Supplementary Online Content

faecal Immunochemical Test Screening (Ages 45–75) Compared to No Screening

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Supplementary Figure 15. Forest Plot of Colorectal Cancer Mortality Risk Ratios for 5-Yearly

Flexible Sigmoidoscopy Screening (Ages 45–75) Compared to No Screening

Supplementary Figure 16. Forest Plot of Colorectal Cancer Incidence Risk Ratios for Biennial faecal Immunochemical Test Screening (Ages 45-75) Compared to No Screening

Supplementary Figure 17. Forest Plot of Colorectal Cancer Mortality Risk Ratios for Biennial faecal Immunochemical Test Screening (Ages 45-75) Compared to No Screening

Supplementary Table 1. Literature Search Strategy Used in PubMed

#1	"adenoma"[MeSH Terms] OR "Colorectal Neoplasms"[MeSH Terms]	344,574
#2	("colorectal"[Title/Abstract] OR "colon"[Title/Abstract] OR "colonic"[Title/Abstract] OR "rectum"[Title/Abstract] OR "rectal"[Title/Abstract]) AND ("cancer*"[Title/Abstract] OR "carcinoma*"[Title/Abstract] OR "neoplas*"[Title/Abstract] OR "tumor"[Title/Abstract] OR "tumors"[Title/Abstract] OR "tumour"[Title/Abstract] OR "tumours"[Title/Abstract] OR "adenocarcinoma*"[Title/Abstract] OR "adenoma*"[Title/Abstract] OR "malignan*"[Title/Abstract])	350,034
#3	#1 OR #2	486,881
#4	"Early Detection of Cancer"[MeSH Terms] OR "Mass screening"[MeSH Terms]	181,886
#5	"screen*"[Title/Abstract] OR "early diagnos*"[Title/Abstract] OR "early detect*"[Title/Abstract]	1,285,675
#6	#4 OR #5	1,334,089
#7	#3 AND #6	48,706
#8	"Incidence"[MeSH Terms] OR "Mortality"[MeSH Terms] OR "Mortality"[MeSH Subheading] OR "Cost-Benefit Analysis"[MeSH Terms]	1,251,811
#9	"effectiveness"[Title/Abstract] OR "incidence*"[Title/Abstract] OR "mortalit*"[Title/Abstract] OR "death*"[Title/Abstract] OR "fatalit*"[Title/Abstract] OR "fatal outcome*"[Title/Abstract] OR "surviv*"[Title/Abstract] OR "life-year*"[Title/Abstract] OR "year-of-life"[Title/Abstract] OR "cost benefit"[Title/Abstract] OR "cost effect*"[Title/Abstract] OR "cost utility"[Title/Abstract] OR "economic-anal*"[Title/Abstract]	4,655,944
#10	#8 OR #9	4,994,547
#11	#7 AND #10	19,253
#12	"models, theoretical"[MeSH Terms] OR "Computer Simulation"[MeSH Terms] OR "Markov Chains"[MeSH Terms] OR "model*"[Title/Abstract] OR "simulat*"[Title/Abstract] OR "markov"[Title/Abstract]	5,689,459
#13	#11 AND #12	4,271
#14	Filters: from 2014/1/1 - 2025/3/3	3,198

Supplementary Table 2. Literature Search Strategy Used in Embase

#1	'colorectal tumor'/exp	516,010
#2	('colorectal':ab,ti,kw OR 'colon':ab,ti,kw OR 'colonic':ab,ti,kw OR 'rectum':ab,ti,kw OR 'rectal':ab,ti,kw) AND ('cancer*':ab,ti,kw OR 'carcinoma*':ab,ti,kw OR 'neoplas*':ab,ti,kw OR 'tumor':ab,ti,kw OR 'tumors':ab,ti,kw OR 'tumour':ab,ti,kw OR 'tumours':ab,ti,kw OR 'adenocarcinoma*':ab,ti,kw OR 'adenoma*':ab,ti,kw OR 'malignan*':ab,ti,kw)	525,124
#3	#1 OR #2	647,185
#4	'early cancer diagnosis'/exp OR 'mass screening'/de OR 'cancer screening'/exp OR 'screening test'/exp	267,507
#5	'screen*':ab,ti,kw OR 'early diagnos*':ab,ti,kw OR 'early detect*':ab,ti,kw	1,804,409
#6	#4 OR #5	1,870,400
#7	#3 AND #6	80,981
#8	'incidence'/exp OR 'mortality'/exp OR 'survival'/exp OR 'cost effectiveness analysis'/exp OR 'cost benefit analysis'/exp	3,616,390
#9	'effectiveness':ab,ti,kw OR 'incidence*':ab,ti,kw OR 'mortalit*':ab,ti,kw OR 'death*':ab,ti,kw OR 'fatalit*':ab,ti,kw OR 'fatal outcome*':ab,ti,kw OR 'surviv*':ab,ti,kw OR 'life-year*':ab,ti,kw OR 'year-of-life':ab,ti,kw OR 'cost benefit':ab,ti,kw OR 'cost effect*':ab,ti,kw OR 'cost utility':ab,ti,kw OR 'economic-anal*':ab,ti,kw	6,555,479
#10	#8 OR #9	7,323,384
#11	#7 AND #10	35,822
#12	'model'/de OR 'simulation'/exp OR 'model'/exp OR 'markov chain'/exp OR 'model*':ti,ab,kw OR 'simulat*':ti,ab,kw OR 'markov':ti,ab,kw	7,631,922
#13	#11 AND #12	8,097
#14	'conference abstract'/it	5,382,065
#15	#13 NOT #14 Filters: from 2014/1/1 - 2025/3/3	3,950

Supplementary Table 3. Literature Search Strategy Used in Web of science

#1	TS=((colorectal OR colon OR colonic OR rectum OR rectal) AND (cancer* OR carcinoma* OR neoplas* OR tumor OR tumors OR tumour OR tumours OR adenocarcinoma* OR adenoma* OR malignan*))	446,693
#2	TS=(screen* OR "early diagnos*" OR "early detect*")	1,360,047
#3	TS=(effectiveness OR incidence* OR mortalit* OR death* OR fatalit* OR "fatal outcome*" OR surviv* OR life-year* OR year-of-life OR "cost benefit" OR "cost effect*" OR "cost utility" OR "economic-anal*")	5,621,523
#4	TS=(model* OR simulat* OR markov)	11,236,981
#5	#1 AND #2 AND #3 AND #4	4,236
#6	Filters: from 2014/1/1 - 2025/3/3	3,212

Supplementary Table 4. Inclusion and Exclusion Criteria

	Included criteria	Excluded criteria
Participants	General population at average risk for colorectal cancer (CRC); screening populations	Focused on CRC patients, middle or high-risk population
Intervention	At least one CRC screening modality, such as faecal immunochemical test (FIT), faecal occult blood test (FOBT), flexible sigmoidoscopy (FS), colonoscopy, CT colonoscopy, faecal DNA testing, and any other screening method not included in this list	Not focused on colorectal cancer screening
Comparator	No screening or alternate CRC screening modality	/
Outcome	CRC incidence, cancer-specific mortality and all-cause mortality	Not reported detailed number for the primary outcomes of interest; Model-based cost-effectiveness analysis that only reported the Incremental Cost-Effectiveness Ratio (ICER), quality-adjusted life-year (QALY) gained or life-year gained (LYG)
Study design	Simulation modelling study	Observational study(cross-sectional study, prospective study, case-control study) or randomised controlled trials (RCTs)
Language of article	Published in English	Not published in English
Publication type	Original study	Review, comments, conference abstract, editorial, or duplicate publications (only the latest publication kept)

Supplementary Table 5. Quality Assessment of Included Studies.

Specific model	**Study (Country, year)**	**Modelling approach:** (1) Adenoma pathway (2) Adenoma/tumor progression (3) Sensitivity analyses (4) Calibration	**Model parameters:** (1) Simulated population all-cause mortality rate (2) Adenoma and CRC incidence rate (3) Adenoma/CRC transition (4) Survival by cancer stage (5) Dynamic or static cohort (6) Sensitivity/specificity of screening methods (7) Adherence rate	**Transparency of data sources or assumptions** (Yes/No)	**External validation** (Yes/No)	**Overall risk of bias** (Low/High)
MISCAN-Colon	USA, 2021[1], USA, 2024[2], USA, 2024[3], USA, 2019[4] [a]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) Yes. Model structure; Sensitivity/specificity of tests; scenarios of CRC risk; sensitivity on benefit metrics[1]. Blood test sensitivity, screening interval and cost[2]. One-way sensitivity analyses (sensitivity and specificity of tests; adherence); probabilistic sensitivity analysis[3]. Sensitivity/specificity of tests; adherence; benefit metrics[4]. (4) Yes.	(1) 2017 US life tables. (2) SEER (1975-1979). (3) Time in each size category for adenoma, overall transition probability at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Yes. SEER. (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. UKFSS Trial, NORCCAP, SCORE.	Low

MISCAN-Colon	Saudi Arabia, 2021[5]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) Yes. Disutility of FIT screening; Life expectancy of 45-year-olds in Saudi Arabia; Costs of terminal care; Costs of FIT and colonoscopy. (4) Yes. MISCAN-Colon was calibrated to replicate the population of Saudi Arabia.	(1) Life tables for Saudi Arabia published by the World Health Organization. (2) CRC incidence in Saudi Arabia. (3) Time in each size category for adenoma, overall transition probability at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) 5-year CRC survival in Saudi Arabia. (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. UKFSS Trial, NORCCAP, SCORE.	Low
MISCAN-Colon	Shanghai, 2022[6]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) Yes. Test characteristics; cost of the validated FITs; international quality of life measurements; alternative surveillance pathway; WTP threshold; Probabilistic sensitivity analysis. (4) Yes.	(1) Life tables and birth tables from China's 6th population census in 2010. (2) Autopsy studies (adenoma prevalence); cancer incidence from Shanghai in 2015. (3) Progressive adenoma probability was fitted to adenoma prevalence in autopsy studies and cancer incidence from Shanghai in 2015; duration from progressive adenoma to preclinical cancer and duration of preclinical cancer was estimated from RCTs. (4) Data from 2015 in Shanghai. (5) Static cohort. (6) Yes.	No	Yes. UKFSS Trial, NORCCAP, SCORE.	Low

			(7) Yes. Full adherence.			
MISCAN-Colon	Norway, 2019[7]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) Yes. (4) Yes.	(1) Sex-specific lifetables for 2007 in Norway. (2) Autopsy studies. (3) The age-specific probability of adenoma-progressivity and the age- and localization-specific transition probabilities between preclinical cancer stages and between preclinical and clinical cancer stages were simultaneously calibrated to data on the age-, stage-, and localization-specific incidence of CRC in Norway during the NORCCAP trial. (4) Sex-, age-, stage-, and localisation-specific colorectal cancer survival as observed in Norway during the timeframe of the NORCCAP trial (1999-2011). (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. NORCCAP.	Low

MISCAN-Colon	the Netherlands, 2019[8]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) No. (4) Yes.	(1) Not reported. (2) Autopsy studies (adenoma prevalence); age-specific, stage-specific, and localization‐specific incidence of colorectal cancer in the Netherlands. (3) Yes. (4) Reported as dependent on cancer stage and age at diagnosis; screen-detected cases assigned one-stage better survival than clinically detected cases (based on RCTs, corrected for lead-time bias). (5) Static cohort. (6) Not applicable. (7) Yes. Realistic adherence.	No	Yes. UKFSS Trial, NORCCAP, SCORE.	High
MISCAN-Colon	USA, 2018[9]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) Yes. Sensitivity of each evaluated screening modality. (4) Yes.	(1) 2013 US life tables by race and sex. (2) Autopsy studies (adenoma prevalence); SEER (1990-1994, CRC incidence). (3) Time in each size category for adenoma, overall transition probability at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Yes. SEER (1975-2003). (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. UKFSS Trial, NORCCAP, SCORE.	Low

MISCAN-Colon	USA, 2018[10]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) Yes. Assumptions (faster adenoma progression to malignancy); incidence rate ratio (IRR). (4) Yes.	(1) 2013 U.S. lifetables. (2) Elevated risk based on trends in incidence under age 40. (3) Time in each size category for adenoma, overall transition probability at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Yes. SEER. (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. UKFSS Trial, NORCCAP, SCORE.	Low
SimCRC	USA, 2021[1], USA, 2024[2], USA, 2024[3], USA, 2019[4]a	(1) Adenoma-carcinoma sequence. (2) All adenomas have the potential to progress to CRC. (3) Yes. Model structure; Sensitivity/specificity of tests; scenarios of CRC risk; sensitivity on benefit metrics[1]. Blood test sensitivity, screening interval and cost[2]. One-way sensitivity analyses (sensitivity and specificity of tests; adherence); probabilistic sensitivity analysis[3]. Sensitivity/specificity of tests; adherence; benefit metrics[4]. (4) Yes.	(1) 2017 US life tables. (2) SEER (1975-1979) (3) Time in each size category for adenoma, overall transition probability at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Yes. SEER. (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. UKFSS Trial.	Low

SimCRC	USA, 2018[9]	(1) Adenoma-carcinoma sequence. (2) All adenomas have the potential to progress to CRC. (3) Yes. Sensitivity of each evaluated screening modality. (4) Yes.	(1) 2013 US life tables by race and sex. (2) Autopsy studies (adenoma prevalence); SEER (1975-1979, CRC incidence). (3) Time in each size category for adenoma, overall transition probability at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Yes. SEER (1975-2003). (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. UKFSS Trial.	Low
CRC-SPIN	USA, 2021[1], USA, 2024[2], USA, 2024[3], USA, 2019[4]a	(1) Adenoma-carcinoma sequence. (2) All adenomas have the potential to progress to CRC. (3) Yes. Model structure; Sensitivity/specificity of tests; Scenarios of CRC risk; Sensitivity on benefit metrics[1]. Blood test sensitivity, screening interval and cost[2]. One-way sensitivity analyses (sensitivity and specificity of tests; adherence); probabilistic sensitivity analysis[3]. Sensitivity/specificity of tests; adherence; benefit metrics[4].	(1) 2017 US life tables. (2) SEER (1975-1979) (3) Growth curve for adenoma, adenoma size at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Yes. SEER. (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. UKFSS Trial.	Low

		(4) Yes.				
CRC-SPIN	USA, 2023[11]	(1) Adenoma-carcinoma sequence. (2) All adenomas have the potential to progress to CRC. (3) Yes. (4) Yes. Recalibrated race-specific CRC-SPIN model.	(1) 2017 US life tables. (2) SEER. (3) Growth curve for adenoma, adenoma size at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Yes. (5) Static cohort. (6) Yes. (7) Not reported.	No	Yes. UKFSS Trial.	High
CRC-SPIN	USA, 2025[12]	(1) Adenoma-carcinoma sequence. (2) All adenomas have the potential to progress to CRC. (3) Yes. WTP threshold and test costs. (4) Yes. CRC-SPIN was recalibrated to predict the 2017-2021 CRC incidence for Hispanic adults aged 45 to 49 years in the Los Angeles Surveillance, Epidemiology, and End Results Registry.	(1) Not reported. (2) 2017-2021 CRC Incidence in the SEER Los Angeles registry. (3) Growth curve for adenoma, adenoma size at transition to preclinical CRC, and time to transition for transition to clinical CRC. (4) Not reported. (5) Static cohort. (6) Yes. (7) Yes. Full adherence and real-world adherence.	No	Yes. UKFSS Trial.	High
MOSAIC	USA, 2018[13]; USA, 2019[14]; USA,	(1) 85% potentially identifiable precursor. (2) Large adenomatous polyp may progress to CRC; normal epithelium may progress to CRC.	(1) U.S. life table data. (2) Autopsy data (polyp prevalence); SEER data (CRC incidence and stage distribution).	No	Yes. Minnesota Colon Cancer Control	Low

	2024[15]; USA, 2024[16]	(3) Yes. All model inputs[13],[14]. Proportion of CRC arising from SSLs; one-way sensitivity analyses and probabilistic Monte Carlo simulation[15]. Test costs and interval; adherence; proportion of CRC arising from SSLs[16]. (4) Yes.	(3) Cross-sectional age-specific prevalence rates (annual transition rate between health states of normal, small polyp, large polyp, localized, regional or disseminated CRC, and dead.) (4) SEER and clinical studies. (5) Static cohort. (6) Yes. (7) Yes.		Study; UKFSS Trial; SCORE; PLCO Trial.	
MOSAIC	Canada, 2019[17]	(1) 85% potentially identifiable precursor. (2) Large polyp may progress to CRC; normal epithelium may progress to CRC. (3) Yes. One-way sensitivity analysis (test characteristics, health utilities, adherence, and cost) and probabilistic sensitivity analysis. (4) Yes.	(1) Statistics Canada. (2) Autopsy data (prevalence of small polyp and large polyp); Alberta Health Service (CRC incidence). (3) The annual transition rate to small polyp from normal, annual transition rate to large polyp from small polyp, annual transition rate to cancer from large polyp, and annual transition rate to cancer without polypoid precursors were derived from model calibration. (4) Yes. Published data. (5) Static cohort. (6) Yes. (7) Yes.	No	Yes. Minnesota Colon Cancer Control Study; UKFSS Trial; SCORE; PLCO Trial.	Low
MOSAIC	USA, 2020[18]	(1) 85% potentially identifiable precursor. (2) Large polyp may progress to CRC; normal epithelium may progress to CRC.	(1) U.S. life table data. (2) Yes. (3) Annual transition rate to small polyp from normal; annual transition rate to large polyp from small polyp; annual	No	Yes. Minnesota Colon Cancer Control	Low

