*Supplementary materials for*

# Dynamics of Colorectal Cancer Screening in Low and Middle-Income Countries: A Modeling Analysis from Thailand

**Modeling files**: All modeling files to replicate the analysis are included in a zipped file.

**Online repository**: [*an online link is available, which shows the same modeling files; however, the link is removed due to ISDC policies about anonymity.*]

**Online simulator**: [*the link is removed due to ISDC policies about anonymity.*]

## Contents


Data input ..... 2
S1: Historical data ..... 2
S2: Model parameters ..... 3
Model development ..... 4
S3: Surveillance colonoscopy ..... 4
Model output ..... 5
S4: Model visualization ..... 5
S5: Calibration ..... 5
S6: Baseline projection ..... 7
S7: Strategy analysis projection ..... 9
S8: Sensitivity analysis ..... 12

# Data input

### S1: Historical data

Table **S1** reported all historical data used in the Colo-Sim. We used data from Thai database to represent colorectal cancer (CRC) care in Thailand. We also used data from UN database and projections as external data to capture the aging trend in Thailand. (See raw data of historical data the online data repository.)

However, historical data on the prevalence and CRC deaths are limited. Thus, we estimated them using data from literature and assumptions. We estimated the initial prevalence of CRC in each stage using calibration. We used the most extensive survival analysis of CRC to represent the crude death rate of symptomatic diagnosed CRC. For undiagnosed and asymptomatic diagnosed CRC, we estimated the crude death rate from the following formulation.

For $\forall X \in \{1,2,3,4\}$,

$$crude\ death\ rate\ of\ undiagnosed\ and\ asymptomatic\ diagnosed\ CRC\ stage\ X = crude\ death\ rate\ of\ symptomatic\ diagnosed\ CRC\ stage\ X * crude\ death\ rate\ ratio\ in\ undiagnosed\ and\ asymptomatic\ diagnosed\ CRC$$

**Table S1.** Source of historical data and projections

| Variable | Unit | Source |
|---|---|---|
| Annual deaths in population 49 years old | People/year | [1] |
| Annual deaths in population 50 years old or more | People/year | [1] |
| Annual deaths in population 75 years old or more | People/year | [1] |
| Colonoscopy for FIT screening per year | People/year | [2] |
| CRC detected by FIT screening per year | People/year | [2] |
| CRC stage 1 detected by symptom per year | People/year | [2–22] |
| CRC stage 2 detected by symptom per year | People/year | [2–22] |
| CRC stage 3 detected by symptom per year | People/year | [2–22] |
| CRC stage 4 detected by symptom per year | People/year | [2–22] |
| FIT participation per year | People/year | [2] |
| FIT positive per year | People/year | [2] |
| Normal results in colonoscopy from FIT screening per year | People/year | [2] |
| Polyp detected by FIT screening per year | People/year | [2] |
| Population 49 years old | People | [1] |
| Population 50 years old or more | People | [1] |
| Population 75 years old or more | People | [1] |

## S2: Model parameters

**Table S2.** Model parameters

| Variable | Value | Unit | Source |
|---|---|---|---|
| Accessibility to FIT ratio in population without tumors | 1.17 | Dmnl | Calibration |
| Average time in FIT positive waiting for a colonoscopy | 1 | Year | Assumption |
| Colonoscopy capacity | 200,000 | People/year | |
| Crude death rate of high-risk polyp (HRP) | 0.017 | Per year | Calibration |
| Crude death rate of low-risk polyp (LRP) | 0.017 | Per year | |
| Crude death rate of population without tumors | 0.017 | Per year | |
| Crude death rate of symptomatic diagnosed CRC stage 1 | 0.05 | Per year | [23] |
| Crude death rate of symptomatic diagnosed CRC stage 2 | 0.08 | Per year | [23] |
| Crude death rate of symptomatic diagnosed CRC stage 3 | 0.18 | Per year | [23] |
| Crude death rate of symptomatic diagnosed CRC stage 4 | 0.4 | Per year | [23] |
| Crude death rate ratio in undiagnosed and asymptomatic diagnosed CRC | 0.47 | Dmnl | Calibration |
| Initial fraction undiagnosed CRC stage 1 | 0.003 | Dmnl | |
| Initial fraction undiagnosed CRC stage 2 | 0.0004 | Dmnl | |
| Initial fraction undiagnosed CRC stage 3 | 0.0007 | Dmnl | |
| Initial fraction undiagnosed CRC stage 4 | 0.0003 | Dmnl | |
| Initial fraction undiagnosed HRP | 0.0137 | Dmnl | |
| Initial fraction undiagnosed LRP | 0.1419 | Dmnl | |
| Progression rate from CRC stage 1 to CRC stage 2 | 0.3 | Per year | [24] |
| Progression rate from CRC stage 2 to CRC stage 3 | 0.45 | Per year | [24] |
| Progression rate from CRC stage 3 to CRC stage 4 | 0.5 | Per year | [24] |
| Progression rate from HRP to CRC stage 1 | 0.05 | Per year | [24] |
| Progression rate from LRP to HRP | 0.015 | Per year | [24] |
| Progression rate from population without tumor to LRP | 0.015 | Per year | Calibration |
| Rate of coming back to observed FIT positive | 0.01 | Per year | Assumption |
| Sensitivity of colonoscopy in CRC | 0.95 | Dmnl | [25] |
| Sensitivity of colonoscopy in HRP | 0.85 | Dmnl | [25] |
| Sensitivity of colonoscopy in LRP | 0.75 | Dmnl | [25] |
| Sensitivity of FIT in CRC | 0.67 | Dmnl | [26] |
| Sensitivity of FIT in HRP | 0.24 | Dmnl | [27] |
| Sensitivity of FIT in LRP | 0.076 | Dmnl | [27] |
| Specificity of FIT | 0.95 | Dmnl | [26] |
| Symptomatic detected rate CRC stage 1 | 0.006 | Per year | Calibration |
| Symptomatic detected rate CRC stage 2 | 0.088 | Per year | |
| Symptomatic detected rate CRC stage 3 | 0.344 | Per year | |
| Symptomatic detected rate CRC stage 4 | 0.657 | Per year | |

**Table S3.** Initial value of health states in 2004

| Variable | Initial value in 2004 | Unit | Source |
|---|---|---|---|
| Diagnosed screened population without tumors | 0 | People | Assumption |
| Diagnosed via symptom CRC stage 1 | 0 | People | |
| Diagnosed via symptom CRC stage 2 | 0 | People | |
| Diagnosed via symptom CRC stage 3 | 0 | People | |
| Diagnosed via symptom CRC stage 4 | 0 | People | |
| FIT false positive population without tumors | 0 | People | |
| FIT true positive CRC stage 1 | 0 | People | |
| FIT true positive CRC stage 2 | 0 | People | |
| FIT true positive CRC stage 3 | 0 | People | |
| FIT true positive CRC stage 4 | 0 | People | |
| FIT true positive HRP | 0 | People | |
| FIT true positive LRP | 0 | People | |
| Lost FIT false positive population without tumor | 0 | People | |

| Variable | Initial value in 2004 | Unit | Source |
|---|---|---|---|
| Lost FIT true positive CRC stage 1 | 0 | People | |
| Lost FIT true positive CRC stage 2 | 0 | People | |
| Lost FIT true positive CRC stage 3 | 0 | People | |
| Lost FIT true positive CRC stage 4 | 0 | People | |
| Lost FIT true positive HRP | 0 | People | |
| Lost FIT true positive LRP | 0 | People | |
| Post-diagnostic colonoscopy CRC stage 1 | 0 | People | |
| Post-diagnostic colonoscopy CRC stage 2 | 0 | People | |
| Post-diagnostic colonoscopy CRC stage 3 | 0 | People | |
| Post-diagnostic colonoscopy CRC stage 4 | 0 | People | |
| Post-diagnostic colonoscopy HRP | 0 | People | |
| Post-diagnostic colonoscopy LRP | 0 | People | |
| Symptomatic Post-diagnostic colonoscopy CRC stage 1 | 0 | People | |
| Symptomatic Post-diagnostic colonoscopy CRC stage 2 | 0 | People | |
| Symptomatic Post-diagnostic colonoscopy CRC stage 3 | 0 | People | |
| Symptomatic Post-diagnostic colonoscopy CRC stage 4 | 0 | People | |
| Undiagnosed population without tumors | 10,926,453 | People | |
| Undiagnosed CRC stage 1 | 43,942 | People | |
| Undiagnosed CRC stage 2 | 5,404 | People | |
| Undiagnosed CRC stage 3 | 9,514 | People | Calibration |
| Undiagnosed CRC stage 4 | 4,389 | People | |
| Undiagnosed HRP | 254,154 | People | |
| Undiagnosed LRP | 2,622,971 | People | |

## Model development

### S3: Surveillance colonoscopy

We estimated the number of surveillance colonoscopies based on National Comprehensive Cancer Network Guidelines® Version 3.2022 Colorectal Cancer Screening. The guideline suggested that patients with a history of a polyp or CRC should get a surveillance colonoscopy. The interval of surveillance colonoscopy depends on various factors, such as the number and grade of polyps found from the latest colonoscopy, type of cancer (colon/rectal cancer), Carcinoembryonic Antigen (CEA) level, preoperative management [28]. Due to those complexities, we simplify it based on staging at first diagnosis and the life expectancy of each stage. Table S4 reported life expectancy after diagnosis of CRC in each stage in Thailand.

