# Evaluation of long-term benefits and cost-effectiveness of nation-wide colorectal cancer screening strategies in China in 2020–2060: a modelling analysis

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## Summary

**Background** Evidence on the long-term benefits and cost-effectiveness of colorectal cancer (CRC) screening strategies in China remains limited. This modelling study aims to address this issue for various CRC screening strategies in China between 2020 and 2060.

**Methods** Using a previously developed microsimulation model (MIMIC-CRC) with Chinese epidemiological data, we evaluated four CRC screening strategies targeting population aged 45–74 years: no screening, colonoscopy every 10 years, biennial faecal immunochemical testing (FIT), and a roll-out FIT screening strategy. Screening coverage (invitation) rates from 5% to 100% were analysed. Single-cohort analysis of 100,000 individuals was conducted to estimate the relative cost-effectiveness of each strategy. A multiple-cohort analysis of 100,000 people aged 40+ over 2020–2060 was conducted to project nation-wide long-term benefits and cost-effectiveness.

**Findings** In single-cohort analysis, all strategies yielded reductions in CRC incidence and mortality compared to no screening, with colonoscopy outperforming FIT-based strategies at the same invitation rates. In multiple-cohort analysis, among people over 40 years of age in China over 2020–2060, compared to no screening, at invitation rate of 5%, screening by colonoscopy, biennial FIT and roll-out FIT-based approach were estimated to avert 1.2, 0.4, and 0.3 million incident CRCs and 0.2, 0.1, and 0.1 million CRC-related deaths, respectively, compared to no screening (25.4 million incident CRCs and 4.4 million CRC-related deaths), and this preventive effect enlarged as the screening coverage rate increased. At full coverage, colonoscopy achieved the largest reductions (38.2% lower incidence and 43.2% lower mortality) but required the most resources. Biennial FIT and roll-out FIT-based approach screening was slightly less effective but had significant reduced colonoscopy needs (reduction of 83.8% and 85.2%, respectively) and overall cost (reduction of 23.4% and 37.8%, respectively) compared to colonoscopy screening.

**Interpretation** Nation-wide implementation of screening would be effective in reducing the burden of CRC in China. Biennial FIT and roll-out FIT-based screening strategies could prevent incident CRC cases and CRC-related deaths with considerably fewer resources than colonoscopy screening. Efforts should be made to increase the screening coverage in China.

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## Research in context

### Evidence before this study

We conducted a systematic literature search in PubMed and Google Scholar from the inception of both databases until April 2024, to identify cost-effectiveness evaluations of colorectal cancer screening in China. One large randomized trial (TARGET-C) has reported 3-year results comparing one-time colonoscopy, annual faecal immunochemical testing, and risk-adapted screening approaches. However, the long-term effects, affordability, and cost-effectiveness of current and potential optimized CRC screening strategies remain unclear. Previous modelling studies from other countries have evaluated different colorectal cancer screening strategies, but comprehensive evaluations specific to the Chinese population were lacking. Some studies examined strategies like colonoscopy, faecal testing, and combined approaches, but did not consider long-term projected outcomes, nationwide resource implications, or tailored screening adaptation based on regional healthcare capacity.

### Added value of this study

To our knowledge, this is the first comprehensive modelling study evaluating the long-term effectiveness, costs, resource utilisation and cost-effectiveness of various population-based colorectal cancer screening strategies for potential nationwide implementation in China from 2020 to 2060. Using a validated microsimulation model adapted with specific Chinese epidemiologic data, the study projected outcomes across strategies under different screening coverage scenarios. The analyses provide crucial evidence on optimizing screening modalities, resource requirements, and strategic tailoring of approaches based on local healthcare contexts across China's diverse regions.

### Implications of all the available evidence

Findings suggest implementing an organised nationwide colorectal cancer screening programme in China would effectively reduce disease burden but require substantial resources and costs. Combining faecal immunochemical testing with diagnostic colonoscopy for positive results, and a stepwise screening roll-out, may help maximize effectiveness while conserving endoscopy capacity and costs. Tailoring regional implementation based on local resources and healthcare access will be crucial. This evidence can guide development of nationwide Chinese screening guidelines and policies for sustainable colorectal cancer screening programmes.