		(3) Yes. The distribution of actual colorectal cancer risk in the average risk population, the risk prediction tool's discriminatory ability, and its cost. (4) Yes.	transition rate to cancer without polypoid precursor; annual transition rate to cancer from large polyp. (4) Yes. (5) Static cohort. (6) Yes. (7) Yes. Full adherence.		Study; UKFSS Trial; SCORE; PLCO Trial.	
MOSAIC	USA, 2022[19]	(1) 85% potentially identifiable precursor. (2) Large adenomatous polyp may progress to CRC; normal epithelium may progress to CRC. (3) No. (4) Yes.	(1) Not reported. (2) Not reported. (3) Annual transition rate to small polyp from normal; annual transition rate to large polyp from small polyp; annual transition rate to cancer without polypoid precursor; annual transition rate to cancer from large polyp. (4) Not reported. (5) Static cohort. (6) Not reported. (7) Not reported.	No	Yes. Minnesota Colon Cancer Control Study; UKFSS Trial; SCORE; PLCO Trial.	High
MOSAIC	Germany, 2014[20]	(1) 85 % of CRCs develop through a potentially identifiable adenoma. (2) Large adenomatous polyp may progress to CRC; normal epithelium may progress to CRC. (3) Yes. One-way sensitivity analyses (all model inputs) and Monte Carlo simulation. (4) Yes.	(1) German national mortality table 2007- 2009. (2) Data from Munich Cancer Registry in 2000. (3) Yes. Annual transition rate between health states of normal, small polyp, large polyp and cancer. (4) Yes. (5) Static cohort. (6) Yes.	No	Yes. Minnesota Colon Cancer Control Study; UKFSS Trial; SCORE; PLCO	Low

			(7) Yes. Full adherence and imperfect adherence.		Trial.	
MOSAIC	Israel, 2024[21]; Israel, 2025[22]	(1) 85 % of CRCs develop through a potentially identifiable adenoma. (2) Large adenomatous polyp may progress to CRC; normal epithelium may progress to CRC. (3) Yes. One-way sensitivity analyses (test sensitivity and specificity, complication rates, CRC health state utilities, test costs, and CRC care costs). (4) Yes. Model was calibrated to predict Israel's National Cancer Registry data on CRC incidence and CRC mortality from 2002 to 2005.	(1) Israeli life tables. (2) Israel's National Cancer Registry data from 2002 to 2005. (3) Yes. Annual transition rate between health states of normal, small polyp, large polyp and cancer. (4) Yes. (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. Minnesota Colon Cancer Control Study; UKFSS Trial; SCORE; PLCO Trial.	Low
CRC-AIM	USA, 2020[23]	(1) Adenoma-carcinoma pathway. (2) Adenomas may grow and transition to preclinical CRC. (3) Yes. (4) Yes.	(1) Sex-specific cohort life tables from the years 1900-2010. (2) No. (3) Log-normal function of sex, adenoma size, individual's age at adenoma initiation, and adenoma location. (4) Parametric regression models based on SEER data (2000-2003). (5) Static cohort. (6) Yes.	No	Yes. UKFSS Trial.	High

			(7) Yes. A Spectrum of adherence including full adherence and real-world adherence.			
CRC-AIM	USA, 2023[24]; USA, 2023[25]; USA, 2024[26]	(1) Adenoma–carcinoma sequence. (2) Adenomas may grow and transition to preclinical CRC. (3) Yes. Adenoma sensitivity of the test[24]. One-way deterministic sensitivity analyses (adherence, costs and utilities) and probabilistic sensitivity analyses[25]. One-way sensitivity analyses and probabilistic sensitivity analyses[26]. (4) Yes.	(1) 2017 U.S. life table. (2) Calibrated to published data and SEER 1975-1979 incidence. (3) Log-normal function of sex, adenoma size, individual's age at adenoma initiation, and adenoma location. (4) Parametric linear regression model derived from cause-specific survival from SEER 2000-2003. (5) Static cohort. (6) Yes. (7) Yes. A spectrum of adherence including real-word adherence and perfect adherence.	No	Yes. UKFSS Trial.	Low
CRC-AIM	USA, 2021[27]	(1) Adenoma-carcinoma pathway. (2) Adenomas may grow and transition to preclinical CRC. (3) No. (4) Yes.	(1) Sex-specific cohort life tables from the years 1900-2010. (2) No. (3) Log-normal function of sex, adenoma size, individual's age at adenoma initiation, and adenoma location. (4) Parametric regression models based on SEER data (2000-2003). (5) Static cohort. (6) Yes.	No	Yes. UKFSS Trial.	High

			(7) Yes. Full adherence and real-world adherence.			
Policy1-Bowel	Australia, 2018[28], Australia, 2018[29]	(1) Adenoma–carcinoma pathway (85%) and the serrated pathway (15%). (2) Advanced adenoma and small sessile serrated adenoma and large sessile serrated adenoma may progress to CRC. (3) Yes. One-way sensitivity analysis and probabilistic sensitivity analysis. (4) Yes.	(1) All causes mortality rate observed in 2011 in Australia. (2) COCOS trial and published data in Australia in 2005-2007. (3) Yes. (4) Published data in Australia in 2000-2003. (5) Static cohort. (6) Yes. (7) Yes. Full adherence, low and high adherence.	No	Yes. Funen trial, Burgundy trial, and Minnesota Colon Cancer Control Study. NORCCAP, SCORE, and UKFSST	Low
Policy1-Bowel	Australia, 2022[30]	(1) Adenoma–carcinoma pathway (85%) and the serrated pathway (15%). (2) Advanced adenoma and small sessile serrated adenoma and large sessile serrated adenoma may progress to CRC. (3) Yes. (4) Yes.	(1) All-causes mortality rates in 2008–2012 for Aboriginal and Torres Strait Islander peoples. (2) National data observed in 2009-2013 for Aboriginal and Torres Strait Islander peoples. (3) Adenoma size progression and regression rate; probability of developing high-grade dysplasia by adenoma size. (4) Yes. Symptomatic survival was calibrated to Western Australia public	No	Yes. Funen trial, Burgundy trial, and Minnesota Colon Cancer Control Study. NORCCAP,	Low

			hospital data; screen-detected survival was adjusted using relative mutipliers. (5) Static cohort. (6) Yes. (7) Yes. Real-world adherence.		SCORE, and UKFSST	
COSIMO	Germany, 2021[31]; Germany, 2021[32]	(1) Adenoma-carcinoma sequence. (2) Advanced adenoma may progress to CRC. (3) Yes. Starting prevalence and transition rates; positivity cut-offs of the test[31]. Starting prevalence and transition rates; screening starting age[32]. (4) Yes.	(1) German population life tables 2010/2012. (2) German screening colonoscopy program. (3) Nationwide screening colonoscopy registry. Annual incidence and transition rates were estimated from prevalences of adenomas in 2003-2011 (2003-2009) and 2004-2012 (2004-2010). (4) Annual CRC-specific mortality rate from the German Cancer Registry. (5) Static cohort. (6) Yes. (7) Yes.	Yes	Yes. SCORE, NORCCAP, UKFSS and PLCO.	Low
CMOST	USA, 2021[33]	(1) Adenoma-carcinoma pathway or direct cancer pathway. (2) Stage 6 adenoma and smaller adenoma (stage 1-4) may progress to CRC. Cancer may progress without adenomatous precursors. (3) Yes. Adherence to screening and follow-up; probability of adenoma detection during	(1) 2008 US Life Table. (2) Publishhed data (adenoma prevalence); SEER (2005-2009, cancer incidence). (3) Yes. Age-dependent adenoma initiation risk was defined by a sigmoidal function; age-dependent early adenoma and advanved adenoma progression risk were defined by a Gaussian funcion.	No	Yes.	Low

		colonoscopy; risk for colonoscopy adverse events; screening and treatment costs; test sensitivity and specificity. (4) Yes.	(4) SEER 2005-2009. (5) Static cohort. (6) Yes. (7) Yes. Full adherence and real-world adherence.			
CMOST	Shenzhen, China, 2024[34]	(1) Adenoma-carcinoma pathway and serrated pathway. (2) Stage 6 adenoma and smaller adenoma (stage 1-4) may progress to CRC. Cancer may progress without adenomatous precursors. (3) Yes. Adherence; screening strategies without surveillance colonoscopies for adenoma and cancer. (4) Yes.	(1) China life table for 2020. (2) Published data (prevalence of advanced adenomas); GBD 2019 (CRC incidence). (3) Same as the original model. (4) Cause of death surveillance data set. (5) Static cohort. (6) Yes. (7) Yes. Real-world adherence.	No	Yes.	Low
MIMIC-CRC	China, 2022[35]	(1) Adenoma-carcinoma pathway. (2) Advanced adenoma may progress to CRC. (3) Yes. One-way sensitivity analyses. (4) Yes.	(1) China Health & Family Planning Statistics Yearbook 2016. (2) Initial prevalence rates were from a large-scale multicenter population-based colonoscopy screening program in China. Adenoma incidence was calibrated based on the data from literature. (3) The annual transition probabilities between CRC-related states were estimated and calibrated based on	No	Yes. UKFSS.	Low

			published studies concerning the natural history of CRC. (4) CRC-related mortality was derived from the China Health & Family Planning Statistics Yearbook 2016. (5) Static cohort. (6) Yes. (7) Yes. Real-world adherence.			
MIMIC-CRC	China, 2024[36]	(1) Adenoma-carcinoma pathway. (2) Advanced adenoma may progress to CRC. (3) Yes. Univariate (one-way) and multivariate deterministic sensitivity analyses (utility, screening costs, diagnostic costs, discount rates, screening completion rates, screening sensitivity, and specificity); probabilistic sensitivity analyses. (4) Yes.	(1) Chinese Population Censes Yearbook 2020. (2) China National Cancer Center and the Global Burden of Disease study. (3) The annual transition probabilities between CRC-related states were estimated and calibrated based on published studies concerning the natural history of CRC. (4) Chinese Population Censes Yearbook 2020 and population-based cancer registration. (5) Static cohort and dynamic cohort. (6) Yes. (7) Yes. Real-world adherence.	No	Yes. UKFSS.	Low
PREDICT	USA, 2020[37]	(1) Adenoma-carcinoma pathway. (2) Advanced adenoma may progress to CRC. (3) Yes. One-way sensitivity analysis.	(1) US life tables. (2) National colonoscopy screening registry from 2003 through 2012 in Germany. (3) Annual age and sex specific progression rates between different	No	Yes. UKFSS, PLCO,.	Low

		(4) Yes.	disease stages (i.e., non-advanced adenoma, advanced adenoma, preclinical CRC, and clinical CRC) from published data from a large data registry. (4) SEER. (5) Static cohort. (6) Yes. (7) Yes. Full adherence and real-world adherence.			
ANSER	USA, 2024[38]	(1) Adenoma-carcinoma sequence and serrated pathway. (2) Advanced adenoma and SSL may progress to CRC. (3) Yes. The plausible range of CRCs arising from SSLs. (4) Yes.	(1) U.S. life tables. (2) Autopsy data (adenoma prevalence) and colonoscopy studies (SSLs prevalence); SEER (1990-1994, cancer incidence). (3) Size and lesion type-specific annual transition probability for lesion growth; age and sex-specific annual transition probability for large lesion progression; age and stage-specific annual transition probability for preclinical CRC stage progression and preclinical CRC symptom development. (4) SEER (2004-2015). (5) Static cohort. (6) Yes. (7) Yes. Full adherence.	No	Yes. Minnesota Colorectal Cancer Control Study, UKFSS.	Low
ASCCA	the Netherlands,	(1) Adenoma–carcinoma pathway. (2) Advanced adenomas can	(1) Dutch Central Bureau of Statistics. (2) Dutch COlonoscopy vs COlonography Screening (COCOS) trial	No	Yes.	Low

	2016[39]	progress to CRC, regression in size allowed. (3) Yes. Natural history parameters; costs of CRC treatment; positivity rate of imaging techniques; costs per imaging test; cost of complications (4) Yes.	(prevalence rates) and Dutch Cancer Registry. (3) Annual transition rate between states were calibrated against the age-, sex- and size-specific prevalence rates in the COCOS trial. (4) Dutch Cancer Registry. (5) Static cohort. (6) Yes. (7) Yes. Real-world adherence.			
EU-TOPIA	Israel, 2025[22]	(1) Adenoma-carcinoma sequence. (2) Progressive adenomas may progress to CRC. (3) No. (4) Yes.	(1) All-cause mortality by age from 2022 in Israel. (2) CRC incidence in Israel (2001–2005). (3) Not reported. (4) Yes. (5) Static cohort. (6) Yes. (7) Not reported.	No	Yes.	High
CAN-SCREEN	USA, 2025[40]	(1) Adenoama-carcinoma pathway. (2) Advanced adenoma may progress to CRC. (3) Yes. Follow-up diagnostic colonoscopy adherence and test interval. (4) Yes.	(1) National Center for Health Statistics. (2) CRC stage distribution (SEER 1975–1979). (3) Yes. (4) Yes. Published data. (5) Static cohort. (6) Yes. (7) Yes. Real-world adherence.	No	No	High
CAN-SCREEN	USA, 2024[41]	(1) Adenoama-carcinoma pathway.	(1) National Center for Health Statistics.	No	No	High

		(2) Advanced adenoma may progress to CRC. (3) Yes. one-way sensitivity analyses (AA sensitivity, adherence and screening interval) (4) Yes.	(2) CRC stage distribution (SEER 1975–1979). (3) Yes. (4) Yes. Published data. (5) Static cohort. (6) Yes. (7) Yes. Full adherence and real-world adherence.			
DECAS	Germany, 2024[42]	(1) adenoma-carcinoma pathway (85%) and serrated pathways. (2) Advanced adenoma and clinically relevant serrated polyp may progress to CRC. (3) Yes. (4) Yes.	(1) German life table 2010–2014. (2) Registry data in 2007-2014 for adenoma prevalence and registry data in 203-2006 for CRC prevalence; the serrated polyp prevalence was calibrated using published data. (3) Yes. (4) Bavarian Cancer Registry data. (5) Static cohort. (6) Yes. (7) Yes. Full adherence, real-world adherence and high adherence.	No	Yes. UKFSS, ZfKD in 2003-2006, a large German colonoscopy cohort study (ESTHER).	Low
Markov model	Ukraine, 2018[43]	(1) Adenoma-carcinoma pathway. (2) Advanced adenoma may progress to CRC. (3) Yes. One-way sensitivity analyses (test characteristics, adherence, rate of complications, and costs of screening and treatment); two and three-way	(1) 2013 Ukrainian life tables. (2) Published data (prevalence of the polyps); National Cancer Registry of Ukraine database (CRC incidence). (3) Age-specific transition probabilities between states including normal mucosa, low risk polyp, high risk polyp, preclinical local cancer, preclinical regional cancer, preclinical distal cancer,	No	No	High

		sensitivity analyses. (4) Yes.	clinical local cancer, clinical regional cancer, clinical distal cancer were derived from published data. (4) SEER. (5) Static cohort. (6) Yes. (7) Yes.			
Markov model	USA, 2023[44]	(1) The polypoid pathway (from a low-risk to high-risk adenoma to CRC) and the nonpolypoid pathway (from a normal health state to CRC). (2) Adenoma and normal colon may progress to CRC. (3) Yes. (4) Yes.	(1) 2018 CDC U.S. Life Tables. (2) Autopsy data (polyp prevalence); SEER 1990-1994; published data. (3) Yes. Annual transition probabilities were derived from published data. (4) Yes. (5) Static cohort. (6) Yes. (7) Yes.	No	Yes. UKFSS, SCORE, MCLIR, NordICC	Low
Markov model	USA, 2022[45]	(1) Adenoma–carcinoma sequence (85%) and denovo pathways. (2) Adenoma and normal colon may progress to CRC. (3) Yes. (4) Yes.	(1) Yes. (2) Endoscopic data (polyp prevalence); SEER (CRC incidence). (3) Transitional probabilities among different health states were derived from a systematic literature search. (4) Published data. (5) Static cohort. (6) Yes. (7) Yes.	No	Yes. UKFSS.	Low
Markov model	USA, 2023[46]	(1) Health-cancer pathway. (2) If patients were not screened, as in the natural history, there	(1) CDC life tables. (2) SEER data prior to 2000.	No	No	High

		was no polyp detection or polyp surveillance, and the cancer state was entered only after diagnostic colonoscopy due to symptomatic presentation. (3) Yes. One-way sensitivity analyses and probabilistic sensitivity analysis. (4) Yes.	(3) Annual transitions between states of health, polyp, cancer, cancer death, and all-cause mortality death. (4) SEER. (5) Static cohort. (6) Yes. (7) Yes.			
Markov model	Japan, 2016[47]	(1) Adenoma-carcinoma pathway. (2) High-risk polyp may progress to CRC. (3) Yes. scenario analyses (uptake rates and screening age); probabilistic sensitivity analysis (transition probabilities, costs, test characteristics, uptake rates and quality of life scales) (4) Yes.	(1) No. (2) Japan's Cancer Registry and Statistics. (3) Yes. The disease progression parameters from normal epithelium to colorectal polyps and cancer were based on CRC incidence data and the polyp prevalence data published in Japan. (4) Yes. (5) Static cohort. (6) Yes. (7) Yes.	No	No	High
Markov model	China, 2022[48]	(1) Adenoma–carcinoma sequence. (2) High-risk adenoma may progress to CRC. (3) Yes. (4) Yes.	(1) China population and Employment Statistics Yearbook in 2017. (2) Yes. 2017 global burden of disease data in China. (3) Yes. (4) Yes. Literature data in Hong Kong. (5) Static cohort. (6) Yes. Published literature.	No	Yes.	Low