**Table S4.** Life expectancy of CRC after diagnosis in Thailand

| Life expectancy | Value* | Unit | Source |
|---|---|---|---|
| CRC stage 1 | 27.55 | Year | [29] |
| CRC stage 2 | 20.05 | Year | |
| CRC stage 3 | 15.2 | Year | |
| CRC stage 4 | 2.15 | Year | |

* Estimated from the weighted average of life expectancy between males and females in Thailand

**Table S5.** Guideline for surveillance colonoscopy for CRC in each stage

| Staging at first diagnosis | Guideline for surveillance colonoscopy | Source |
|---|---|---|
| Normal colonoscopy | No need to get surveillance colonoscopy. They need FIT screening after 10 years. | [28,30] |
| Low-risk polyp | | |
| High-risk polyp | Repeat colonoscopy 3, 8 years after diagnosis. | |
| CRC stage 1 | Repeat colonoscopy 1, 4 years after diagnosis. Then every 5 years | |
| CRC stage 2 | | |
| CRC stage 3 | | |
| CRC stage 4 | | |

## Model output

### S4: Model visualization

The model used CRC disease progression based on the adenoma-carcinoma sequence. Population without tumors can generate tumors by the transition to low-risk polyp, high-risk polyp, CRC stage 1-4, respectively. We presented the overview of the Colo-Sim below.

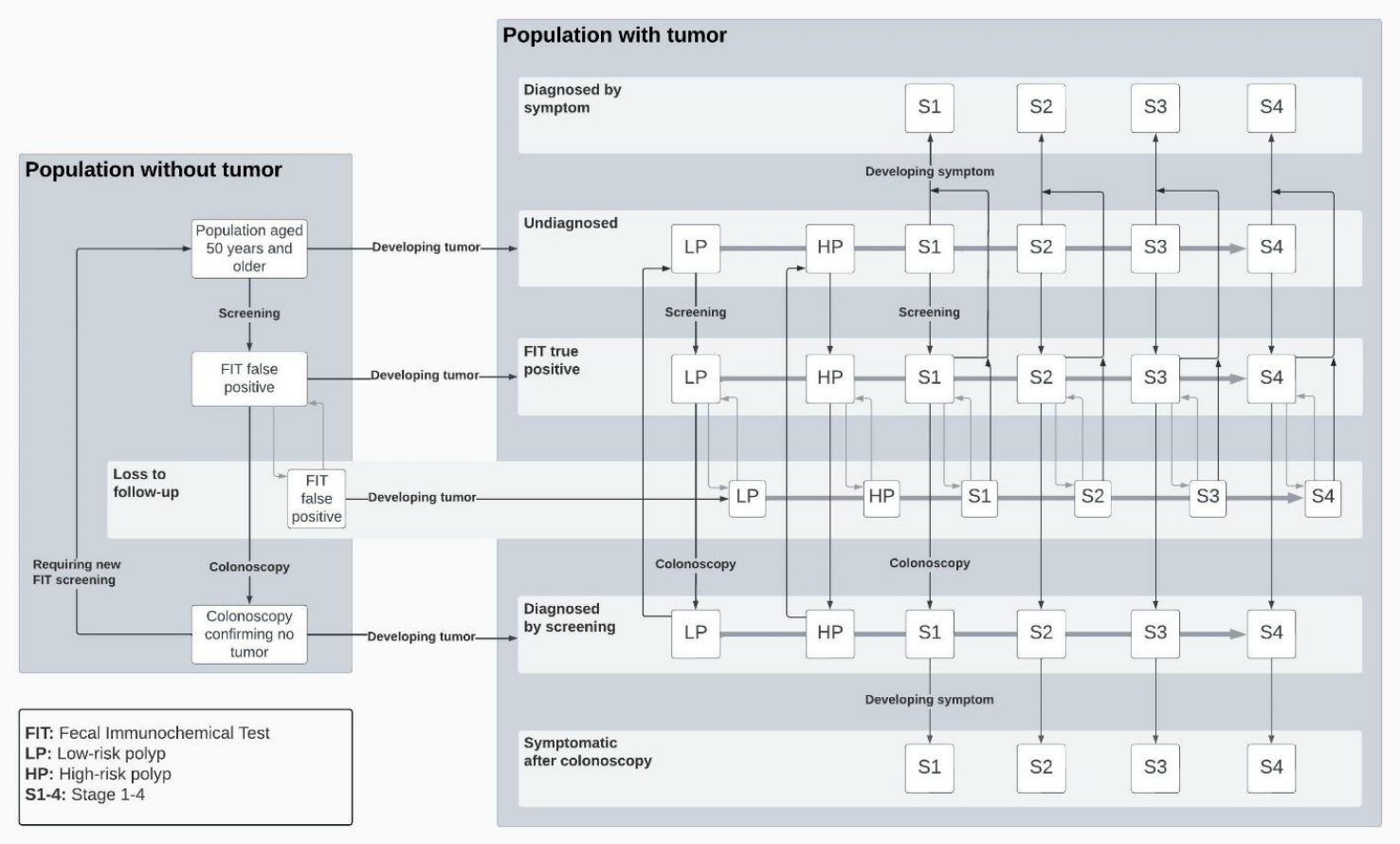
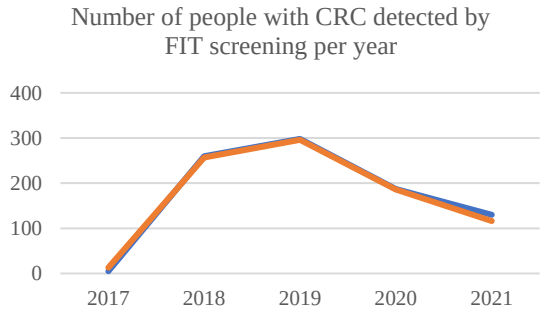


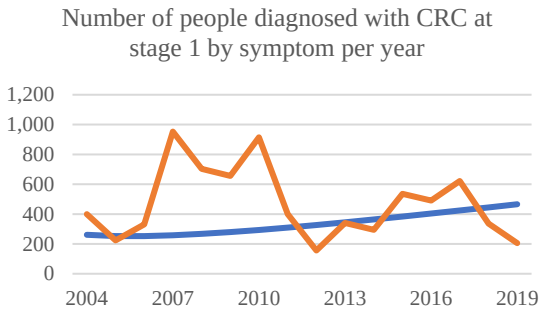

**Fig. S1.** Overview of the Colo-Sim model

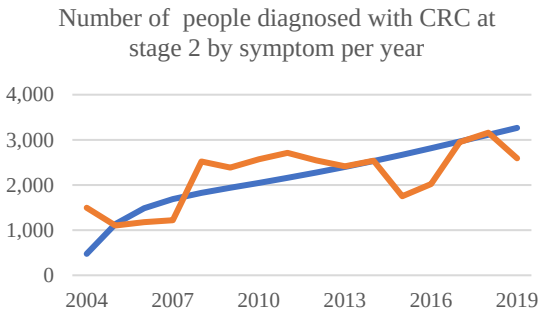
### S5: Calibration

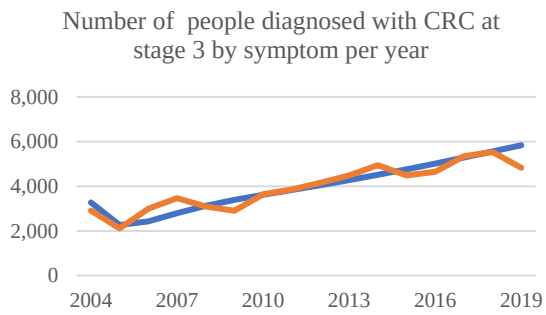
We performed calibration using nine sets of historical data from S1 (others were used as external data) to optimize 14 unknown parameters in S2. We used mean absolute percentage error

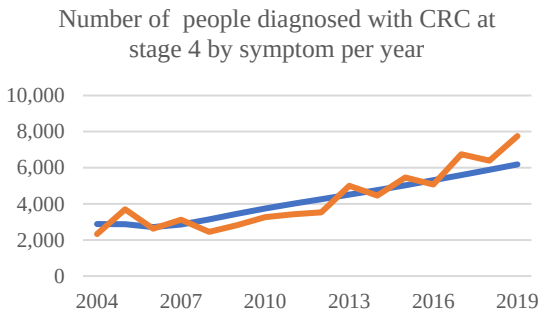
calculated from historical data and model output by the Powell optimization method. We replicated historical data as follows.

