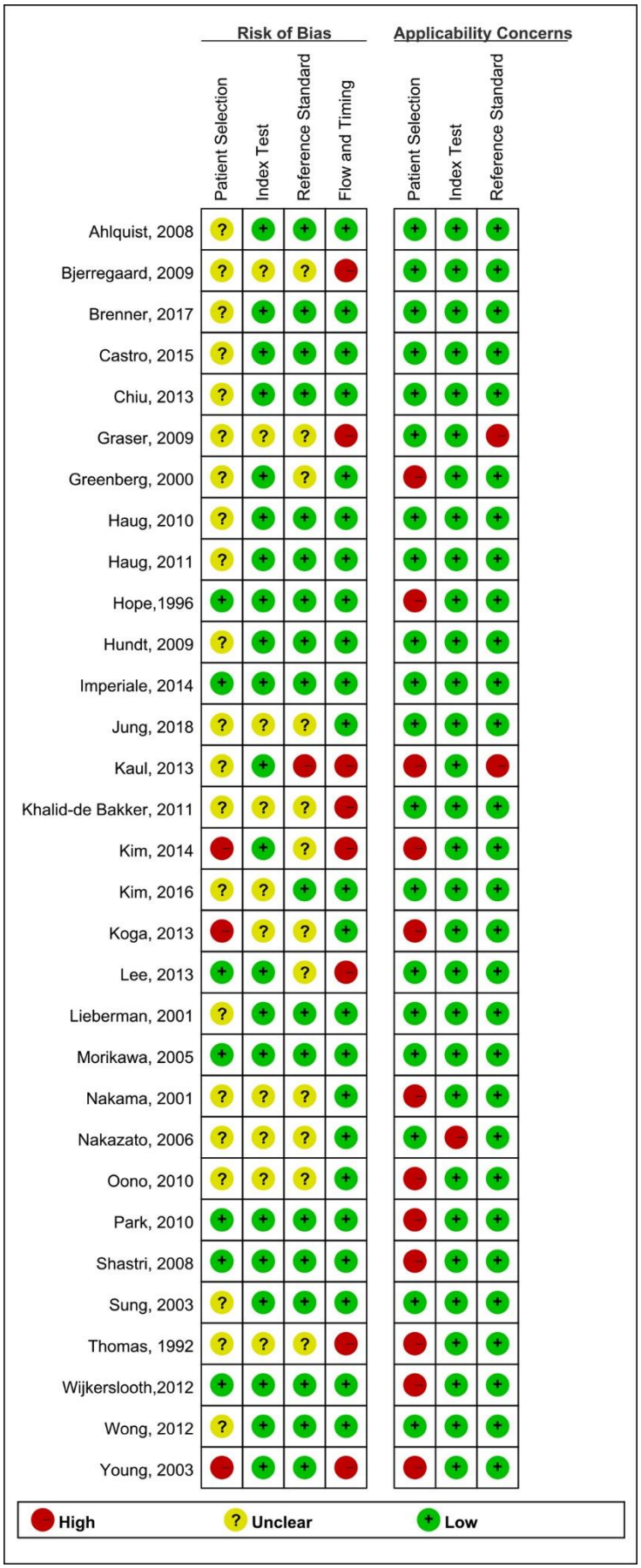
(E) for testing publication bias of detecting advanced neoplasia by using guaiac-occult blood test



(F) for testing publication bias of detecting advanced neoplasia by using immunochemical fecal occult blood test




Patient Selection
Index Test
Reference Standard
Flow and Timing
3
21
7
10
21
1
12
18
8
23
12
19
1
30
2
29
0%
25%
50%
75%
100%
Risk of Bias
Applicability Concerns
High
Unclear
Low


Risk of Bias
Applicability Concerns
Patient Selection
Index Test
Reference Standard
Flow and Timing
Patient Selection
Index Test
Reference Standard
Ahlquist, 2008
Bjerregaard, 2009
Brenner, 2017
Castro, 2015
Chiu, 2013
Graser, 2009
Greenberg, 2000
Haug, 2010
Haug, 2011
Hope,1996
Hundt, 2009
Imperiale, 2014
Jung, 2018
Kaul, 2013
Khalid-de Bakker, 2011
Kim, 2014
Kim, 2016
Koga, 2013
Lee, 2013
Lieberman, 2001
Morikawa, 2005
Nakama, 2001
Nakazato, 2006
Oono, 2010
Park, 2010
Shastri, 2008
Sung, 2003
Thomas, 1992
Wijkerslooth,2012
Wong, 2012
Young, 2003
High
Unclear
Low

Protocol 1. Description of the QUADAS-2 critical appraisal checklist

Domain 1. Patient selection

Risk of bias: Could the selection of patients have introduced bias?
Signaling question 1: Was a consecutive or random sample of patients enrolled?