			(7) Yes.			
Decision analysis model	Asia, 2023[49]	(1) Not based on tumor progression. (2) Not based on tumor progression. (3) Yes. Sensitivity of M3CRC, compliance rates of screening tests, and cost of colonoscopy. (4) No.	(1) No. (2) Yearly age-specific incidence rates of CRC in Hong Kong. (3) Yes. The transition probabilities were derived from published data in Asian countries. (4) Yes. Annual mortality of CRC patients at various stages of disease. (5) Static cohort. (6) Yes. (7) Yes.	No	No	High
Markov model	China, 2016[50]	(1) Not based on tumor progression. (2) Not based on tumor progression. (3) Yes. One-way sensitivity analyses (specificity of FS, compliance, colonoscopy costs) and probabilistic analysis. (4) No	(1) No. (2) Age-stratified incidence of CRC of the Hong Kong population. (3) Not appliable. (4) The annual mortality rate of CRC was extrapolated from the Hong Kong Cancer Registry. (5) Static cohort. (6) Yes. (7) Yes.	No	No	High
Markov model	China, 2025[51]	(1) Not based on tumor progression. (2) Not based on tumor progression. (3) Yes. (4) No.	(1) No. (2) CRC risk after screening tests. (3) Not appliable. (4) The annual mortality rate of CRC patients at various stages was extrapolated from the data of the Hong	No	No	High

			Kong Cancer Registry and a study on survival modeling of CRC. (5) Static cohort. (6) Yes. (7) Yes.			
Markov model	USA, 2017[52]	(1) Not based on tumor progression. (2) Not based on tumor progression. (3) Yes. (4) No.	(1) Period Life Table, 2010. (2) SEER 1990-1995. (3) CRC risk after screening tests. (4) The model predicted the mortality using the natural history of CRC after incidence reduction and stage-shift for the screened population. (5) Static cohort. (6) Yes. (7) Yes.	No	No	High
Markov model	USA, 2025[53]	(1) Adenoma-carcinoma pathway. (2) Yes. Advanced adenoma may progress to CRC. (3) Yes. One-way sensitivity analyses (all model inputs) and probabilistic sensitivity analysis. (4) Yes.	(1) Yes. US Life Tables (World Health Organization; RRID:SCR_008505). (2) Published data. (3) Yes. Surveillance, Epidemiology, and End Results (SEER) data (RRID:SCR_006902) and published data were used to estimate the transition probability to model adenoma and CRC progression over time. (4) Static cohort. (5) Yes. (6) Yes.	No	No	High

Abbreviations: CRC, colorectal cancer; MISCAN-Colon, MIcrosimulation SCreening ANalysisColon; USA, United States of America; SEER,

Surveillance, Epidemiology, and End Results; UKFSS, UK Flexible Sigmoidoscopy Screening Trial; NORCCAP, Norwegian Colorectal Cancer Prevention Trial; SCORE, Screening for Colon and Rectum Trial; SimCRC, Simulation Model of Colorectal Cancer; CRC-SPIN, CRC Simulated Population Model for Incidence and Natural History; WTP, willingness-to-pay; MOSAIC, Model of Screening and Surveillance for Colorectal Cancer; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; CRC-AIM, Colorectal Cancer and Adenoma Incidence and Mortality Microsimulation Model; COSIMO, Colorectal Cancer Multistate Simulation Model; CMOST, Colon Modeling Open Source Tool; MIMIC-CRC, MIcrosimulation Model for prevention and Intervention of Colorectal Cancer; PREDICT, Predictive modeling, Evidence integration, and Decision analysis In Clinical Therapeutics; ANSER, Adenoma aNd SERrated pathway; ASCCA, Adenoma and Serrated pathway to Colorectal CAncer; EU-TOPIA, Towards Improved Screening for breast, cervical and colorectal cancer in All of Europe; CAN-SCREEN, Colorectal cANcer SCReening Economics and adherENce; DECAS, Discrete Event simulation model for the natural history of colorectal cancer from the Adenoma and Serrated neoplasia pathways; MCLIR, Maximum Clinical Incidence Reduction; NordICC, Nordic-European Initiative on Colorectal Cancer.

[a] Studies used the same model inputs and assumptions.

Supplementary Table 6. Sensitivity Analyses of Pooled Risk Ratios Using Alternative Assumed Cohort Sizes (1,000 vs 10,000 Participants per Arm)

Screening strategies[a] (modality, age range, interval)	**No. of studies**	**No. of scenarios**	**RR of CRC incidence (95% CI)**		**No.of studies**	**No. of scenarios**	**RR of CRC mortality (95% CI)**[b]	
Perfect adherence			***n=1000***	***n=10000***			***n=1000***	***n=10000***
Colonoscopy, 45-75, 10	13	23	0.23 (0.19-0.28)	0.22 (0.18-0.26)	13	23	0.17 (0.14-0.21)	0.15 (0.12-0.18)
FIT, 45-75, 1	17	28	0.36 (0.32-0.41)	0.35 (0.31-0.40)	17	28	0.23 (0.20-0.27)	0.22 (0.20-0.25)
CTC, 45-75, 5	5	26	0.35 (0.30-0.41)	0.33 (0.29-0.39)	5	26	0.24 (0.20-0.28)	0.22 (0.19-0.25)
mSEPT9, 50-75, 1	3	4	0.46 (0.38-0.57)	0.45 (0.36-0.56)	2	2	0.25 (0.13-0.52)	0.25 (0.11-0.54)
mt-sDNA, 45-75, 3	11	20	0.40 (0.36-0.45)	0.39 (0.35-0.44)	11	20	0.26 (0.22-0.31)	0.26 (0.24-0.28)
FS, 45-75, 5	6	29	0.39 (0.36-0.42)	0.38 (0.35-0.41)	6	29	0.28 (0.25-0.33)	0.28 (0.26-0.30)
FIT, 45-75, 2	10	19	0.51 (0.46-0.57)	0.51 (0.45-0.56)	10	19	0.31 (0.26-0.36)	0.30 (0.27-0.33)
Realistic adherence								
Colonoscopy, 45-75, 10	6	6	0.50 (0.42-0.60)	0.50 (0.44-0.57)	5	5	0.43 (0.31-0.60)	0.43 (0.33-0.56)
FIT, 45-75, 1	9	9	0.60 (0.52-0.70)	0.60 (0.52-0.69)	8	8	0.49 (0.39-0.62)	0.47 (0.38-0.59)
CTC, 45-75, 5	2	2	0.84 (0.66-1.06)	0.83 (0.69-0.99)	3	3	0.71 (0.51-0.97)	0.68 (0.53-0.87)
mSEPT9, 50-75, 1	2	2	0.50 (0.37-0.67)	0.49 (0.37-0.65)	2	2	0.33 (0.18-0.58)	0.32 (0.17-0.60)
mt-sDNA, 45-75, 3	7	7	0.48 (0.37-0.61)	0.47 (0.37-0.61)	7	7	0.38 (0.28-0.50)	0.38 (0.28-0.50)
FS, 45-75, 5	4	4	0.78 (0.64-0.95)	0.78 (0.70-0.87)	3	3	0.66 (0.46-0.94)	0.66 (0.59-0.73)
FIT, 45-75, 2	5	5	0.76 (0.64-0.91)	0.74 (0.64-0.87)	5	5	0.63 (0.46-0.87)	0.60 (0.49-0.74)

Abbreviations: CI, confidence interval; CRC, colorectal cancer; CTC, computed tomography colonography; FIT, fecal immunochemical test; FS, flexible sigmoidoscopy; mSEPT9, methylated Septin 9 DNA blood test; mt-sDNA, multitarget stool-based DNA; RR, risk ratios.

[a] Screening strategies are presented as screening modality, age to begin-age to end screening, screening interval

[b] Lifetime effects compared with no screening

Supplementary Table 7. Summary of Screening Effectiveness for Hybrid Strategies[a]

Study	Screening age	Screening modality	Screening interval	Adherence	CRC incidence (RRR)	CRC mortality (RRR)
Barzi, 2017	50-75	FS, FIT	5_1	realistic 0.63	8.00%	14.00%
Barzi, 2017	50-75	FS, FIT	5_2	realistic	7.00%	17.00%
Lew, 2018	55-74	FS, FIT	Once-off FS screening at 55 years combined with 2-yearly FIT at 60-74 years	realistic	12%	18%
Barzi, 2017	50-75	FS, FOBT	5_1	realistic 0.63	14.00%	19.00%
Barzi, 2017	50-75	FS, FOBT	5_2	realistic	13.00%	21.00%
Lwin, 2024	50-65	FIT, colonoscopy	Men: 2 colonoscopies at age 50 and 60 years; Women: annual FIT for age 50–54 years followed by 2 colonoscopies at 55 and 65 years	realistic	15.38%	26.43%
Lwin, 2024	45-60	FIT, colonoscopy	FIT(1y, 45-49); colonoscopy(10y, 50-60)	realistic	16.33%	27.28%
Lwin, 2024	45-70	FIT, colonoscopy	FIT(1y, 45-49); colonoscopy(10y, 50-70)	realistic	17.58%	28.21%
Lew, 2018	50-74	FS, FIT	2-yearly FIT screening at 50-74 years combined with FS at age 50 for negative FIT	realistic	23%	37%

Lew, 2018	50-74	FS, FIT	2-yearly FIT screening at 50-74 years combined with FS at 54, 64 and 74 years for negative FIT	realistic	25%	38%
Lew, 2018	50-74	FIT, mSEPT9	2-yearly FIT screening at 50-74 years combined with mSEPT9 in underscreened individuals	realistic	24%	39%
Lew, 2018	50-74	FIT, colonoscopy	Once-off colonoscopy screening at 50 years combined with 2-yearly FIT at 52-74 years	realistic	26%	39%
Aziz, 2023	45-75	colonoscopy, liquid biopsy	10y	realistic 60.6% for screening colonoscopy; the unscreened underwent LB	42.31%	43.75%
Lu, 2022	50-65	FIT, colonoscopy	FIT biennually at 50-54, colonoscopy at 55 and 65	realistic 94% for FIT, 42% for colonoscopy	49%	57.00%
Lu, 2022	50-65	FIT, colonoscopy	FIT annually at 50-54, colonoscopy at 55 and 65	realistic 94% for FIT, 42% for colonoscopy	55%	62.00%
Sharaf, 2022	65-75	FIT, colonoscopy	FIT(65);colonoscopy(10y, 66-75)	100%	56.00%	63.00%
Sharaf, 2022	65-75	FIT, colonoscopy	FIT(65,66);colonoscopy(10y, 67-75)	100%	55.00%	64.00%
Melnitchouk, 2018	50-75	FS, FOBT	5_1	realistic 0.75	NA	64.00%
Rui, 2025	45-75	FS, FIT	10_1	realistic	40.39%	66.02%
Lew, 2018	55-74	FS, FIT	Once-off FS screening at 55 years combined with 2-yearly FIT at 60-74 years	100%	53%	69%
Knudsen, 2021	50-75	FS, FIT	10_1	100%	51.85%	70.59%

Lwin, 2024	50-65	FIT, colonoscopy	Men: 2 colonoscopies at age 50 and 60 years; Women: annual FIT for age 50–54 years followed by 2 colonoscopies at 55 and 65 years	100%	64.04%	72.05%
Knudsen, 2021	45-75	FS, FIT	10_1	100%	54.32%	73.53%
Ladabaum, 2019	45-75	FS, FIT	FS(once, at 45); FIT(1y, 50-75)	100%	62.30%	74.40%
Lwin, 2024	45-60	FIT, colonoscopy	FIT(1y, 45-49); colonoscopy(10y, 50-60)	100%	66.07%	74.94%
Sharaf, 2022	50-75	FIT, colonoscopy	FIT(once,50); colonoscopy(10y,51-75)	100%	70.00%	75.00%
Sharaf, 2022	50-75	FIT, colonoscopy	FIT(1y, 50-51);colonoscopy(10y, 52-75)	100%	70.00%	76.00%
Lwin, 2024	45-70	FIT, colonoscopy	FIT(1y, 45-49); colonoscopy(10y, 50-70)	100%	67.92%	76.45%
Ladabaum, 2019	45-75	FS, colonoscopy	sigmoidoscopy(once, at 45); colonoscopy(10y, 50-75)	100%	70.80%	76.70%
Ladabaum, 2019	45-75	FIT, colonoscopy	FIT(1y, 45-49); colonoscopy(10y, 50-75)	100%	70.80%	76.70%
Lew, 2018	50-74	FS, FIT	2-yearly FIT screening at 50-74 years combined with FS at age 50 for negative FIT	100%	59%	77.00%
Rui, 2025	45-75	FS, FIT	10_1	100%	70.06%	77.70%
Lew, 2018	50-74	FIT, colonoscopy	Once-off colonoscopy screening at 50 years combined with 2-yearly FIT at 52-74 years	100%	62%	78.00%

Naber, 2019	50-75	FS, FIT	10_1	100%	59.70%	78.60%
Naber, 2019	50-75	FS, FOBT	10_1	100%	59.70%	78.60%
Lew, 2018	50-74	FS, FIT	2-yearly FIT screening at 50-74 years combined with FS at 54, 64 and 74 years for negative FIT	100%	65%	80.00%
Knudsen, 2021	50-75	FS, FIT	10_1	100%	76.62%	81.25%
Ladabaum, 2018	50-80	FS, FOBT	10_1	100%	71%	82.00%
Heisser, 2021	50-75	FIT, colonoscopy	1y(FIT,50-54), 10y(Colonoscopy,55,65)	100%	76.00%	82.00%
Knudsen, 2021	50-75	FS, FIT	10_1	100%	74.12%	82.35%
Ladabaum, 2018	50-80	FS, FIT	10_1	100%	73%	83.00%
Knudsen, 2021	45-75	FS, FIT	10_1	100%	80.52%	84.38%
Heisser, 2021	50-75	FIT, colonoscopy	1y(FIT,50-54), 10y(Colonoscopy,55,65)	100%	78.00%	86.00%
Heisser, 2021	50-78	FIT, colonoscopy	10y(Colonoscopy,50,60), 2y(FIT,70-78)	100%	78.00%	86.00%
Knudsen, 2021	45-75	FS, FIT	10_1	100%	78.82%	88.24%
Naber, 2019	50-75	FS, FIT	10_1	100%	81.90%	88.90%
Naber, 2019	50-75	FS, FOBT	10_1	100%	83.30%	88.90%

Heisser, 2021	50-78	FIT, colonoscopy	10y(Colonoscopy,50,60), 2y(FIT,70-78)	100%	81.00%	89.00%
Naber, 2019	50-75	FS, FIT	10_1	100%	78.57%	89.29%
Naber, 2019	50-75	FS, FOBT	10_1	100%	80.00%	89.29%
Ladabaum, 2014	50-75	FOBT, colonoscopy	FOBT(1y, 50-54) ; FOBT(2y, 55-75) /colonoscopy(10y, 60-70)	100%	63%	NA
Ladabaum, 2014	50-75	FOBT, colonoscopy	FOBT(1y, 50-54) ; FOBT(2y, 55-75) /colonoscopy(10y, 55-65)	100%	64%	NA
Ladabaum, 2020	50-80	FIT, colonoscopy	FIT for low- and moderate risk, colonoscopy every 5 years for high risk	100%	64.00%	NA
Ladabaum, 2014	50-75	FIT, colonoscopy	FIT(1y, 50-54) ; FIT(2y, 55-75) /colonoscopy(10y, 60-70)	100%	65%	NA
Ladabaum, 2014	50-75	FIT, colonoscopy	FIT(1y, 50-54) ; FIT(2y, 55-75) /colonoscopy(10y, 55-65)	100%	65%	NA
Wong, 2016	50-70	FS, colonoscopy	FS(female, 50-70, 5); colonoscopy(male, 50-70, 10)	colonoscopy(98.9%); FS(90%)	44.90%	NA
Wong, 2016	50-70	FS, colonoscopy	FS(female, 50-65, 5); colonoscopy(female, 70; male, 50-70, 10)	colonoscopy(98.9%); FS(90%)	45.80%	NA
Wong, 2016	50-70	FS, colonoscopy	FS(female, 50-55, 5); colonoscopy(female, 60-70, 10; male, 50-70, 10)	colonoscopy(98.9%); FS(90%)	50.40%	NA
Sekiguchi, 2016	40+	FIT, colonoscopy	FIT(1y, 40-49y)； colonoscopy(50y, did not undergo total colonoscopy)	60%	61.40%	NA

Abbreviations: CRC, colorectal cancer; RRR, relative risk reduction; FS, flexible sigmoidoscopy; FIT, fecal immunochemical test; FOBT, fecal occult

blood testing; mSEPT9, methylated Septin 9 DNA blood test.