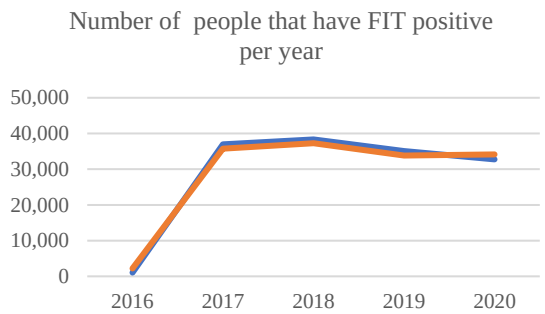


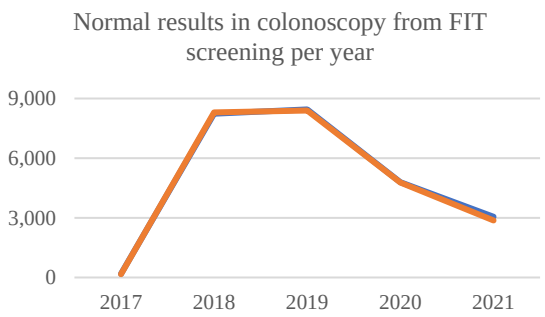



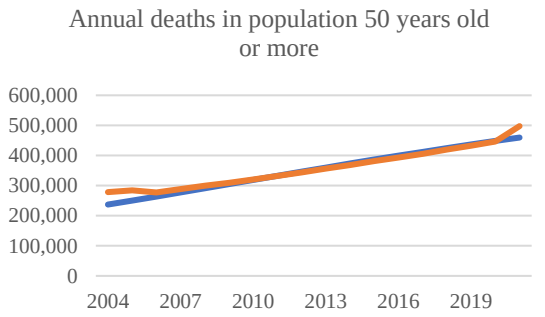



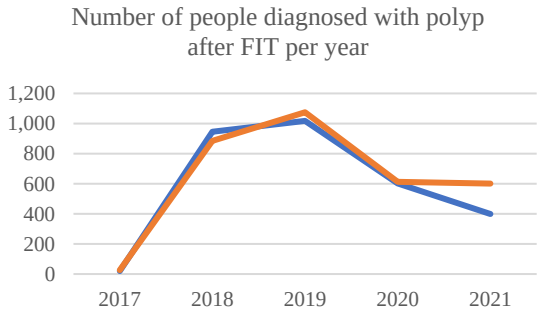



**Fig. S2.** Graphs compared between model projection (blue lines) and historical data from Thailand (red lines)

## S6: Baseline projection

In 2022, projected FIT accessibility and accessibility to diagnostic colonoscopy are 3% and 10%, respectively. For all stages of CRC, the mean sojourn time is estimated as nine years in Thailand compared to five years in the USA [31,32]. Also, only 30% of CRC are diagnosed.

After calibrating the model with the historical data, we projected all outcomes to 2022. We estimated accessibility to FIT and diagnostic colonoscopy from the formulation below.

$$accessibility\ to\ FIT = \frac{number\ of\ FIT\ screening\ per\ year}{undiagnosed\ population\ in\ 50-75\ years\ old}$$

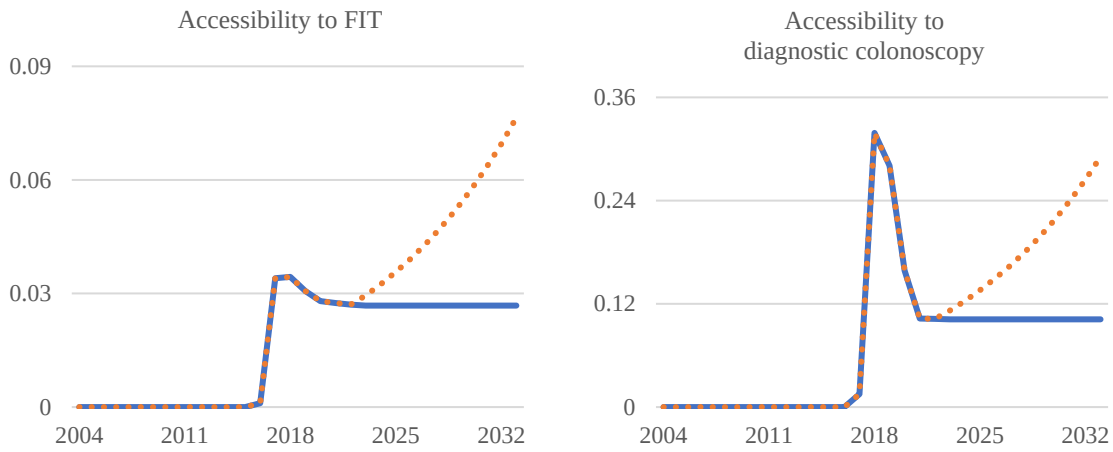
$$accessibility\ to\ diagnostic\ colonoscopy = \frac{number\ of\ diagnostic\ colonoscopy\ after\ FIT}{FIT\ positive\ population}$$

We cannot directly quantify accessibility to symptom evaluation (AS). So, we estimated accessibility to symptom evaluation (relative to the baseline) (ASR) from the formulation below. Denote symptomatic detection rate (SDR). For $\forall X \in \{1,2,3,4\}$,

$$ASR_{new} = \frac{AS_{new}}{AS_{baseline}} = \frac{SDR\ CRC\ stage\ X_{new}}{SDR\ CRC\ stage\ X_{baseline}}$$

$$SDR\ CRC\ stage\ X = \frac{CRC\ stage\ X\ diagnosed\ by\ symptom\ per\ year}{Undiagnosed\ CRC\ stage\ X}$$

In the main baseline assumption, we assumed that access to screening (i.e., accessibility to FIT, and accessibility to diagnostic colonoscopy) and access to symptom evaluation are projected as constants to their values in 2022. We also considered the alternative baseline of gradual increase in those access by multiplying them with 1.1 each year. Fig. S3 showed the historical and projected results of access to screening (i.e., accessibility to FIT, accessibility to diagnostic colonoscopy) and ASR in the main and alternative baseline assumptions.



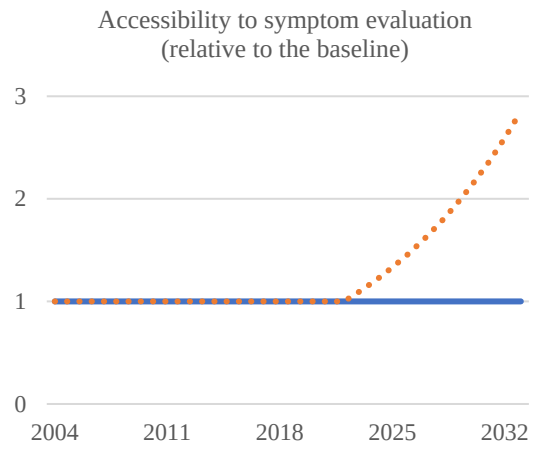



**Fig. S3.** Historical data and projections of access to screening and symptom evaluation in the main (blue lines) and alternative baseline assumptions (red dot lines)

Fig. S4 showed projections of the main outcomes in both baseline assumptions. The results are largely consistent. Fig. S5-Fig. S6 compare the colonoscopy capacity, availability of diagnostic colonoscopy, and people with FIT positive per year (demands for diagnostic colonoscopy per year) in the main baseline and alternative baseline assumptions, respectively.