- We scored "Yes" if a consecutive or random sample of eligible patients was enrolled; "No" if patients were selected by convenience; and "Unclear" if the study did not report the manner in which patients were enrolled.

Signaling question 2: Was a case-control design avoided?

- We scored "Yes" if a case-control design was avoided; "No" if the study employed a case-control design; and "Unclear" if study design was not reported.

Signaling question 3: Did the study avoid inappropriate exclusions?

- We scored "Yes" if no inappropriate exclusion was noted; "No" if inappropriate exclusions were noted such as patients were excluded because of prior knowledge about them other than their intestinal-related diseases status; "Unclear" if exclusion standards were not reported.

- We considered Risk of Bias to be "Low Risk" if we scored "Yes" for all of the three signaling questions; "High Risk" if we scored "No" for one out of the three signaling question; and "Unclear" if we scored "unclear" for one out of the three signaling question.

Concerns regarding applicability: Is there concern that the included patients do not match the review question?

- Our study aimed to investigate the diagnostic performance of fecal occult blood test (FOBT) in detecting colorectal neoplasms by anatomical site. We judged "Low Applicability Concern" if we scored "Yes" for studies that has already excluded patients who had history of colorectal cancer, inflammatory of bowel disease, and who had history of colonoscopy in the preceding 5 years; "High Applicability Concern" if we scored "No" for studies that has not excluded patients who had history of colorectal cancer, inflammatory of bowel disease, and were at active bleeding, or who had history of colonoscopy in the preceding 5 years; and "Unclear Applicability Concern" if we could not tell.

- ## Domain 2. Index Test

Risk of bias: Could the conduct or interpretation of the test have introduced bias?
Signaling question 1: Were the FOBT test results interpreted without knowledge of the results of colonoscopy?

- We scored "Yes" if the FOBT test results were interpreted without knowledge of the results of colonoscopy; "No" if blinding to test results were not done; and "Unclear" if this was not stated.

Signaling question 2: If a threshold was used, was it pre-specified?

- We scored "Yes" if an FOBT cut-off value was pre-specified or it was stated that "the cut-off value as per the manufacturer's guidelines was used"; and "No" if this was not stated.

- We considered Risk of Bias to be "Low Risk" if we scored "Yes" for both signaling questions; "High Risk" if we scored "No" for either of the questions; and "Unclear" if we were unclear about blinding status or cut-off value.

Concerns regarding applicability: Is there concern that FOBT test, its conduct, or interpretation differ from the review question?

- We judged "Low Applicability Concern" if interpretation of test results was blinded, threshold value was specified, and the test was performed as per the manufacturer's guidelines. We judged "High Applicability Concern" if blinding in test result interpretation was not done, threshold value was not specified or the test was not carried out as per the manufacturer's recommendations. We judged "Unclear Applicability Concern" if the blinding status of the study and threshold value were unclear.

Domain 3. Reference standard

Risk of bias: Could the conduct or interpretation of the test have introduced bias?

Signaling question 1: Is the reference standard likely to correctly classify the target condition?

- We scored "Yes" if diagnoses were confirmed by colonoscopy; "No" if diagnosis were not done by colonoscopy; and "Unclear" if this was not stated.

Signaling question 2: Were results of colonoscopy interpreted without knowledge of the results of FOBT test?

- We scored "Yes" if the results of colonoscopy were interpreted without knowledge of the results of FOBT test; "No" if blinding to test results were not done; and "Unclear" if this was not stated.

Concerns regarding applicability: Is there concern that TST test, its conduct, or interpretation differ from the review question?

- We judged "Low Applicability Concern" if interpretation of test results was blinded and diagnoses were referred to colonoscopy. We judged "High Applicability Concern" if blinding in test result interpretation was not done or diagnoses were not confirmed by colonoscopy. We judged "Unclear Applicability Concern" if the blinding status of the study and diagnosis tests were unclear.

Domain 4. Flow and timing

Risk of bias: Could the patient flow have introduced bias?

Signaling question 1: Did all patients received a reference standard?
We scored “Yes” if the all patients received a reference standard; “No” if not all of patients received a reference standard

Signaling question 2: Were all patients included in the analysis?
We scored “Yes” if all patients included in the analysis; “No” if not all of patients included in the study.