[a] The efficacy of various screening strategies is presented in ascending order based on the magnitude of colorectal cancer (CRC) mortality reduction.

Supplementary Table 8. All-Cause Mortality Outcomes for Colorectal Cancer Screening Strategies

Study	Model	Country	Time horizon	Screening strategies[a]	Adherence rate	All-cause mortality reduction
Buskermolen, 2019[7]	MISCAN-Colon	Norway	15y	colonoscopy, 50-79, once	100%	1.40%
Ren, 2022[48]	13-state Markov model	China	25y	colonoscopy, 50-75, 10	61.25%	3.17%
Ren, 2022[48]	13-state Markov model	China	25y	colonoscopy, 50-75, 5	61.25%	3.85%
Ren, 2022[48]	13-state Markov model	China	35y	colonoscopy, 40-75, 10	61.25%	5.37%
Ren, 2022[48]	13-state Markov model	China	35y	colonoscopy, 40-75, 5	61.25%	6.41%
Buskermolen, 2019[7]	MISCAN-colon	Norway	15y	FIT, 50-79, 2	100%	1.10%
Buskermolen, 2019[7]	MISCAN-colon	Norway	15y	FIT, 50-79, 1	100%	1.30%
Ren, 2022[48]	13-state Markov model	China	25y	FIT, 50-75, 2	60%	3.37%
Ren, 2022[48]	13-state Markov model	China	25y	FIT, 50-75, 1	60%	4.10%
Ren, 2022[48]	13-state Markov model	China	35y	FIT, 40-75, 2	60%	5.59%
Ren, 2022[48]	13-state Markov model	China	35y	FIT, 40-75, 1	60%	6.67%
Heijnsdijk, 2019[8]	MISCAN-colon	the Netherlands	15y	FS, 55-75, once	realistic 73%	0.62%
Buskermolen, 2019[7]	MISCAN-colon	Norway	15y	FS, 50-79, once	100%	1.10%

Abbreviations: MISCAN-Colon, MIcrosimulation SCreening ANalysisColon; FIT, faecal immunochemical test; FS, flexible sigmoidoscopy.

[a] Screening strategies are presented as screening modality, age to begin-age to end screening, screening interval.

Supplementary Table 9. Cost-Effectiveness Analysis of Colorectal Cancer Screening Strategies Compared to No Screening Under Perfect Adherence Conditions

Study	Country	Screening strategies (modality, age range, interval) [a]	Modeling setting	ICER (/LYG)[b]	ICER (/QALY gained)[b]	Cost effectiveness compared to no screening[c]
Common screening strategies						
Cenin, 2022[6]	China	FIT, 45-75, 1y	Discount rate: 3%; 2019 Chinese Renminbi (RMB, ¥); WTP: ¥ 193931RMB	4618.2	NA	cost-effective
Ladabaum, 2024[16]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2023 US dollars; WTP:$100,000-150,000/ QALYG	NA	-	cost-saving
Ladabaum, 2024[16]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2023 US dollars; WTP:$100,000-150,000/ QALYG	NA	-	cost-saving
Nascimento De Lima, 2024[2]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2021 US dollars; WTP: 100,000/QALYG	NA	NA	cost-saving
van den Puttelaar, 2024[3]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2021 US dollars; WTP: 100,000/QALYG	NA	-	cost-saving
Meester, 2024[38]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2020 US dollars; WTP: $100,000/QALY gained	NA	-	cost-saving
Ladabaum, 2024[15]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2023 US dollars; WTP: $100,000–$150,000/ QALY gained	NA	NA	cost-saving

Rui, 2025[53]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2024 dollars; WTP: $100,000/QALYG	NA	952	cost-effective
Ladabaum, 2019[14]	USA	FIT, 45-75, 1y	Discount rate: 3%; 2018 dollars; WTP: $100,000/QALYG	NA	-	cost-saving
Lew, 2018[28]	Australia	FIT, 45-74, 2y	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$8,848	NA	cost-effective
Cenin, 2022[6]	China	FIT, 45-75, 2y	Discount rate: 3%; 2019 Chinese Renminbi (RMB, ¥); WTP: ¥ 193,931RMB	2996.4	NA	cost-effective
Ladabaum, 2024[15]	USA	FIT, 45-75, 2y	Discount rate: 3%	NA	NA	cost-saving
Thiruvengadam, 2023[44]	USA	colonoscopy, 45-75, 10y	Discount rate: 3%; 2020 US dollars; WTP: $100,000/QALYG	NA	$3,218	cost-effective
Naber, 2021[5]	Saudi Arabia	colonoscopy, 45-75, 10y	Discount rate: 3%	$33,552	$29,485	cost-effective
Meester, 2024[38]	USA	colonoscopy, 45-75, 10y	Discount rate: 3%; 2020 US dollars; WTP: $100,000/QALYG	NA	-	cost-saving
Ladabaum, 2024[15]	USA	colonoscopy, 45-75, 10y	Discount rate: 3%; 2023 US dollars; WTP: $100,000–$150,000/ QALYG	NA	-	cost-saving
Ladabaum, 2024[16]	USA	colonoscopy, 45-75, 10y	Discount rate: 3%; 2023 US dollars; WTP: $100,000–$150,000/ QALYG	NA	-	cost-saving
van den Puttelaar, 2024[3]	USA	colonoscopy, 45-75, 10y	Discount rate: 3%; 2021 US dollars; WTP: $100,000/QALYG	NA	-	cost-saving
Ladabaum, 2019[14]	USA	colonoscopy, 45-75, 10y	Discount rate: 3%; 2018 dollars; WTP: $100,000/QALYG	NA	-	cost-saving

Rui, 2025[53]	USA	colonoscopy, 45-75, 10y	Discount rate: 3%; 2024 dollars; WTP: $100,000/QALYG	NA	261	cost-effective
Meester, 2024[38]	USA	mt-sDNA, 45-75, 3y	Discount rate: 3%; 2020 US dollars; WTP: $100,000/QALY gained	NA	12100	cost-effective
Ladabaum, 2024[15]	USA	mt-sDNA, 45-75, 3y	Discount rate: 3%; 2023 US dollars; WTP: $100,000–$150,000/ QALY gained	NA	6300	cost-effective
Ladabaum, 2024[16]	USA	mt-sDNA, 45-75, 3y	Discount rate: 3%; 2023 US dollars; WTP:$100,000-150000/ QALY gained	NA	6300	cost-effective
van den Puttelaar, 2024[3]	USA	mt-sDNA, 45-75, 3y	Discount rate: 3%; 2021 US dollars; WTP: $100,000 per QALY gained	NA	6,200-22,000	cost-effective
Rui, 2025[53]	USA	mt-sDNA, 45-75, 3y	Discount rate: 3%; 2024 dollars; WTP: $100,000/QALYG	NA	20216	cost-effective
Deibel, 2021[33]	USA	mSEPT9, 50-75, 1y	Discount rate: 3%; 2018 US dollars; WTP: $100,000/LYG	$12,209	NA	cost-effective
Ladabaum, 2014[20]	Germany	mSEPT9-2well, 50-75, 1y	Discount rate: 3%; 2011 euros	NA	€ 3,600	cost-effective
Ladabaum, 2014[20]	Germany	mSEPT9-3well, 50-75, 1y	Discount rate: 3%; 2011 euros	NA	€ 800	cost-effective
Rui, 2025[53]	USA	CTC, 45-75, 5y	Discount rate: 3%; 2024 dollars; WTP: $100,000/QALYG	NA	2139	cost-effective
Rui, 2025[53]	USA	FS, 45-75, 5y	Discount rate: 3%; 2024 dollars; WTP: $100,000/QALYG	NA	4673	cost-effective
Naber, 2019[4]	USA	FS, 50-75, 5y	Discount rate: 3%; 2017 dollars; WTP: $100,000/LYG	-	NA	cost-saving
Naber, 2019[4]	USA	FS, 50-75, 5y	Discount rate: 3%; 2017 dollars; WTP: $100,000/LYG	3947	NA	cost-effective

Naber, 2019[4]	USA	FS, 50-75, 5y	Discount rate: 3%; 2017 dollars; WTP: $100,000/LYG	-	NA	cost-saving
Novel potential screening strategies						
Meester, 2024[38]	USA	ngMT-sDNA(Exact Sciences), 45-75, 1y	Discount rate: 3%; 2020 US dollars; WTP: $100,000/QALY gained	NA	48600	cost-effective
Ladabaum, 2024[16]	USA	ngMT-sDNA(Exact Sciences), 45-75, 1y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	46000	cost-effective
Rui, 2025[53]	USA	ngMT-sDNA(Exact Sciences), 45-75, 1y	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	48792	cost-effective
Ladabaum, 2024[16]	USA	ngMT-sDNA(Exact Sciences), 45-75, 2y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	17600	cost-effective
Ladabaum, 2024[16]	USA	ngMT-sDNA(Exact Sciences), 45-75, 3y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	6500	cost-effective
Ladabaum, 2024[16]	USA	ngMT-sDNA(Exact Sciences), 45-75, 3y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	6600	cost-effective
Meester, 2024[38]	USA	ngMT-sDNA(Exact Sciences), 45-75, 3y	Discount rate: 3%; 2020 S dollars; WTP: $100 000/QALY gained	NA	13700	cost-effective
Rui, 2025[53]	USA	ngMT-sDNA(Exact Sciences), 45-75, 3y	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	17226	cost-effective
Ladabaum, 2024[16]	USA	cf-bDNA(Guardant Shield), 45-75, 2y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	107900	cost-effective
Ladabaum, 2024[15]	USA	cf-bDNA(Guardant Shield), 45-75, 3y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	23600	cost-effective

Ladabaum, 2024[16]	USA	cf-bDNA(Guardant Shield), 45-75, 3y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	89600	cost-effective
Ladabaum, 2024[16]	USA	cf-bDNA(Guardant Shield), 45-75, 3y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	90600	cost-effective
van den Puttelaar, 2024[3]	USA	cf-bDNA(Guardant Shield), 45-75, 3y	Discount rate: 3%; 2021 US dollars; WTP: $100,000/ QALY gained	NA	22,200-41,000	cost-effective
Rui, 2025[53]	USA	cf-bDNA(Guardant Shield), 45-75, 3y	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	63320	cost-effective
Nascimento De Lima, 2025[12]	Hispanic or Latino patient population; Southern California	cf-bDNA(Guardant Shield), 50-75, 3y	Discount rate: 3%; 2021 US dollars; WTP: $100,000/ QALY gained	NA	54740	cost-effective
Rui, 2025[53]	USA	mt-sRNA, 45-75, 1y	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	52862	cost-effective
Rui, 2025[53]	USA	mt-sRNA, 45-75, 3y	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	17716	cost-effective
Ladabaum, 2024[16]	USA	cf-bDNA(Guardant Shield), 45-75, 1y	Discount rate: 3%; 2023 US dollars;WTP: $100,000-150000/ QALY gained	NA	160900	not cost-effective
Aziz, 2023[46]	USA	liquid biopsy, 45-75, 3y	Discount rate: 3%; 2022 US dollars; WTP: $100,000/LYG	1325428.6	NA	not cost-effective
Deibel, 2021[33]	USA	UMT, 50-75, 3y	Discount rate: 3%; 2018 US dollars; WTP: $100,000/LYG	-2696	NA	cost-saving

Areia, 2022[45]	USA	AI-assisted colonoscopy, 50-80, 10y	Discount rate: 3%; US dollars	NA	4714	cost-effective
Hybrid strategies						
Rui, 2025[53]	USA	(FS, FIT), 45-75, 10_1[d]	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	4670	cost-effective
Naber, 2019[4]	USA	(FS, FIT), 50-75, 10_1[d]	Discount rate: 3%; 2017 US dollars; WTP: $100,000 per LYG	/	NA	cost-saving
Naber, 2019[4]	USA	(FS, FIT), 50-75, 10_1[d]	Discount rate: 3%; 2017 US dollars; WTP: $100,000 per LYG	1433	NA	cost-effective
Naber, 2019[4]	USA	(FS, FIT), 50-75, 10_1[d]	Discount rate: 3%; 2017 US dollars; WTP: $100,000 per LYG	/	NA	cost-saving
Ladabaum, 2018[13]	USA	(FS, FIT), 50-80, 10_1[d]	Discount rate: 3%; WTP: $100,000/QALYG	NA	$8,300	cost-effective
Lew, 2018[29]	Australia	2-yearly FIT screening at 50-74 years combined with FS at 54, 64 and 74 years for negative FIT	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$34,279	NA	cost-effective
Lew, 2018[29]	Australia	2-yearly FIT screening at 50-74 years combined with FS at age 50 for negative FIT	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$26,011	NA	cost-effective
Ladabaum, 2019[14]	USA	FS(45, once); FIT(50-75, 1y)[e]	Discount rate: 3%; 2018 dollars; WTP: $100,000/QALYG	NA	-	cost-saving
Lew, 2018[29]	Australia	Once-off FS screening at 55 years combined with 2-yearly FIT at 60-74 years	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$21,478	NA	cost-effective
Ladabaum, 2020[18]	USA	FIT for low and moderate risk, colonoscopy every 5	Discount rate: 3%; 2013 US dollars; WTP: $50,000-100,000/QALY	NA	-	cost-saving

Ladabaum, 2019[14]	USA	years for high risk from ages 50 through 80 FIT(45-49, 1y); colonoscopy(50-75, 10y)[f]	Discount rate: 3%; 2018 dollars; WTP: $100,000/QALYG	NA	-	cost-saving
Ladabaum, 2014[20]	Germany	FIT(50-54, 1y) ; FIT(55-75, 2y) /colonoscopy (55-65, 10y)[g]	Discount rate: 3%; 2011 euros	NA	-	cost-saving
Ladabaum, 2014[20]	Germany	FIT(50-54, 1y) ; FIT(55-75, 2y) /colonoscopy (60-70, 10y)[h]	Discount rate: 3%; 2011 euros	NA	-	cost-saving
Lew, 2018[29]	Australia	Once-off colonoscopy at 50 years combined with 2-yearly FIT at 52-74 years for those who did not participate in colonoscopy	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	26990	NA	cost-effective
Naber, 2019[4]	USA	(FS, FOBT), 50-75, 10_1[i]	Discount rate: 3%; 2017 US dollars; WTP: $100,000 per LYG	/	NA	cost-saving
Naber, 2019[4]	USA	(FS, FOBT), 50-75, 10_1[i]	Discount rate: 3%; 2017 US dollars; WTP: $100,000 per LYG	850	NA	cost-effective
Naber, 2019[4]	USA	(FS, FOBT), 50-75, 10_1[i]	Discount rate: 3%; 2017 US dollars; WTP: $100,000 per LYG	/	NA	cost-saving
Ladabaum, 2018[13]	USA	(FS, FOBT), 50-80, 10_1[i]	Discount rate: 3%; WTP: $100,000/QALYG	NA	$5,700	cost-effective
Ladabaum, 2014[20]	Germany	FOBT(50-54, 1y) ; FOBT(55-75, 2y) /colonoscopy (55-65, 10y)[j]	Discount rate: 3%; 2011 euros	NA	-	cost-saving
Ladabaum, 2014[20]	Germany	FOBT(50-54, 1y) ; FOBT(55-75, 2y)	Discount rate: 3%; 2011 euros	NA	-	cost-saving

Ladabaum, 2019[14]	USA	/colonoscopy (60-70, 10y)[k] sigmoidoscopy(once, at 45); colonoscopy(10y, 50-75)	Discount rate: 3%; 2018 US dollars; WTP: $100,000/QALYG	NA	-	cost-saving

Abbreviations: ICER, incremental cost-effectiveness ratios; LYG, life-year gained; QALYG, quality-adjusted life-year gained; WTP, willingness-to-pay; FIT, faecal immunochemical test; CTC, computed tomography colonography; mSEPT9, methylated Septin 9 DNA blood test; mt-sDNA, multitargeted stool-based DNA; FS, flexible sigmoidoscopy; AI, artificial intelligence; ngMT-sDNA, next-generation MT-sDNA;mt-sRNA, multitarget stool RNA; cf-bDNA, cell-free DNA blood test; UMT, urine metabolomic-based test; FOBT, faecal occult blood testing.

[a] Screening strategies are presented as screening modality, age to begin-age to end screening, screening interval.