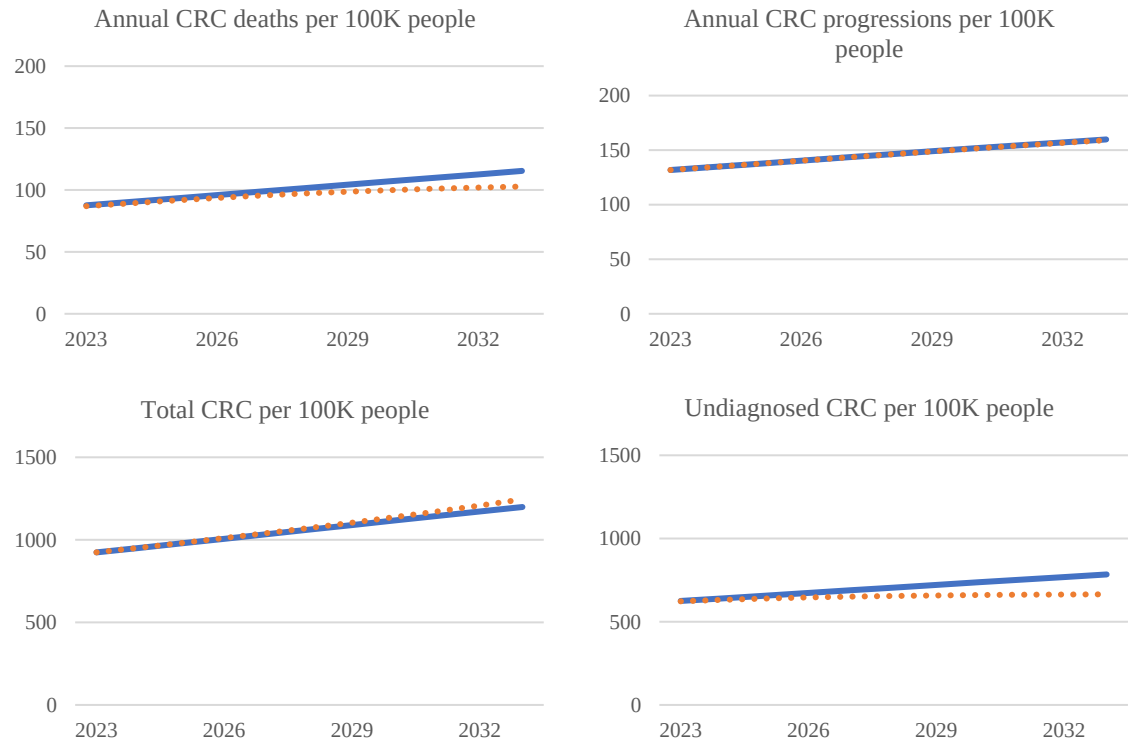



**Fig. S4.** Projected outcomes normalized for 100K people in the main baseline (blue lines), and the alternative baseline assumption (red dot lines) for people 50 years or older. Including annual CRC deaths (per 100K people), annual CRC progressions (per 100K people), total CRC (per 100K people), undiagnosed CRC (per 100K people)

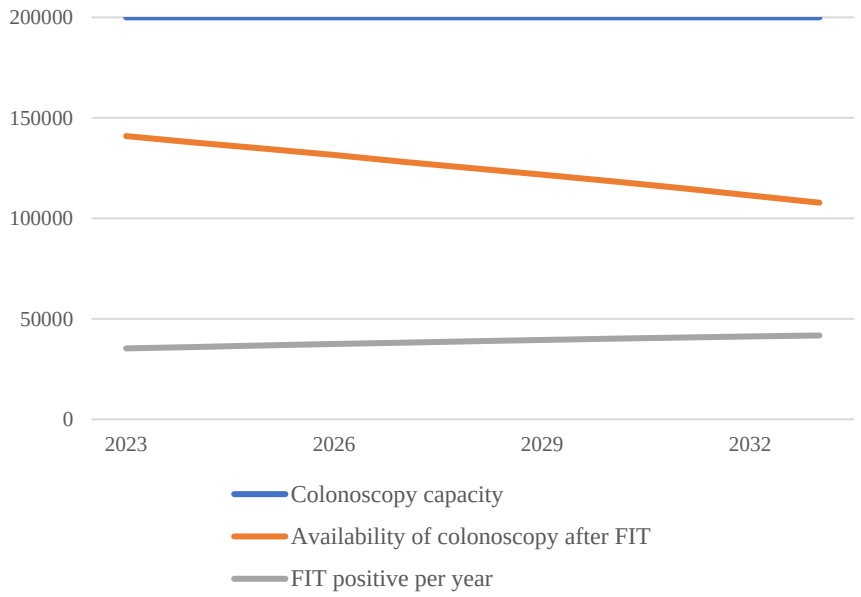



**Fig. S5.** Projected outcomes in the main baseline: comparison among the colonoscopy capacity, the availability of diagnostic colonoscopy for FIT positive, and FIT positive per year

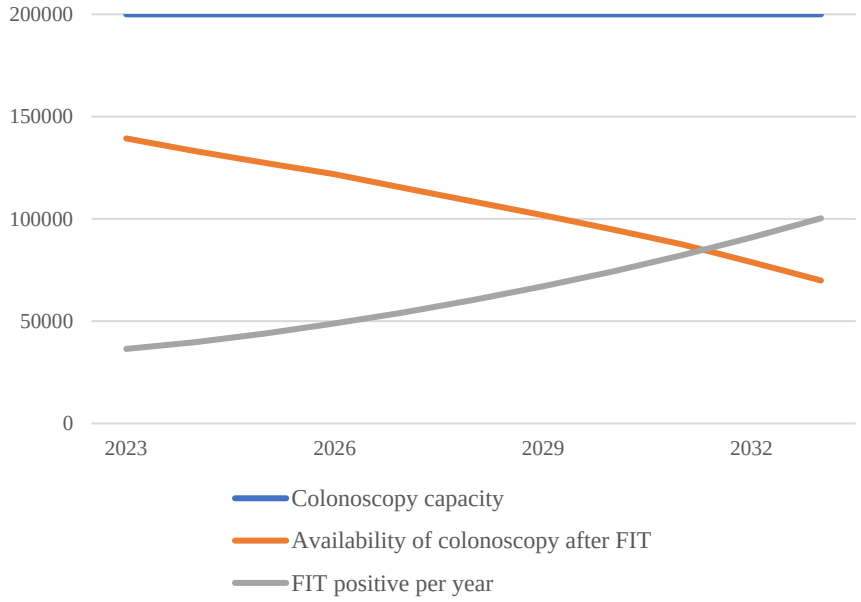



**Fig. S6.** Projected outcomes in the alternative baseline assumption: comparison among the colonoscopy capacity, the availability of diagnostic colonoscopy for FIT positive, and FIT positive per year

## S7: Strategy analysis projection

In the strategy analysis, we aimed to compare strategies in current colonoscopy (200K people/year) and sufficient colonoscopy capacity (681K people/year). To calculate the sufficient colonoscopy that can satisfy all strategies, we first performed the analysis on an extremely high colonoscopy capacity (e.g., 50 times of the current capacity). Estimated colonoscopy demand from each strategy was present below. From Fig. S7, maximum colonoscopy demand from the baseline and

three strategies during 2023-2032 is 681K people. Thus, we concluded that sufficient colonoscopy capacity is 681K people/year.