[b] When not reported, incremental cost-effectiveness ratios (ICERs) were manually calculated by dividing the incremental cost by incremental life-years (LYs) or quality-adjusted life-years (QALYs) and rounded to the nearest integer.

[c] Cost-effectiveness outcomes were classified into three categories according to the willingness-to-pay (WTP) thresholds established in the original studies: (1) cost-saving/dominant (defined as interventions that were both less costly and more effective than the comparator, indicated in blue); (2) cost-effective (ICER ≤ WTP threshold, indicated in orange); or (3) not cost-effective (ICER > WTP threshold, indicated in gray).

[e] Once-off FS screening at 45 years combined with yearly FIT at 50-75 years.

[f] FIT yearly for ages 45 through 49 and 10-yearly colonoscopy for ages 50 through 75.

[g] FIT yearly for ages 50 through 54 and then every 2 years for ages 55 through 75, and hybrid strategies with FIT and colonoscopy at age 55 and 65.

[h] FIT yearly for ages 50 through 54 and then every 2 years for ages 55 through 75, and hybrid strategies with FIT and colonoscopy at age 60 and 70.

[i] The first interval is for FS and the second interval is for FOBT.

[j] FOBT yearly for ages 50 through 54 and then every 2 years for ages 55 through 75, and hybrid strategies with FOBT and colonoscopy at age 55 and 65.

[k] FOBT yearly for ages 50 through 54 and then every 2 years for ages 55 through 75, and hybrid strategies with FOBT and colonoscopy at age 60 and 70.

Supplementary Table 10. Cost-Effectiveness Analysis of Colorectal Cancer Screening Strategies Compared to No Screening Under Realistic Adherence Conditions

Study	Country	Screening strategies (modality, age range, interval) a	Adherence	Modelling setting	ICER (/LYG)[b]	ICER (/QALY gained)[b]	Cost effectiveness compared to no screening[c]
Common screening strategies							
Huang, 2025[51]	China	FIT, 45-75, 1y	realistic 50.0%	Discount rate: 3%; US dollars	67892	NA	WTP was not reported
Aziz, 2023[46]	USA	FIT, 45-75, 1y	realistic 60.6%	Discount rate: 3%; 2022 US dollars; WTP: $100,000/LYG	38780	NA	cost-effective
van den Puttelaar, 2024[3]	USA	FIT, 45-75, 1y	60%	Discount rate: 3%; 2021 US dollars; WTP: 100,000 per QALY gained	NA	-	cost-saving
Rui, 2025[53]	USA	FIT, 45-75, 1y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	4118	cost-effective
Lew, 2018[28]	Australia	FIT, 45-74, 2y	realistic 41%	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/life-year saved (LYS)	$5,471	NA	cost-effective
Lew, 2022[30]	Aboriginal and Torres Strait Islander	FIT, 45-74, 2y	42% psr. (iFOBT)/53% (follow-up colonoscopy)/8	Discount rate: 5%; 2018 Australian dollars; WTP: $50,000/LYS	$14,615	NA	cost-effective

	peoples in Australian		0% (surveillance colonoscopy)				
Lu, 2024[36]	China	FIT, 45-74, 2y	80%	Discount rate: 5%; Chinese Yuan (CHY); WTP: CNY 35,446 and 141,784 per QALY gained as strongly and weakly cost-effective	NA	7500	cost-effective
Lu, 2024[36]	China	colonoscopy, 45-74, 10y	20%	Discount rate: 5%; Chinese Yuan (CHY); WTP: CNY 35,446 and 141,784 per QALY gained as strongly and weakly cost-effective	NA	11229	cost-effective
Huang, 2025[51]	China	colonoscopy, 45-75, 10y	realistic 44.0%	Discount rate: 3%; US dollars	$312,848	NA	WTP was not reported
Thiruvengadam,2023[44]	USA	colonoscopy, 45-75, 10y	Age-Adjusted	Discount rate: 3%; 2020 US dollars; WTP: 100,000/QALYG	NA	$3,555	cost-effective
Aziz, 2023[46]	USA	colonoscopy, 45-75, 10y	realistic 60.6%	Discount rate: 3%; 2022 US dollars; WTP: $100,000/LYG	$28,092	NA	cost-effective
van den Puttelaar, 2024[3]	USA	colonoscopy, 45-75, 10y	60%	Discount rate: 3%; 2021 US dollars; WTP: 100,000 per QALY gained	NA	-	cost-saving
Rui, 2025[53]	USA	colonoscopy, 45-75, 10y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	/	cost-saving
Aziz, 2023[46]	USA	mt-sDNA, 45-75, 3y	realistic 60.6%	Discount rate: 3%; 2022 US dollars; WTP: $100,000/LYG	79089.6	NA	cost-effective

van den Puttelaar, 2024[3]	USA	mt-sDNA, 45-75, 3y	60%	Discount rate: 3%; 2021 USdollars; WTP: $100,000 per QALY gained	NA	6,200 - 22,000	cost-effective
Rui, 2025[53]	USA	mt-sDNA, 45-75, 3y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	11543	cost-effective
Greuter, 2016[39]	the Netherlands	CTC, 55-75, 5y	realistic 34% (screening)/96 % (diagnostic/surveillance colonoscopy)	Discount rate: 3%; 2014 Euros; WTP: €35,916/LYG	-	NA	cost-saving
Rui, 2025[53]	USA	CTC, 45-75, 5y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	/	cost-saving
Barzi, 2017[52]	USA	FS, 50-75, 5y	realistic	Discount rate: 3%; WTP: $50,000/LYG	-	NA	cost-saving
Wong, 2016[50]	China	FS, 50-70, 5y	colonoscopy(98.9%); FS(90%)	Discount rate: 3%; US dollars	NA	56510	WTP was not reported
Rui, 2025[53]	USA	FS, 45-75, 5y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	/	cost-saving
Deibel, 2021[33]	USA	mSEPT9, 50-75, 1y	realistic 0.68(screening)/ 0.82(diagnostic and surveillance col)	Discount rate: 3%; 2018 US dollars; WTP: 100,000 dUSD per dLYGs	$7,530	NA	cost-effective

Novel potential screening strategies

Greuter, 2016[39]	the Netherlands	MRC, 55-75, 5y	34%(screening) /96% (diagnostic/surveillance colonoscopy)	Discount rate: 3%; 2014 Euros; WTP: €35,916/LYG	-	NA	cost-saving
Greuter, 2016[39]	the Netherlands	MRC, 55-65, 10y	34%(screening) /96% (diagnostic/surveillance colonoscopy)	Discount rate: 3%; 2014 Euros; WTP: €35,916/LYG	-	NA	cost-saving
Greuter, 2016[39]	the Netherlands	MRC, 55-75, 10y	34%(screening) /96% (diagnostic/surveillance colonoscopy)	Discount rate: 3%; 2014 Euros; WTP: €35,916/LYG	-	NA	cost-saving
Greuter, 2016[39]	the Netherlands	MRC, 50-80, 10y	34%(screening) /96% (diagnostic/surveillance colonoscopy)	Discount rate: 3%; 2014 Euros; WTP: €35,916/LYG	-	NA	cost-saving
Donderici, 2025[40]	USA	cf-bDNA(Guardant Shield), 45-75, 3y	90%	Discount rate: 3%; 2023 US dollars; WTP: 100,000 per QALY gained	NA	48662	cost-effective
Nascimento De Lima, 2025[12]	Southern California	cf-bDNA(Guardant Shield), 50-75, 3y	realistic 0.625	Discount rate: 3%; 2021 US dolllars; WTP: $100,000/ QALY gained	NA	137217	not cost-effective
Rui, 2025[53]	USA	cf-bDNA(Guardant Shield), 45-75, 3y	realistic 99.5%	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	69799	cost-effective

Rui, 2025[53]	USA	mt-sRNA, 45-75, 3y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	8242	cost-effective
Rui, 2025[53]	USA	mt-sRNA, 45-75, 1y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	33973	cost-effective
Rui, 2025[53]	USA	ngMT-sDNA(Exact Sciences), 45-75, 3y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	8427	cost-effective
Rui, 2025[53]	USA	ngMT-sDNA(Exact Sciences), 45-75, 1y	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	32620	cost-effective
Barichello, 2019[17]	Canada	UMT, 50-74, 1y	realistic 0.836	Discount rate: 1.5%; 2018 Canadian dollars; WTP: $50,000/QALY	NA	42325	cost-effective
Deibel, 2021[33]	USA	UMT, 50-75, 3y	realistic 0.51(screening)/ 0.82(diagnostic and surveillance col)	Discount rate: 3%; 2018 US dollars; WTP: 100,000 dUSD per dLYGs	-4931	NA	cost-saving
Hybrid strategies							
Barzi, 2017[52]	USA	(FS, FIT), 50-75, 5_1[d]	realistic 0.63	Discount rate: 3%; WTP: $50,000/LYG	-	NA	cost-saving
Barzi, 2017[52]	USA	(FS, FIT), 50-75, 5_2[d]	realistic	Discount rate: 3%; WTP: $50,000/LYG	-	NA	cost-saving
Lew, 2018[29]	Australia	Once-off FS at 55 years combined with 2-yearly FIT at 60-74 years	realistic	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$11,694	NA	cost-effective

Lew, 2018[29]	Australia	2-yearly FIT screening at 50-74 years combined with FS at age 50 for negative FIT	realistic	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$4,914	NA	cost-effective
Lew, 2018[29]	Australia	2-yearly FIT screening at 50-74 years combined with FS at 54, 64 and 74 years for negative FIT	realistic	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$7,943	NA	cost-effective
Rui, 2025[53]	USA	(FS, FIT), 45-75, 10_1[d]	realistic	Discount rate: 3%; 2024 US dollars; WTP: $100,000/QALY gained	NA	/	cost-saving
Barzi, 2017[52]	USA	(FS, FOBT), 50-75, 5_1[e]	realistic 0.63	Discount rate: 3%; WTP: $50,000/LYG	-	NA	cost-saving
Barzi, 2017[52]	USA	(FS, FOBT), 50-75, 5_2[e]	realistic	Discount rate: 3%; WTP: $50,000/LYG	-	NA	cost-saving
Melnitchouk, 2018[43]	Ukraine	(FS, FOBT), 50-75, 5_1[e]	realistic 0.75	Discount rate: 3%; 2012 US dollars; WTP: $11,700 US dollars/QALYG	NA	NA	cost-saving
Lew, 2018[29]	Australia	Once-off colonoscopy at 50 years combined with 2-yearly FIT at 52-74 years for those who did not participate in colonoscopy	realistic	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	$9,221	NA	cost-effective
Sekiguchi, 2016[47]	Japan	FIT(40-49y, 1y);colonoscopy(50y, did not undergo total colonoscopy)	60%	Discount rate: 3%; Japanese Yen (JPY); WTP: JPY 5–6 million per QALY gained	NA	-	cost-saving

Aziz, 2023[46]	USA	colonoscopy-liquid biopsy, 45-75, 10y	realistic 60.6% for screening colonoscopy; the unscreened underwent LB	Discount rate: 3%; 2022 US dollars; WTP: $100,000/LYG	53981.1	NA	cost-effective
Wong, 2016[50]	China	FS (female, 50-55, 5); colonoscopy(female, 60-70, 10; male, 50-70, 10)	colonoscopy(98.9%); FS(90%)	Discount rate: 3%; US dollars	NA	43517	WTP was not reported
Wong, 2016[50]	China	FS(female, 50-65, 5); colonoscopy(female, 70; male, 50-70, 10)	colonoscopy(98.9%); FS(90%)	Discount rate: 3%; US dollars	NA	47710	WTP was not reported
Wong, 2016[50]	China	FS(female, 50-70, 5); colonoscopy(male, 50-70, 10)	colonoscopy(98.9%); FS(90%)	Discount rate: 3%; US dollars	NA	42,515	the most cost-effective
Lew, 2018[29]	Australia	2-yearly FIT screening at 50-74 years combined with mSEPT9 in underscreened individuals	realistic	Discount rate: 5%; 2015 Australian dollars; WTP: $50,000/LYS	6702	NA	cost-effective

Abbreviations: ICER, incremental cost-effectiveness ratios; LYG, life-year gained; QALYG, quality-adjusted life-year gained; WTP, willingness-to-pay; FIT, faecal immunochemical test; mt-sDNA, multitargeted stool-based DNA; CTC, computed tomography colonography; FS, flexible sigmoidoscopy; mSEPT9, methylated Septin 9 DNA blood test; MRC, MR colonography; cf-bDNA, cell-free DNA blood test; mt-sRNA, multitarget stool RNA; ngMT-sDNA, next-generation MT-sDNA; UMT, urine metabolomic-based test; FOBT, faecal occult blood testing.

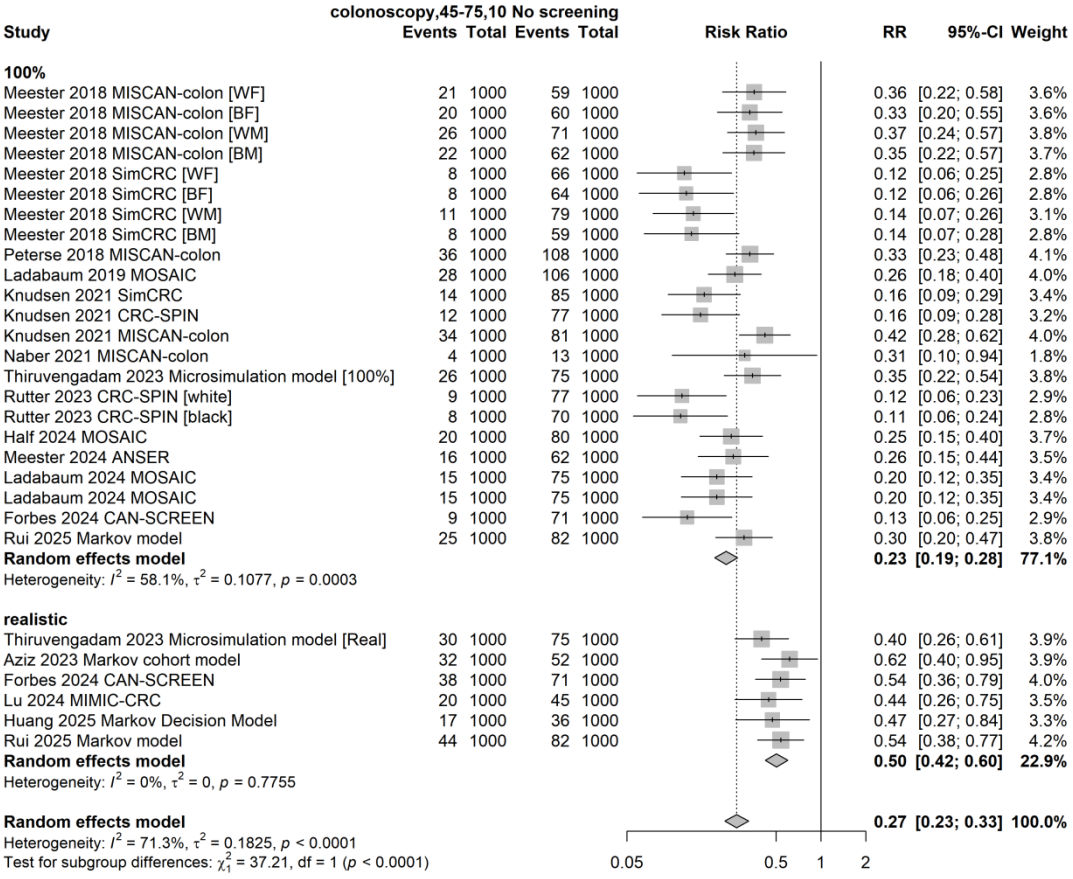
[a] Screening strategies are presented as screening modality, age to begin-age to end screening, screening interval.

[b] When not reported, incremental cost-effectiveness ratios (ICERs) were manually calculated by dividing the incremental cost by incremental life-years (LYs) or quality-adjusted life-years (QALYs) and rounded to the nearest integer.