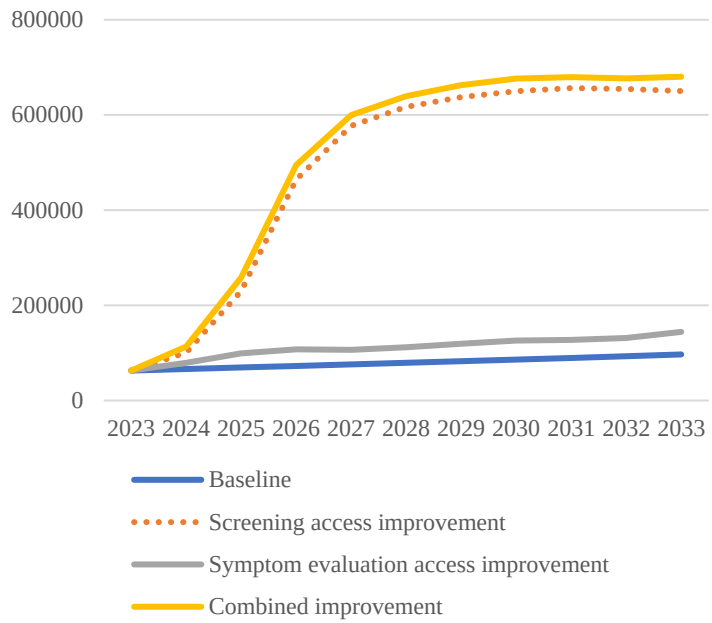



**Fig. S7.** Colonoscopy demand in 10M people/year colonoscopy capacity

We gathered the target value of accessibility to FIT, and diagnostic colonoscopy from literature. We estimated the target value of AS (relative to the baseline) using the formulation below. Denote mean sojourn time (MST), transition rate between undiagnosed to diagnosed CRC by symptom (TRA), symptomatic detection rate (SDR). For CRC stage 1-4,

$$ASR_{\ target\ value} = \frac{AS_{target\ value}}{AS_{baseline}} = \frac{SDR\ CRC\ stage\ X_{target\ value}}{SDR\ CRC\ stage\ X_{baseline}}$$

Thus,

$$SDR\ CRC\ stage\ X_{target\ value} = ASR_{\ target\ value} * SDR\ CRC\ stage\ X_{baseline}$$

$$SDR\ CRC\ stage\ X = \frac{CRC\ stage\ X\ diagnosed\ by\ symptom\ per\ year}{Undiagnosed\ CRC\ stage\ X}$$

The literature shows the formulation of mean sojourn time below [32].

$$MST = \frac{1}{TRA} = \frac{\sum_{X=I}^{IV} CRC\ stage\ X\ diagnosed\ by\ symptom\ per\ year}{\sum_{X=I}^{IV} Undiagnosed\ CRC\ stage\ X}$$

we estimated $ASRB_{\ target\ value}$ = 343%, resulting in a mean sojourn time of 5 years in 2032 (the levels equal to the USA in 1997-2010). In other words, accessibility to symptom evaluation in Thailand is 29% of the level in the USA.

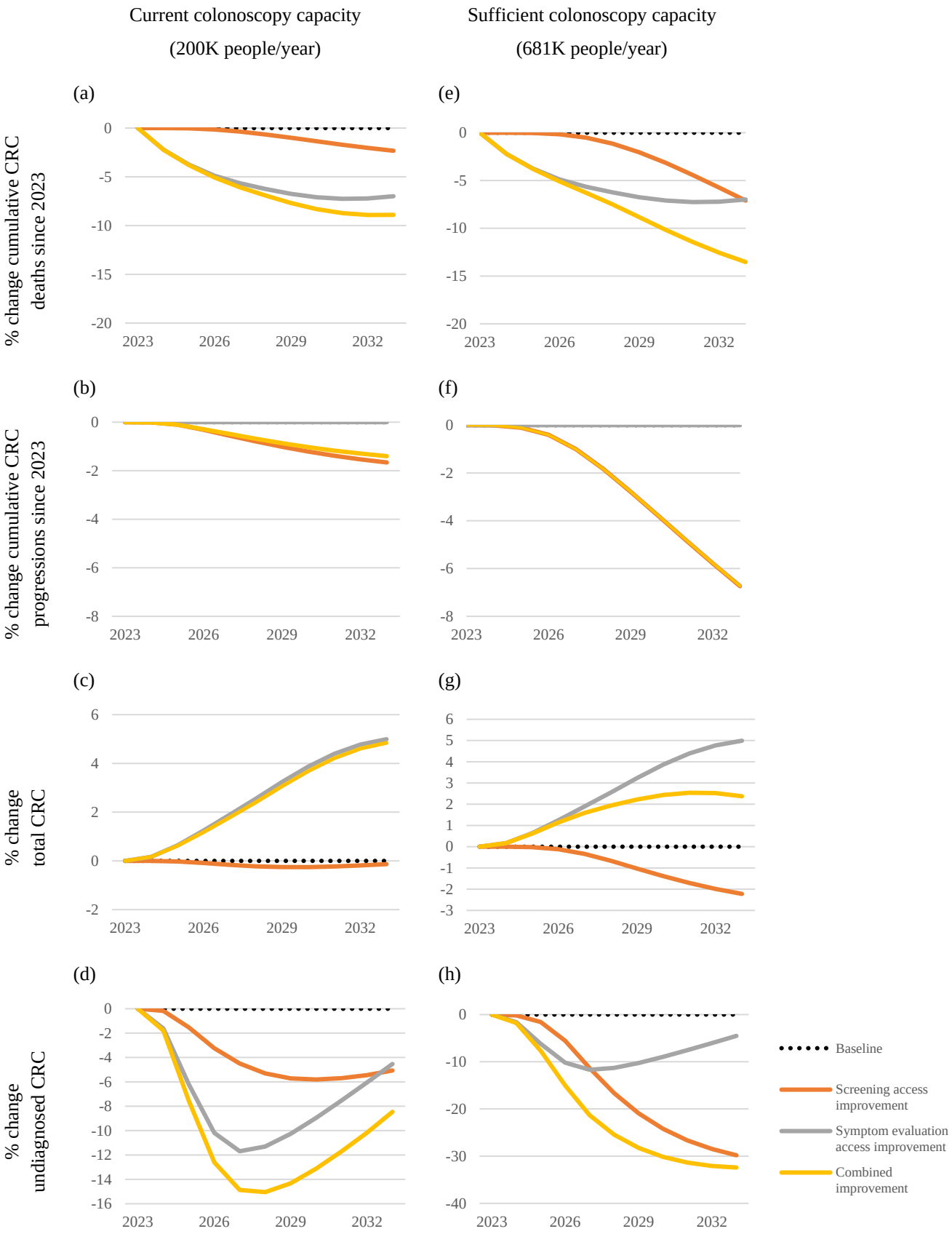



**Fig. S8.** Simulated outcomes' trajectories from each strategy compared to alternative baseline assumption, under current and sufficient colonoscopy capacities.
% change cumulative CRC deaths since 2023 (a, e), % change cumulative CRC progressions since 2023 (b, f), % change total CRC (c, g), and % change of undiagnosed CRC (d, h)

## S8: Sensitivity analysis

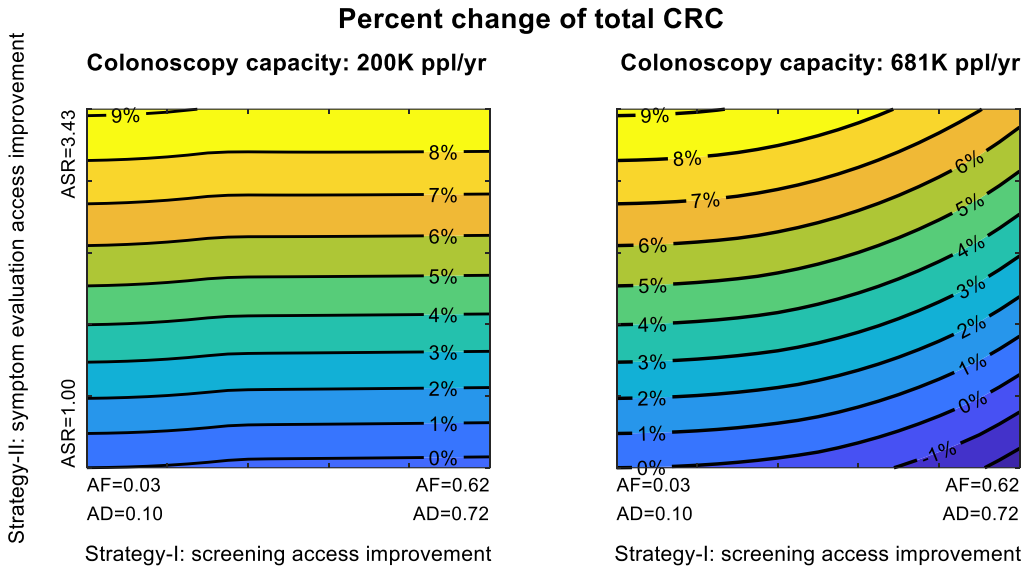



**Fig. S9.** Projected changes in total CRC based on various levels of 'Strategy-I: screening access improvement' and 'Strategy-II: symptom evaluation access improvement.'
AF: accessibility to FIT; AD: accessibility to diagnostic colonoscopy; ASR: accessibility to symptom evaluation relative to the baseline