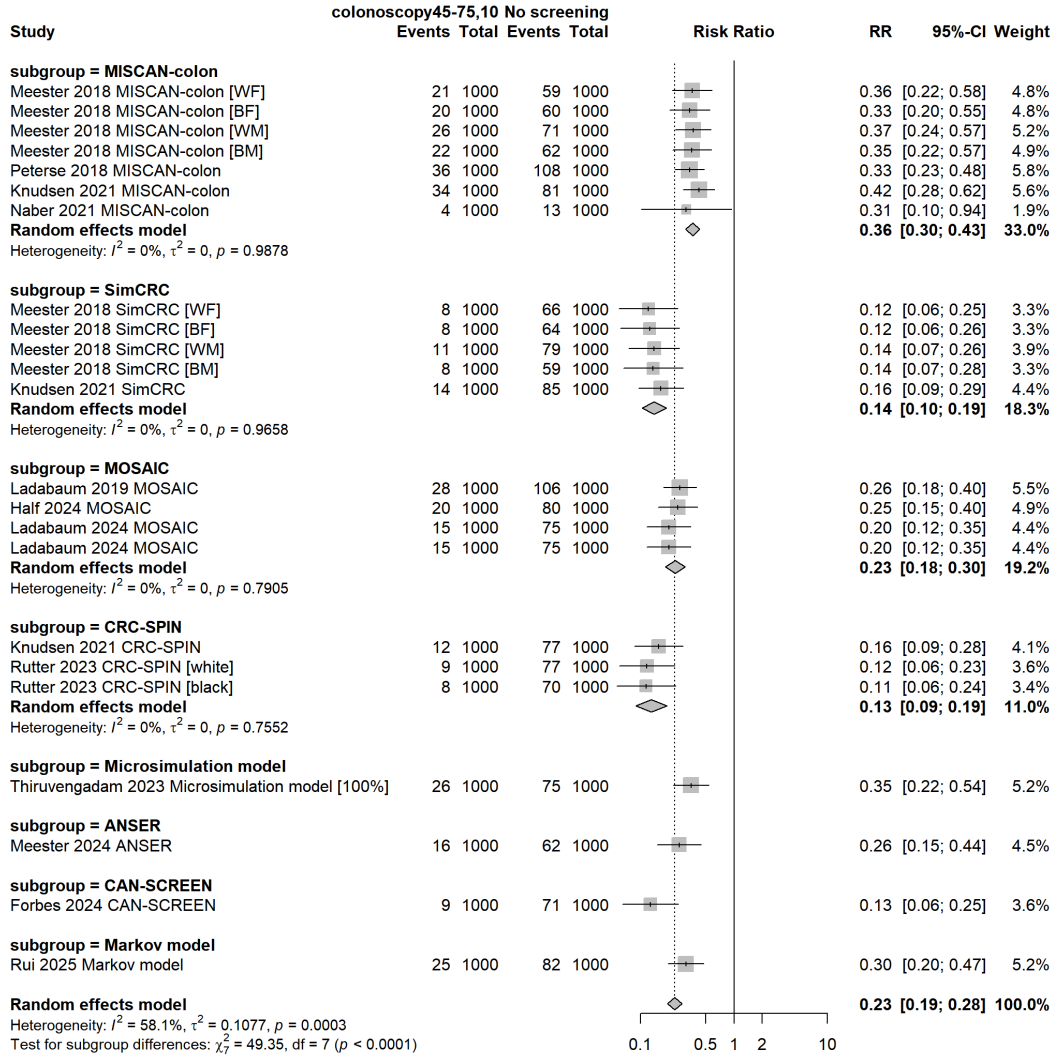
[c] Cost-effectiveness outcomes were classified into three categories according to the willingness-to-pay (WTP) thresholds established in the original studies: (1) cost-saving/dominant (defined as interventions that were both less costly and more effective than the comparator, indicated in blue); (2) cost-effective (ICER ≤ WTP threshold, indicated in orange); or (3) not cost-effective (ICER > WTP threshold, indicated in gray).

[d] The first interval is for FS and the second interval is for FIT.
[e] The first interval is for FS and the second interval is for FOBT.

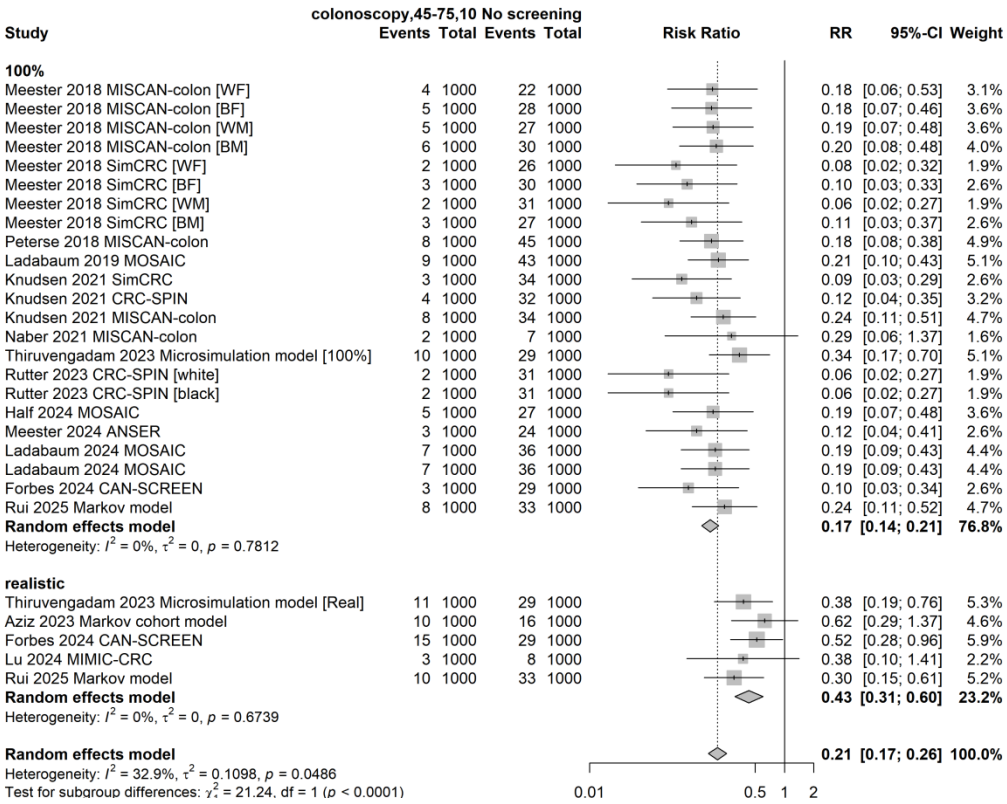
Supplementary Figure 1. Forest Plot of Colorectal Cancer Incidence Risk Ratios for 10-Yearly Colonoscopy Screening (Ages 45–75) Compared to No Screening



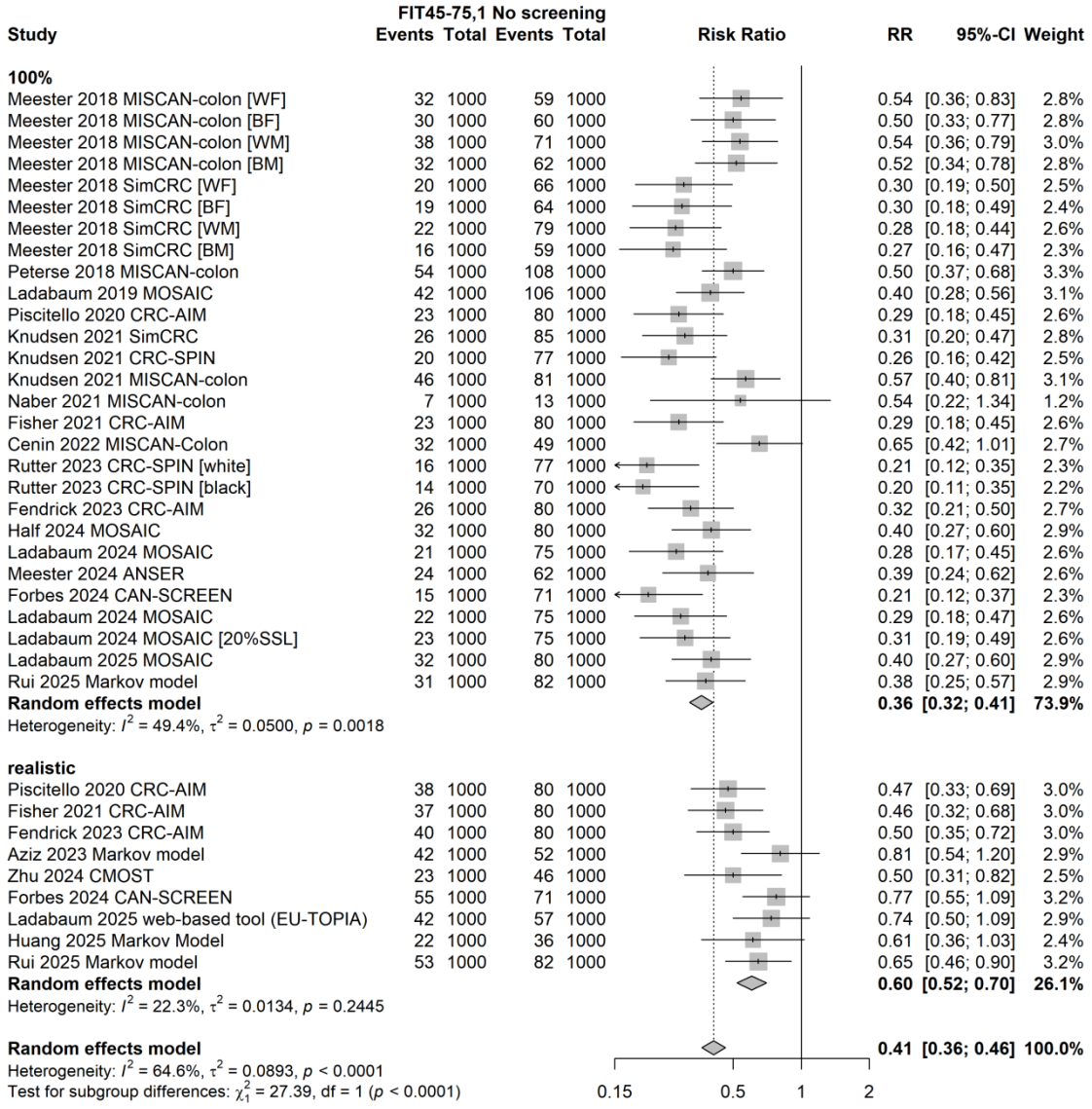
Supplementary Figure 2. Colorectal Cancer Incidence Risk Ratios by Model for 10-Yearly Colonoscopy Screening (Ages 45–75, Perfect Adherence)



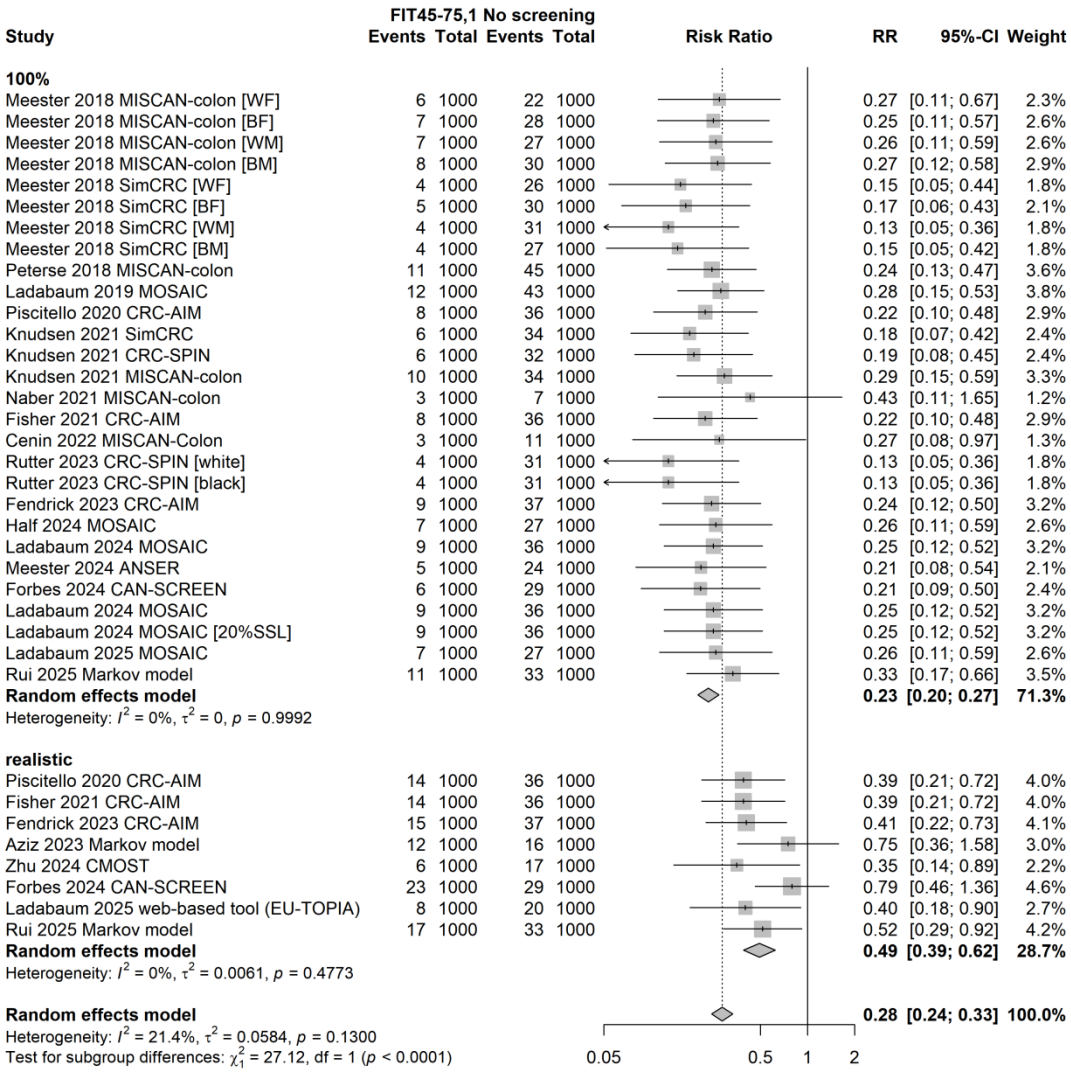
Supplementary Figure 3. Forest Plot of Colorectal Cancer Mortality Risk Ratios for 10-Yearly Colonoscopy Screening (Ages 45–75) Compared to No Screening



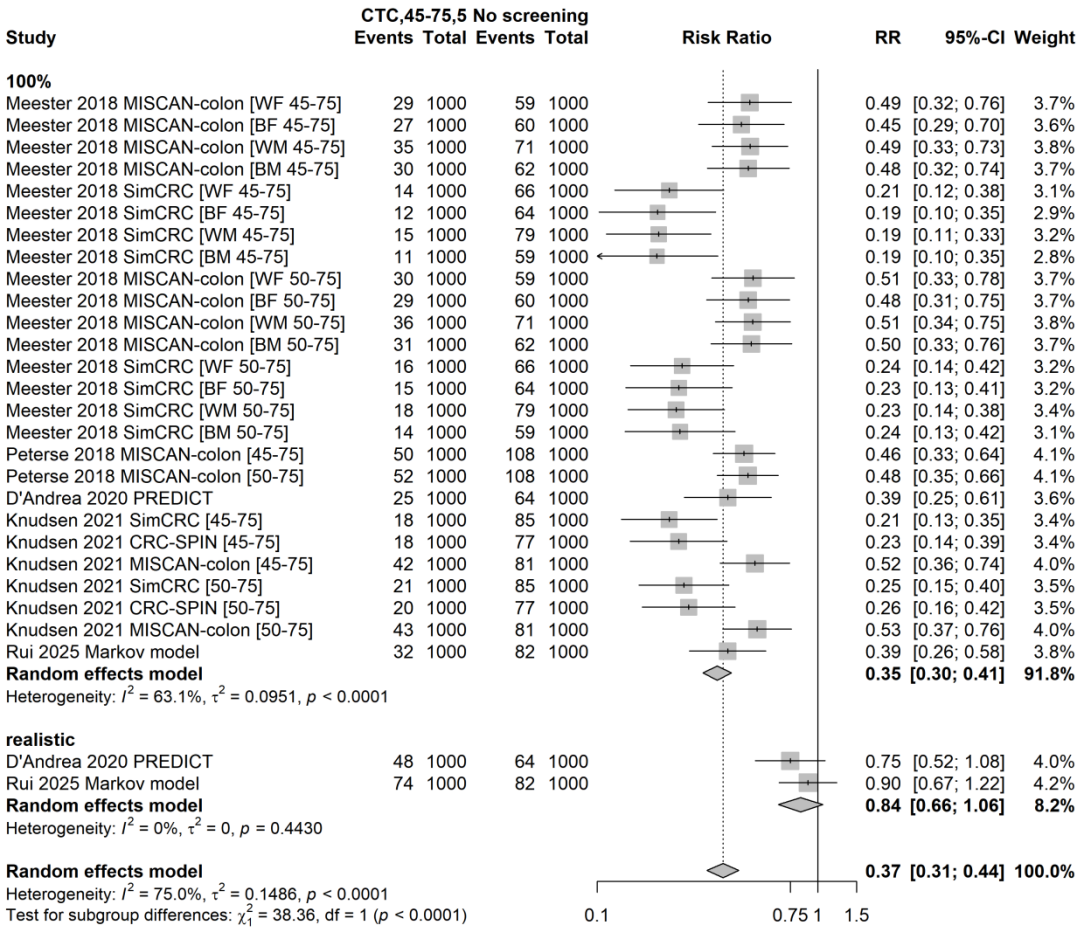
Supplementary Figure 4. Forest Plot of Colorectal Cancer Incidence Risk Ratios for Annual faecal Immunochemical Test Screening (Ages 45–75) Compared to No Screening