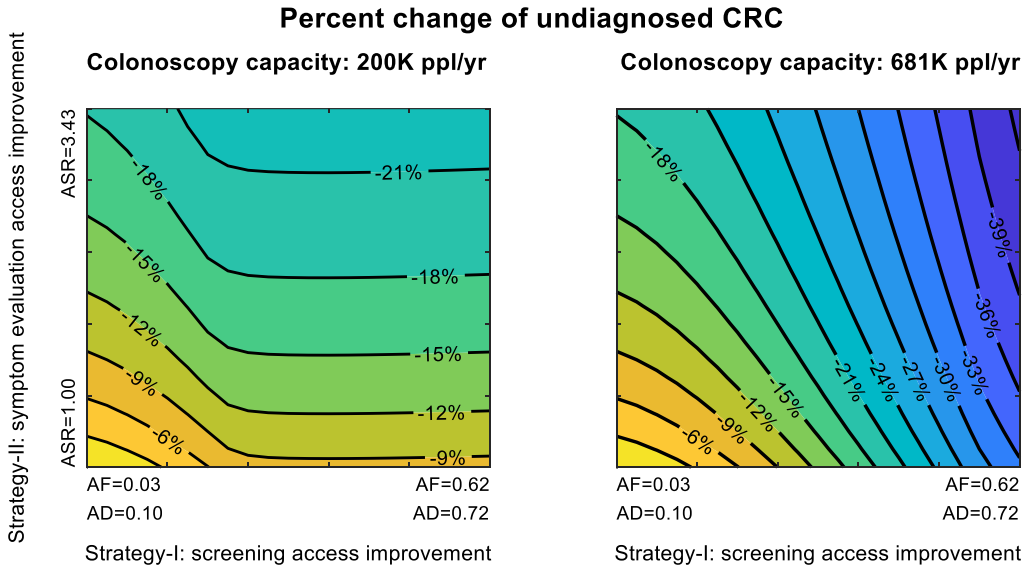



**Fig. S10.** Projected changes in undiagnosed CRC based on various levels of 'Strategy-I: screening access improvement' and 'Strategy-II: symptom evaluation access improvement.'
AF: accessibility to FIT; AD: accessibility to diagnostic colonoscopy; ASR: accessibility to symptom evaluation relative to the baseline

We performed one-way sensitivity analysis on model parameters with ±20% range in uniform distribution. Fig. S11-Fig. S14 are tornado diagrams representing uncertainty from each parameter on primary outcomes (i.e., annual CRC deaths, annual CRC progressions) and secondary outcomes (i.e., total CRC, undiagnosed CRC), respectively. We reported all outcomes per cohort of 100K people

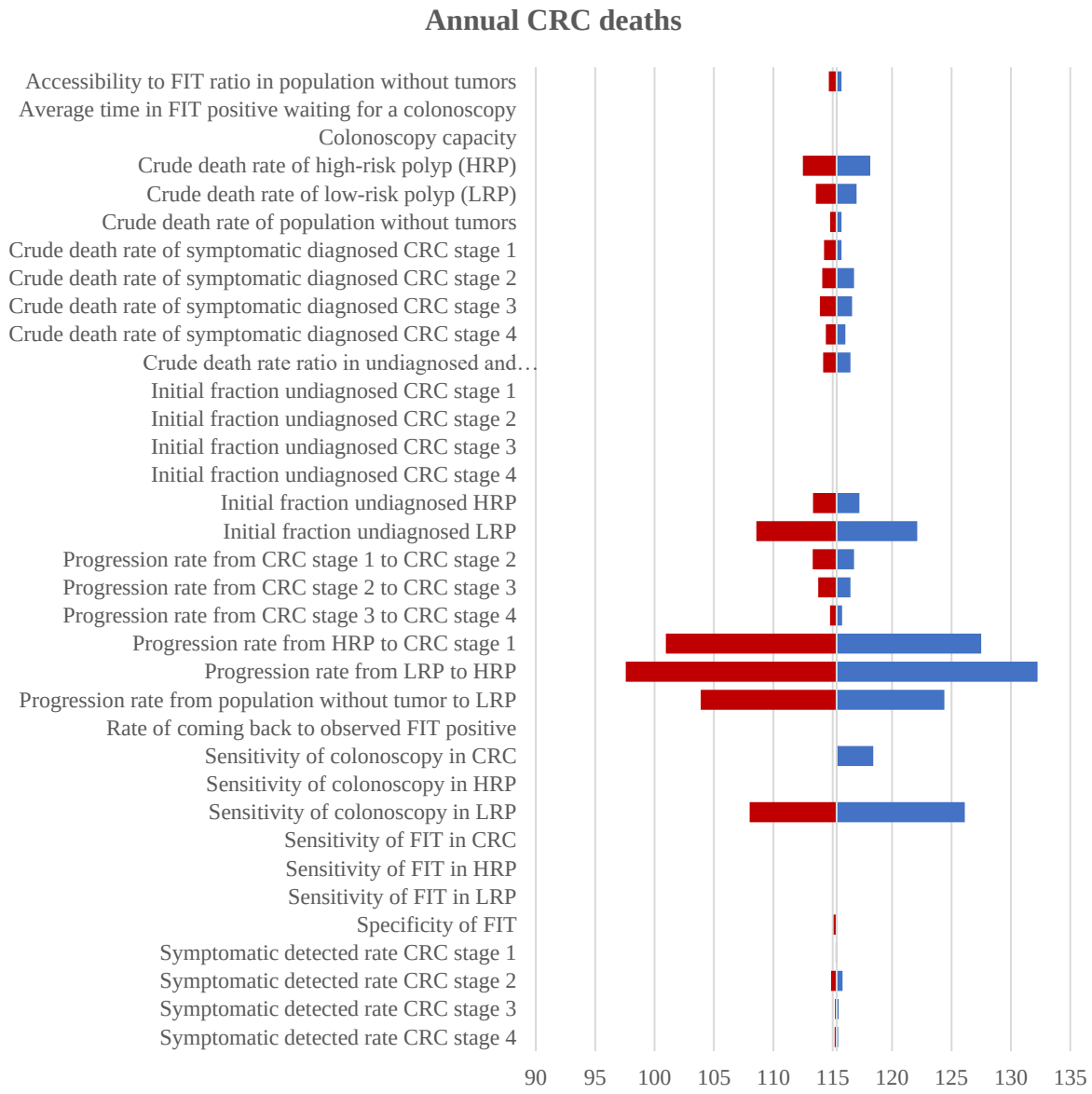



**Fig. S11.** One-way sensitivity analysis represented annual CRC deaths per 100K people in baseline projections (baseline value: 115 people) over ten years