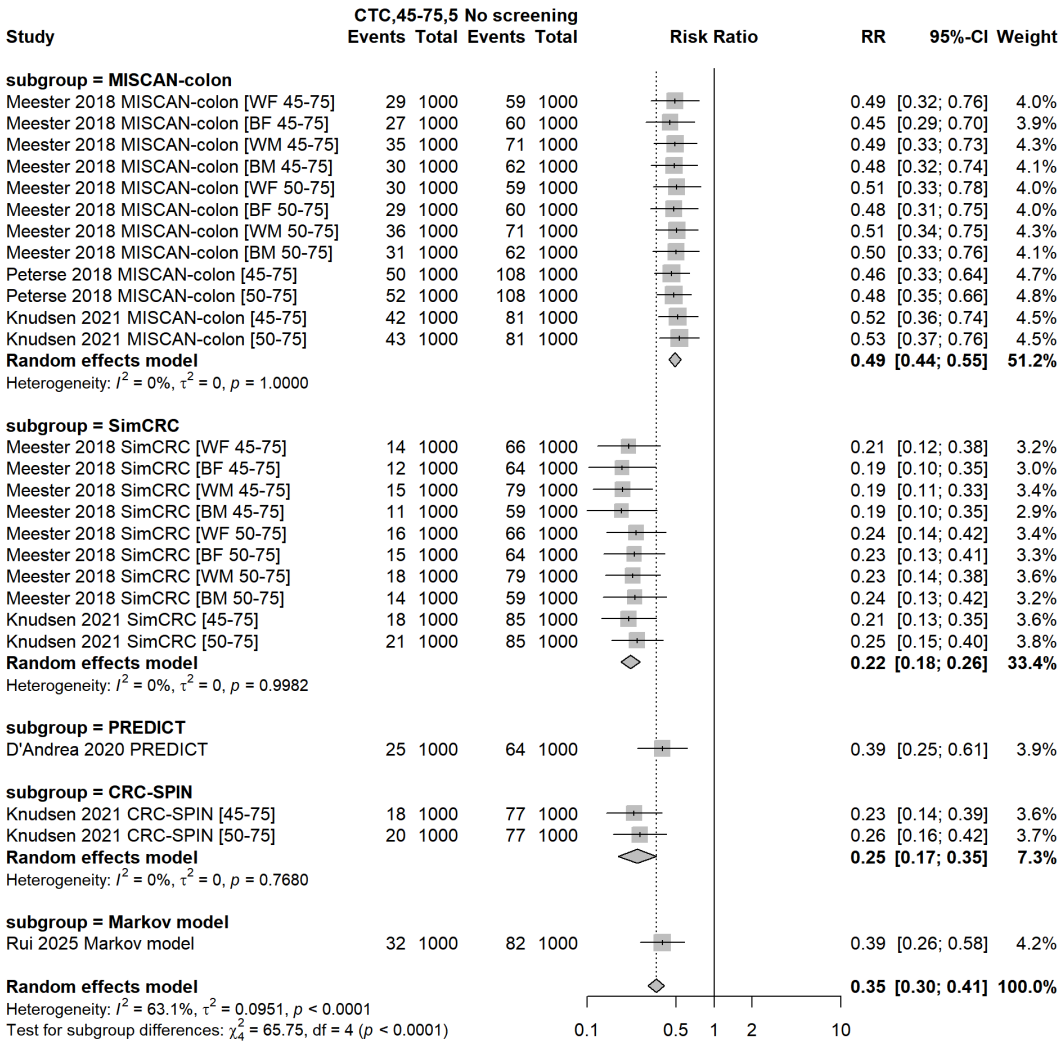
Supplementary Figure 5. Forest Plot of Colorectal Cancer Mortality Risk Ratios for Annual faecal Immunochemical Test Screening (Ages 45–75) Compared to No Screening



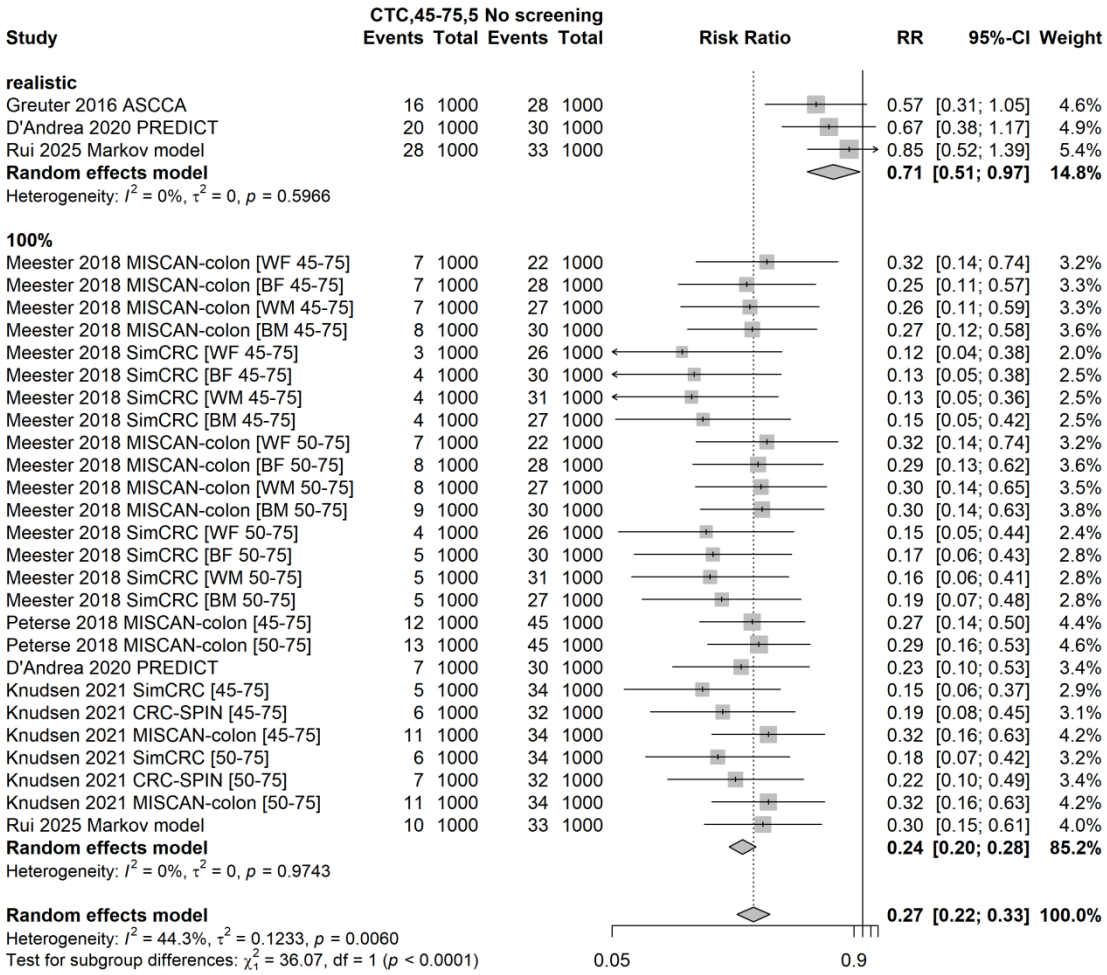
Supplementary Figure 6. Forest Plot of Colorectal Cancer Incidence Risk Ratios for 5-Yearly Computed Tomography Colonography Screening (Ages 45–75) Compared to No Screening



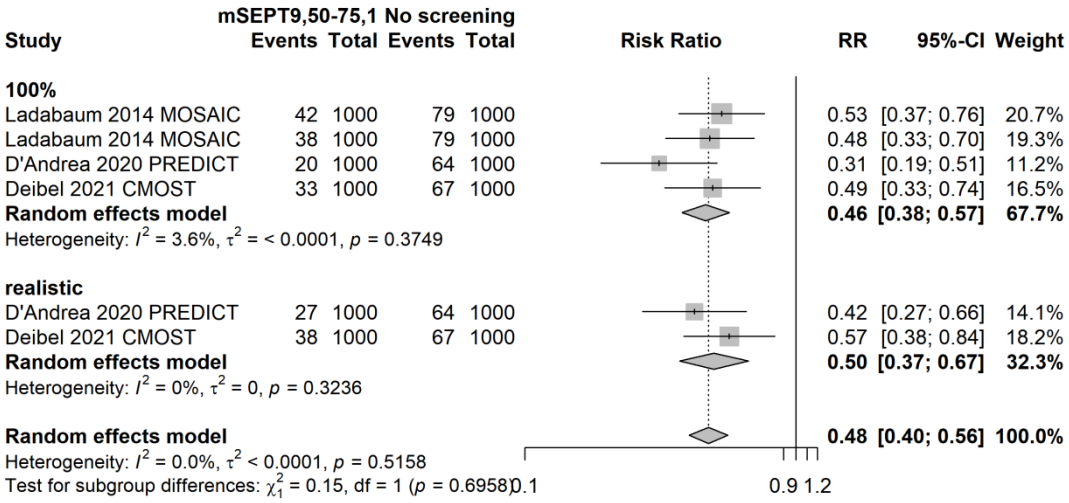
Supplementary Figure 7. Colorectal Cancer Incidence Risk Ratios by Model for 5-Yearly Computed Tomography Colonography Screening (Ages 45–75, Perfect Adherence)



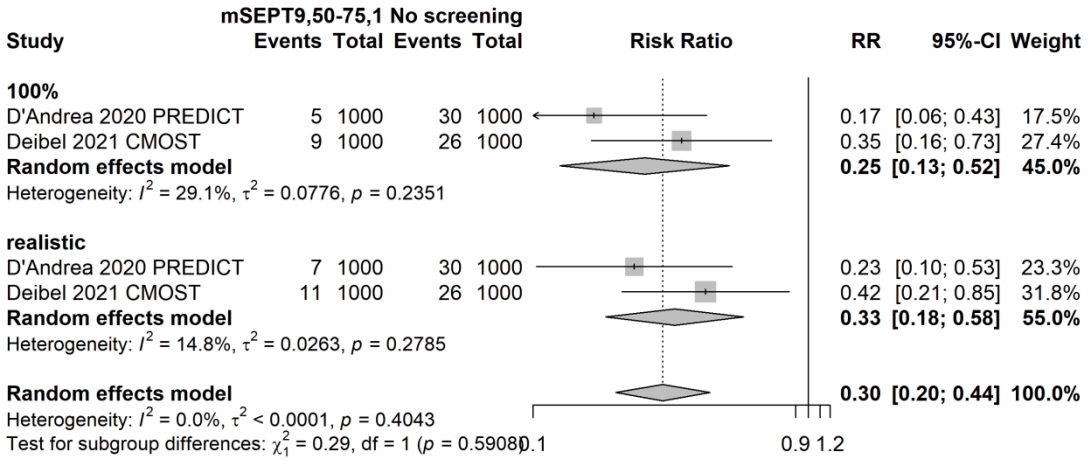
Supplementary Figure 8. Forest Plot of Colorectal Cancer Mortality Risk Ratios for 5-Yearly Computed Tomography Colonography Screening (Ages 45–75) Compared to No Screening



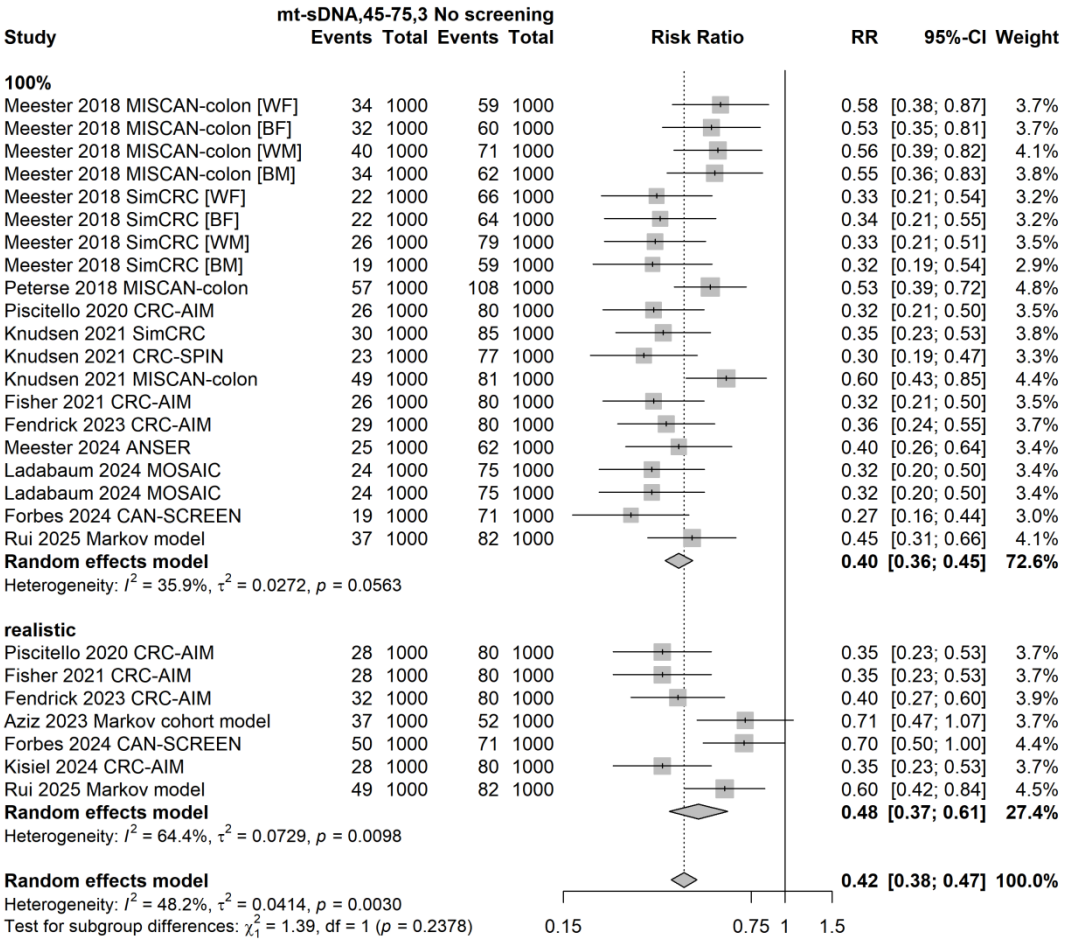
Supplementary Figure 9. Forest Plot of Colorectal Cancer Incidence Risk Ratios for Annual mSEPT9 Screening (Ages 50–75) Compared to No Screening



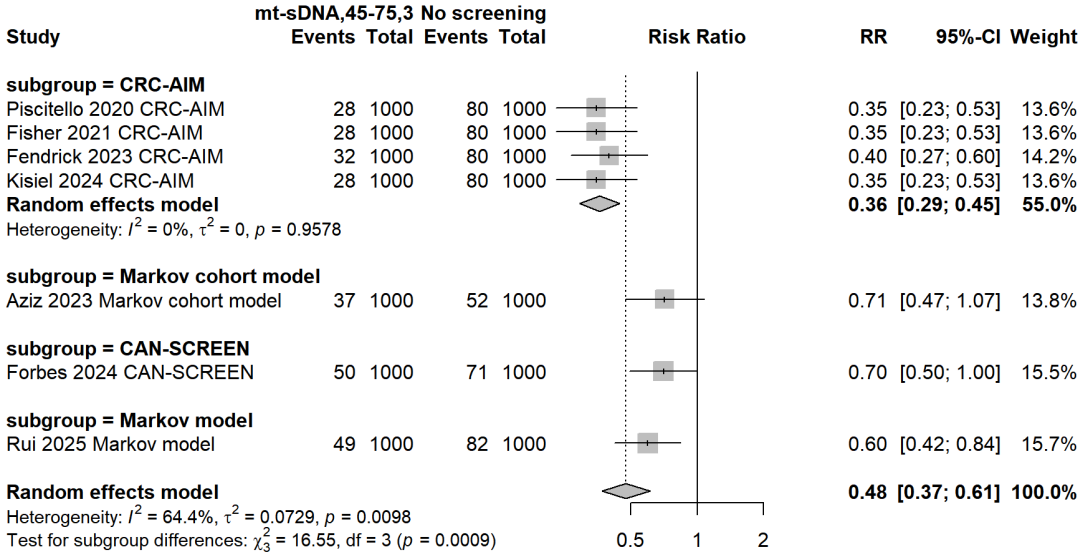
Supplementary Figure 10. Forest Plot of Colorectal Cancer Mortality Risk Ratios for Annual mSEPT9 Screening (Ages 50–75) Compared to No Screening