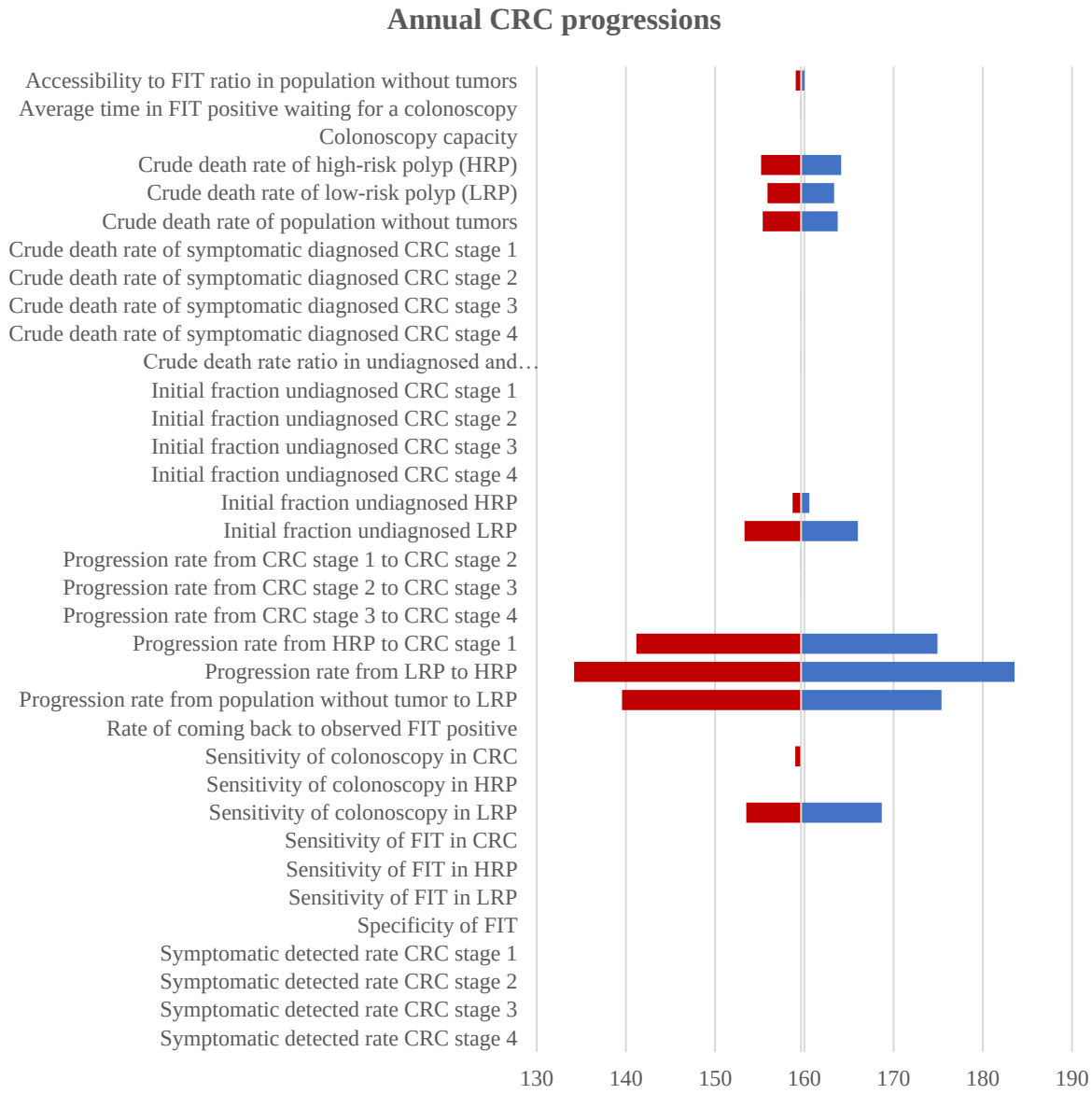



**Fig. S12.** One-way sensitivity analysis represented annual CRC progressions per 100K people in baseline projections (baseline value: 160 people) over ten years

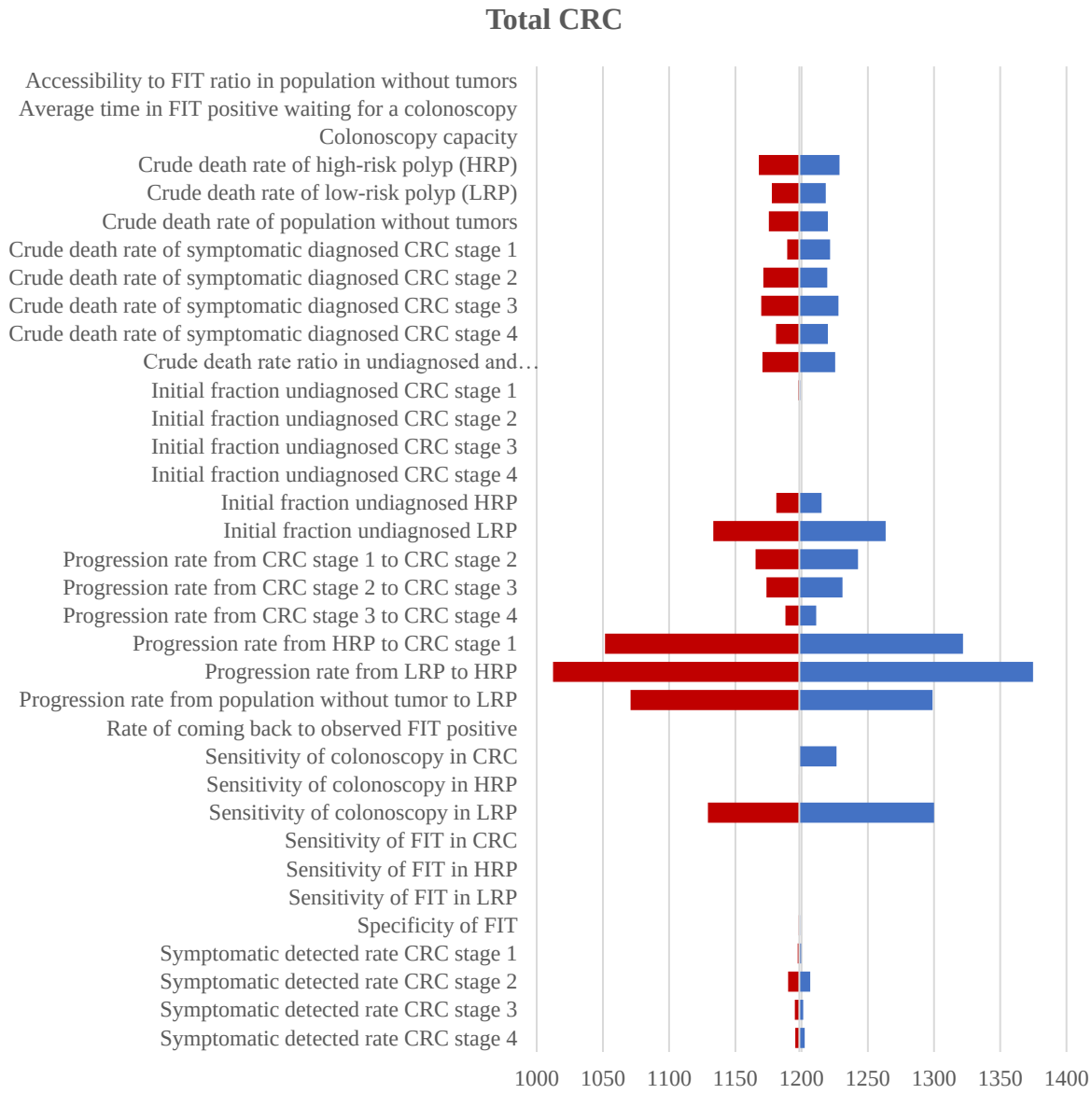



**Fig. S13.** One-way sensitivity analysis represented total CRC per 100K people in baseline projections (baseline value: 1,198 people) over ten years

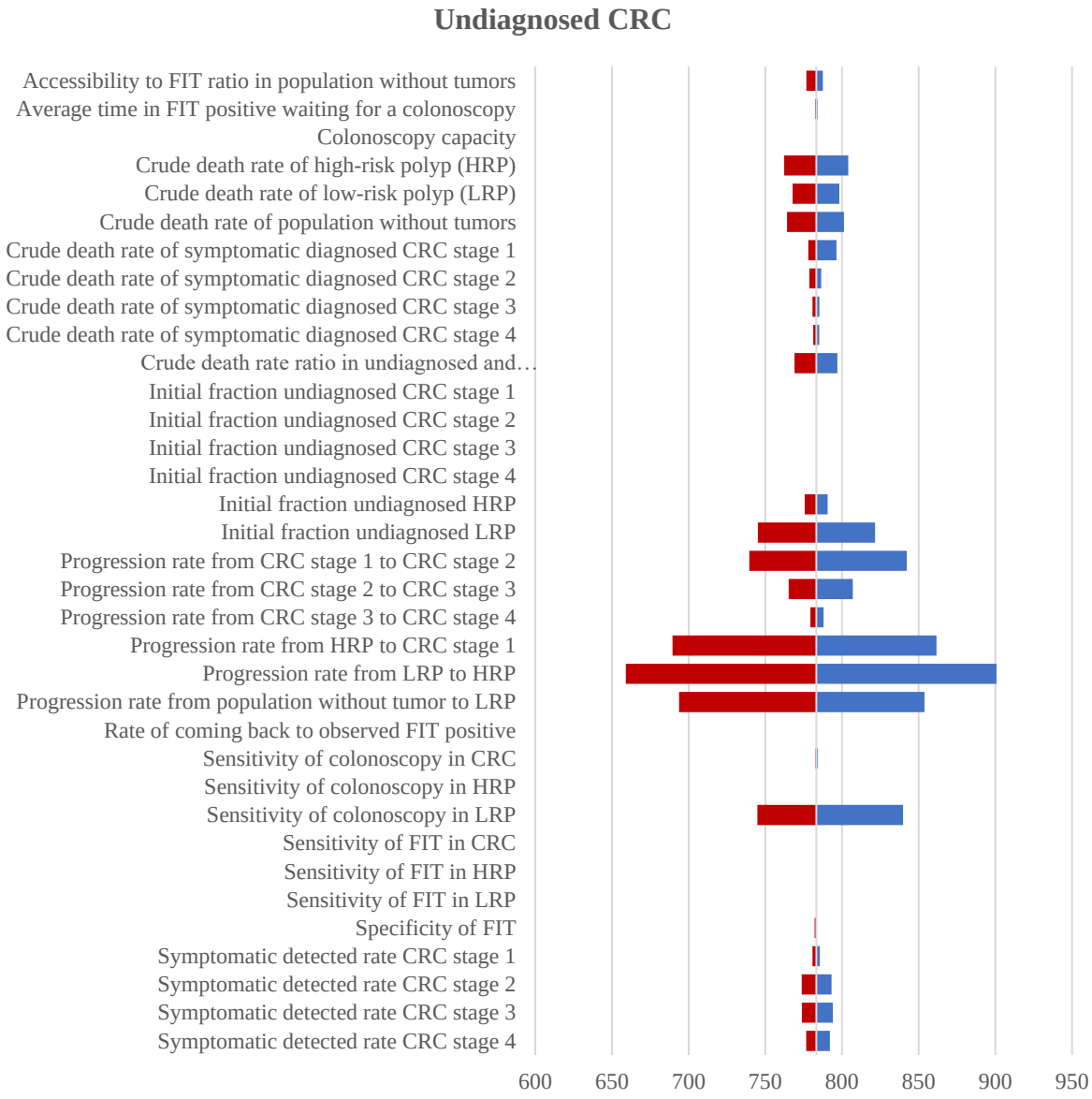



**Fig. S14.** One-way sensitivity analysis represented undiagnosed CRC per 100K people in baseline projections (baseline value: 783 people) over ten years

**References:**


1 United Nations, Department of Economic and Social Affairs, Population Division (2022). World Population Prospects 2022, Online Edition.

2 Health data center of ministry of public health of Thailand. ประชากรกลุ่มเป้าหมายได้รับการคัดกรองโรคมะเร็งลำไส้ใหญ่และลำไส้ตรง. 2019. https://hdcservice.moph.go.th/hdc/reports/report.php?source=pformated/format1.php&cat_id=59acae7a68f02c8e2c0cb88dfc6df3b3&id=6c88a8d6cbd2779301d3198b82a45cdf (accessed 1 Oct 2022).

3 Attasara pattarawin. *Hospital-based cancer registry, 2004*. National Cancer Institute, department of medical services, Ministry of Public Health

4 Attasara P. *Hospital-based cancer registry, 2005*. National Cancer Institute, department of medical services, Ministry of Public Health

5 Attasara P. *Hospital-based cancer registry, 2006*. National Cancer Institute, department of medical services, Ministry of Public Health

6 Attasara P, Buasom R. *Hospital-based cancer registry, 2007*. National Cancer Institute, department of medical services, Ministry of Public Health 2008.

7 Attasara P, Buasom R. *Hospital-based cancer registry, 2008*. National Cancer Institute, department of medical services, Ministry of Public Health 2009.

8 Attasara P, Buasom R. *Hospital-based cancer registry, 2009*. National Cancer Institute, department of medical services, Ministry of Public Health 2010.

9 Attasara P, Buasom R. *Hospital-based cancer registry, 2010*. National Cancer Institute, department of medical services, Ministry of Public Health 2011. http://www.nci.go.th

10 Attasara P, Buasom R. *Hospital-based cancer registry, 2011*. National Cancer Institute, department of medical services, Ministry of Public Health 2012.

11 Chaiwerawattana A, Laowahutanont P, Suwankaysorn P. *Hospital-based cancer registry, annual report 2012*. National Cancer Institute, department of medical services, Ministry of Public Health 2014.

12 Chaiwerawattana A, Laowahutanont P, Suwankaysorn P. *Hospital-based cancer registry, annual report 2013*. National Cancer Institute, department of medical services, Ministry of Public Health 2015.

13 Chaiwerawattana A, Sangrajrang S, Laowahutanont P, *et al. Hospital-based cancer registry,, annual report 2014*. National Cancer Institute, department of medical services, Ministry of Public Health 2016.

14 Chaiwerawattana A, Sangrajrang S, Laowahutanont P, *et al. Hospital-based cancer registry, annual report 2015*. National Cancer Institute, department of medical services, Ministry of Public Health 2017. http://www.nci.go.th

15 Sangrajrang S, Laowahutanont P, Sangariyawanich A, *et al. Hospital-based cancer registry, annual report 2016*. National Cancer Institute, department of medical services, Ministry of Public Health 2018.

16 Sangrajrang S, Laowahutanont P, Sangariyawanich A, *et al. Hospital-based cancer registry, annual report 2017*. National Cancer Institute, department of medical services, Ministry of Public Health 2018.

17 Sangariyawanich A, Buasom R. *hospital-based cancer registry, annual report 2018*. National Cancer Institute, department of medical services, Ministry of Public Health 2019.

18 Khuhaprema T, Attasara P, Sriplung H, *et al. Cancer in Thailand Volume VI, 2004-2006*. Bangkok: : National Cancer Institute Thailand, Ministry of public health 2012.

19 Khuhaprema T, Attasara P, Sriplung H, *et al. Cancer in Thailand Volume VII, 2007-2009*. Bangkok: : National Cancer Institute Thailand, Ministry of public health 2013.
20 Imsamran W, Chaiwerawattana A, Wiangnon S, *et al. Cancer in Thailand Vol. VIII, 2010-2012*. Bangkok: : National Cancer Institute Thailand, Ministry of public health 2015.
21 Imsamran W, Pattatang A, Supaattagorn P, *et al. Cancer in Thailand Vol. IX, 2013-2015*. Bangkok: : National Cancer Institute Thailand, Ministry of public health 2018.
22 Rojanamatin J, Ukranun W, Supaattagorn P, *et al. Cancer in Thailand Vol. X, 2016-2018*. Bangkok: : National Cancer Institute Thailand, Ministry of public health 2021.
23 Kittrongsiri K, Wanitsuwan W, Prechawittayakul P, *et al.* Survival analysis of colorectal cancer patients in a Thai hospital-based cancer registry. *Expert Rev Gastroenterol Hepatol* 2020;**14**:291–300. doi:10.1080/17474124.2020.1740087
24 Heresbach D, Chauvin P, Grolier J, *et al.* Cost-effectiveness of colorectal cancer screening with computed tomography colonography or fecal blood tests. *Eur J Gastroenterol Hepatol* 2010;**22**:1372–9. doi:10.1097/MEG.0b013e32833eaa71
25 Knudsen AB, Rutter CM, Peterse EFP, *et al.* Colorectal Cancer Screening: An Updated Decision Analysis for the U.S. Preventive Services Task Force Acknowledgments. 2021. www.ahrq.gov
26 Lee JK, Liles EG, Bent S, *et al.* Accuracy of Fecal Immunochemical Tests for Colorectal Cancer. *Ann Intern Med* 2014;**160**:171–81. doi:10.7326/m13-1484
27 Lin JS, Perdue LA, Henrikson NB, *et al.* Evidence Synthesis Number 202 Screening for Colorectal Cancer: An Evidence Update for the U.S. Preventive Services Task Force. 2021. www.ahrq.gov
28 Benson AB, Al-Hawary MM, Azad N, *et al.* NCCN Guidelines Version 2.2022 Colon Cancer Continue NCCN Guidelines Panel Disclosures. 2022. https://www.nccn.org/home/member-
29 Soerjomataram I, Thong MSY, Ezzati M, *et al.* Most colorectal cancer survivors live a large proportion of their remaining life in good health. *Cancer Causes and Control* 2012;**23**:1421–8. doi:10.1007/s10552-012-0010-2
30 Ness RM, Llor X, Chair V, *et al.* Continue NCCN Guidelines Panel Disclosures NCCN Guidelines Version 1.2022 Colorectal Cancer Screening. 2022. https://www.nccn.org/home/member-
31 Zheng W, Rutter CM. Estimated mean sojourn time associated with hemoccult sensa for detection of proximal and distal colorectal cancer. *Cancer Epidemiology Biomarkers and Prevention* 2012;**21**:1722–30. doi:10.1158/1055-9965.EPI-12-0561
32 Brenner H, Altenhofen L, Katalinic A, *et al.* Sojourn time of preclinical colorectal cancer by sex and age: Estimates from the german national screening colonoscopy database. *Am J Epidemiol* 2011;**174**:1140–6. doi:10.1093/aje/kwr188