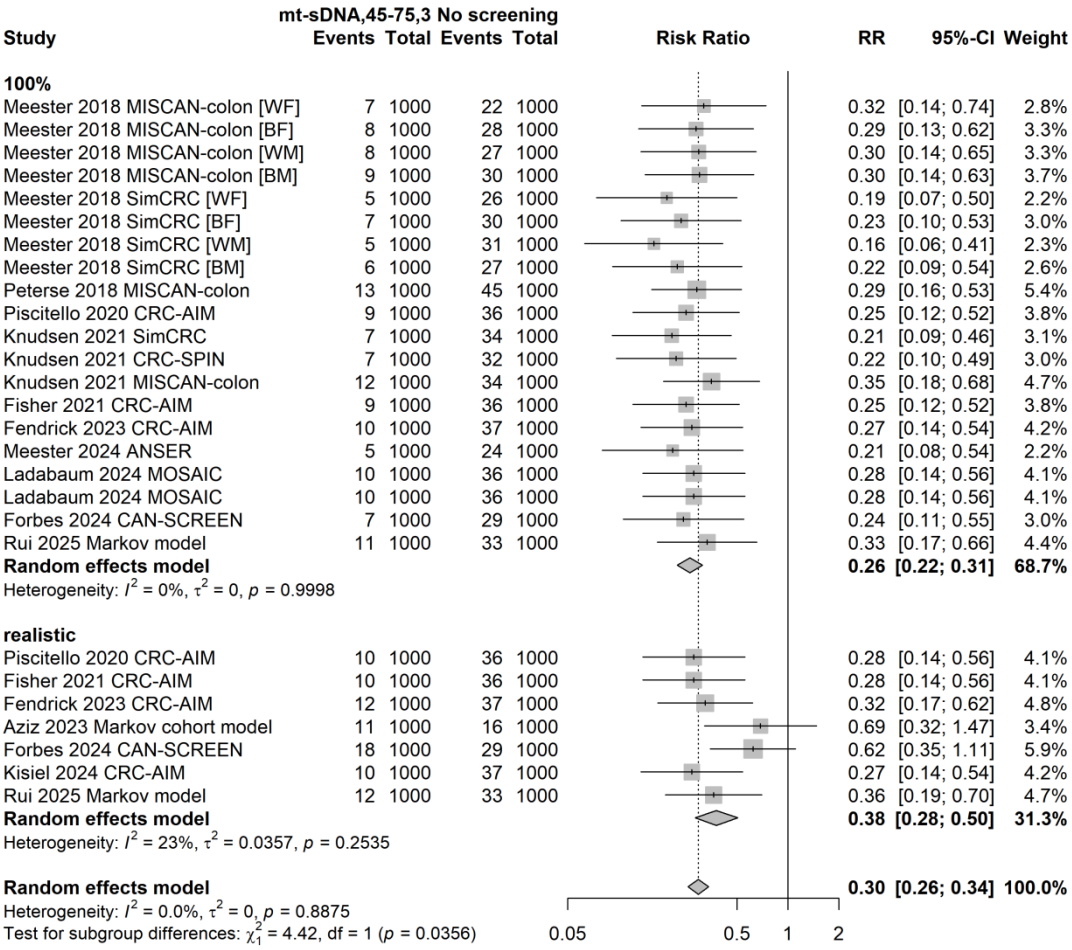
Supplementary Figure 11. Forest Plot of Colorectal Cancer Incidence Risk Ratios for Triennial Multi-Target Stool DNA Screening (Ages 45–75) Compared to No Screening



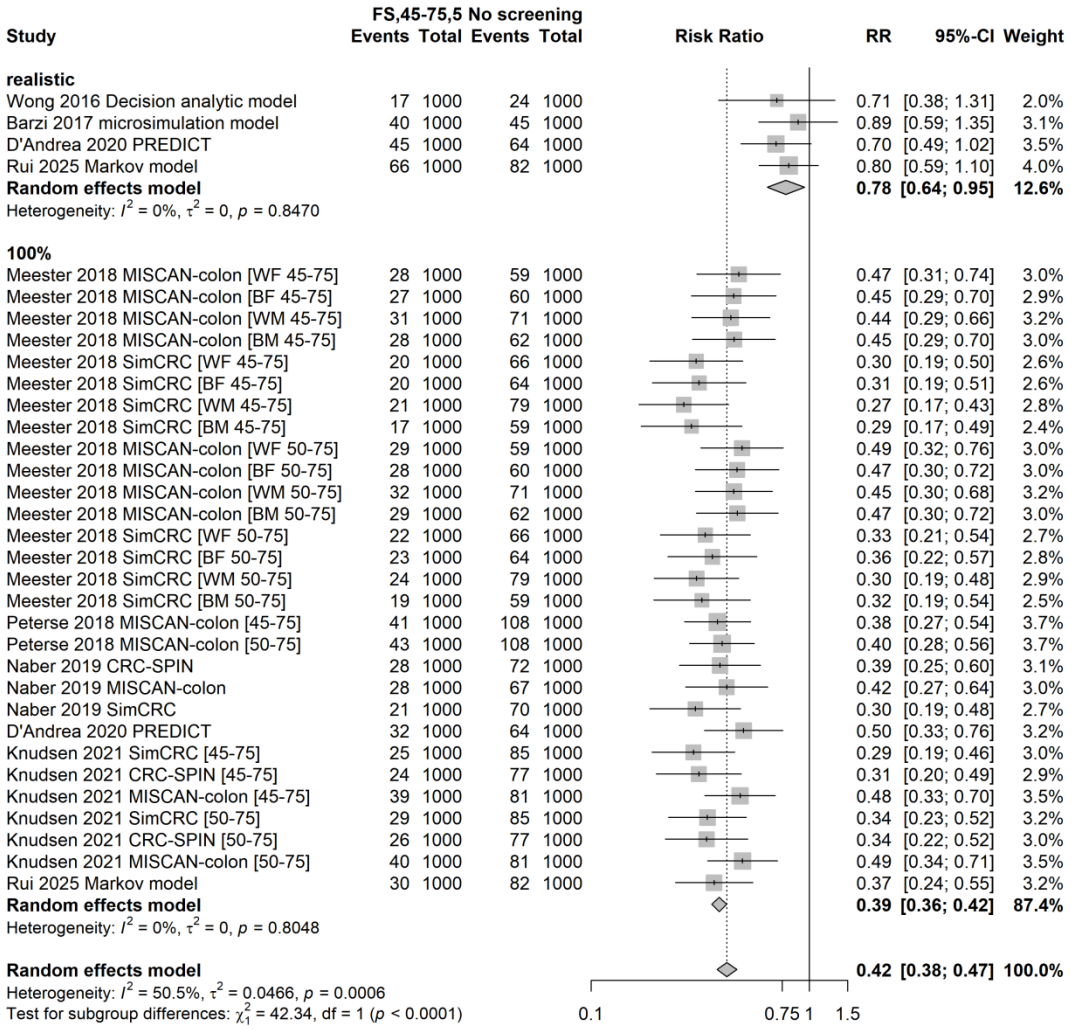
Supplementary Figure 12. CRC Incidence Risk Ratios by Model for Triennial Multi-Target Stool DNA (Ages 45–75, Realistic Adherence)



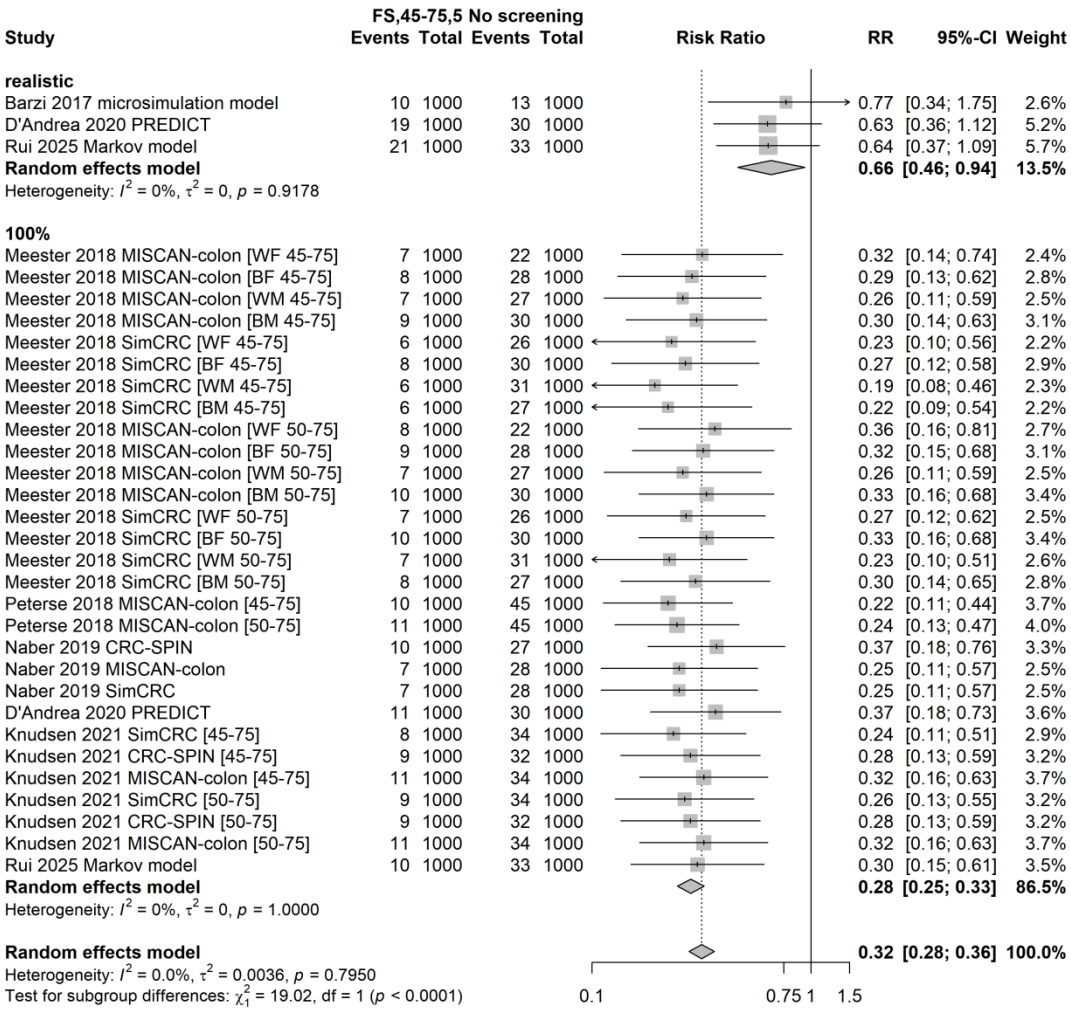
Supplementary Figure 13. Forest Plot of Colorectal Cancer Mortality Risk Ratios for Triennial Multi-Target Stool DNA Screening (Ages 45–75) Compared to No Screening



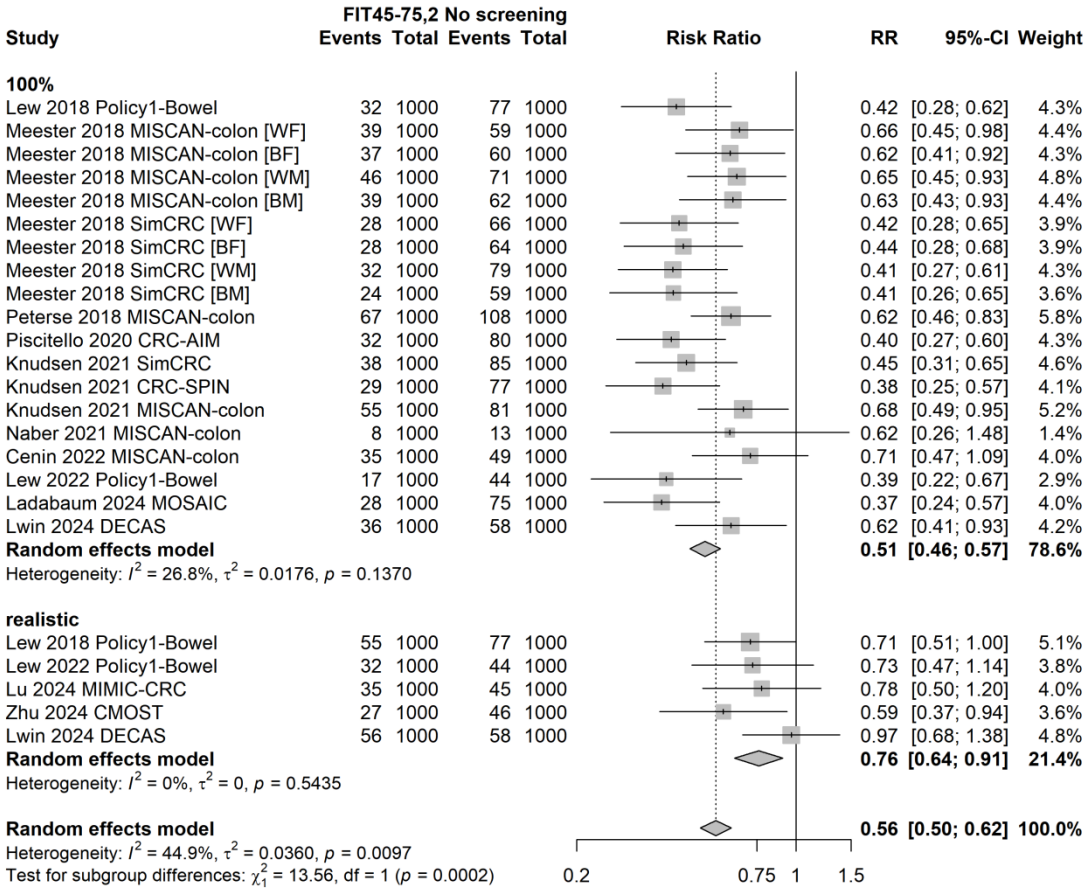
Supplementary Figure 14. Forest Plot of Colorectal Cancer Incidence Risk Ratios for 5-Yearly Flexible Sigmoidoscopy Screening (Ages 45–75) Compared to No Screening



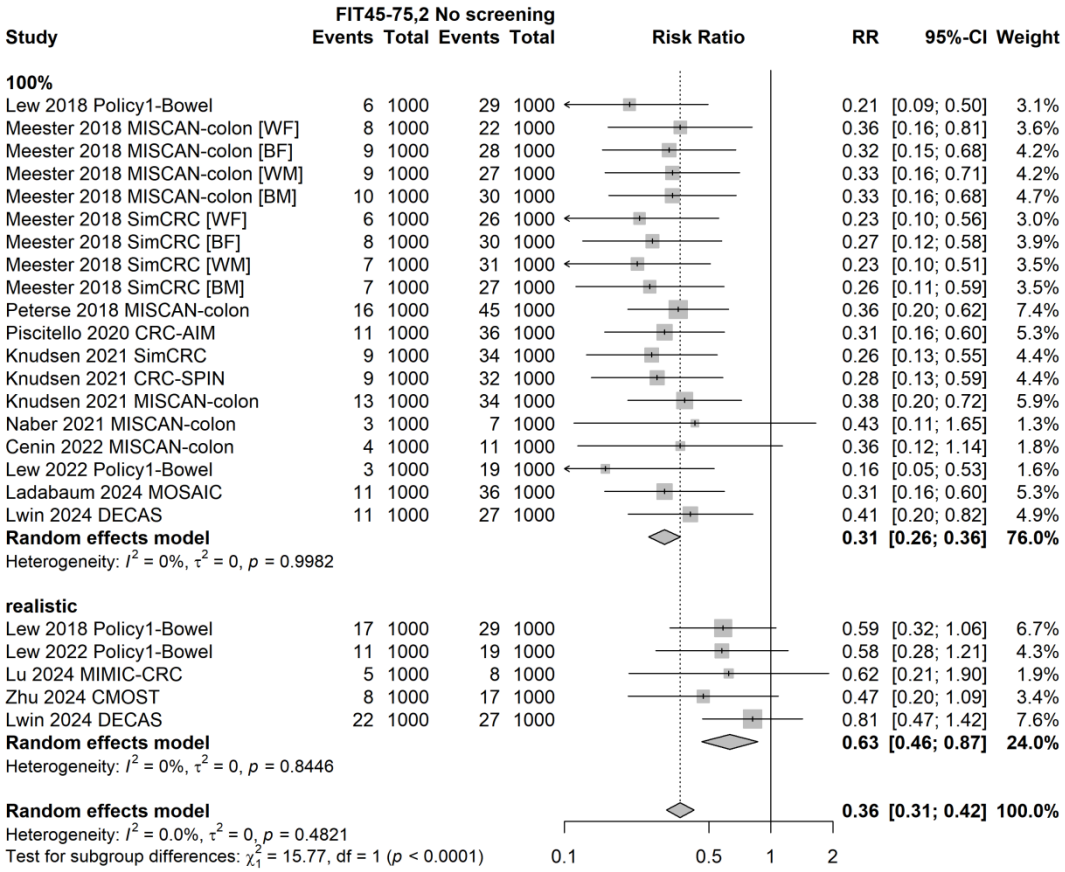
Supplementary Figure 15. Forest Plot of Colorectal Cancer Mortality Risk Ratios for 5-Yearly Flexible Sigmoidoscopy Screening (Ages 45–75) Compared to No Screening



Supplementary Figure 16. Forest Plot of Colorectal Cancer Incidence Risk Ratios for Biennial faecal Immunochemical Test Screening (Ages 45-75) Compared to No Screening



Supplementary Figure 17. Forest Plot of Colorectal Cancer Mortality Risk Ratios for Biennial faecal Immunochemical Test Screening (Ages 45-75) Compared to No Screening



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