## Introduction

Colorectal cancer (CRC) is a leading cause of cancer-related deaths and poses a significant public health burden worldwide, with approximately 1,925,828 individuals diagnosed with CRC and 903,643 deaths from the disease in 2022.[1] Nearly 30% of global new CRC cases and deaths occur in China annually, with 517,100 new cases of CRC diagnosed and 240,000 CRC deaths reported in 2022.[2] While screening has proven effective in reducing CRC incidence and mortality,[3] developing optimised screening strategies is crucial to maximise the cost-effectiveness of nationwide screening programmes, especially in resource-limited regions.

Several population-based organised CRC screening programmes, such as the Cancer Screening Programme in Rural China (initiated in 2005) and the Cancer Screening Programme in Urban China (initiated in 2012), have been launched in China under the support of central or local governments via key public health service programmes.[4] However, China currently lacks a nationwide organised CRC screening programme covering all eligible populations, and also lacks the high-quality evidence to guide nationwide screening strategies. Due to regional variations in CRC epidemiology,[2] ethnic composition, and healthcare resources, evidence from other countries may not be directly applicable to China. This highlights the necessity of conducting research specific to China's unique context to develop effective and applicable CRC screening strategies. In 2018, researchers in China initiated the first large-scale multicentre randomised controlled trial to evaluate the effectiveness of different CRC screening strategies, including one-time colonoscopy, annual faecal immunochemical test (FIT), and annual risk-adapted screening strategies (TARGET-C trial).[5] The preliminary result of this trial for the three rounds of screening has been reported, but the long-term effects, affordability, and cost-effectiveness of current and potential optimised CRC screening strategies remain unexplored.[6]

As the implementation period of nationally representative screening programmes in China has been too short to provide long-term evidence, a model-based cost-effectiveness analysis of different screening scenarios can serve as a reference for decision-makers to select the optimal screening strategy. Microsimulation modelling studies have been utilised to evaluate and compare the relative performance of various CRC screening strategies internationally as well as to assess the cost-effectiveness of implementing nationwide screening programmes. Findings from these studies have also informed guideline updates.[7] Nevertheless, CRC epidemiology in China differs significantly from Western countries which exist modelling studies, making a China-specific modelling study essential.[8–10] Given the substantial CRC burden and the current screening landscape in China, model-based evaluations can provide valuable guidance for optimising CRC screening efforts.

A micro-simulation model for the prevention and intervention of CRC in China (MIMIC-CRC)[11] has been developed to evaluate the natural history of CRC in China. The current modelling analysis was based on the

updated MIMIC-CRC framework, to evaluate the impact of implementing various screening strategies in China from 2020 to 2060, including projecting the impact on disease outcomes, costs, utilities, resource use, and cost-effectiveness; comparing the relative advantages of different strategies under varying screening coverage rates and financial and medical supplements; and identifying the optimal screening strategy for nationwide implementation in China.

## Methods

### Model construction, calibration and validation

A Chinese-adapted microsimulation model to simulate the natural history of CRC (MIMIC-CRC) has been developed.[11] The carcinogenesis process (Supplementary material p 2) was primarily based on adenoma-carcinoma sequence, which accounts for over 95% of cases in the Asian population and has been the most extensively studied.[12] The model assumes that initially, there are no lesions in the colorectal epithelium. As each simulated person ages, the normal colorectal epithelium is at risk of developing non-advanced adenomas and advanced adenomas (≥10 mm in size, with villous components, or high-grade intraepithelial neoplasia).[13] Advanced adenomas can progress to preclinical CRC (stages I-IV), which may develop into clinical (symptom-detected or screening-detected) CRC (stages I-IV). Disease progression may be interrupted due to CRC-related or other causes of death, while screening and removal of adenomas can prevent the occurrence of CRC and the status of the person changes back to no lesion. Other assumptions are presented in the Supplementary material (pp. 2–4).

The model parameters and inputs were synthesised from various sources (Supplementary material, pp. 3–4). The natural history parameters were obtained from recent large-scale pooled analyses and high-quality meta-analyses of Chinese studies. When unavailable, parameters were adapted from other modelling studied.[14] We used sex-, age-, and region-specific parameter values for factors sensitive to these variables. Population data were extracted from the 2020 China Population Census,[15] while all-cause mortality rates were obtained from the National Mortality Surveillance Report.[16] The latest registry-based cancer incidence and mortality statistics in 2016 were sourced from reports by the China National Cancer Center, which providing comprehensive data stratified by age and sex. To complement the long-term data, we also incorporated estimates in 2010–2019 from the Global Burden of Disease study.[17,18] From a societal perspective, costs included those associated with FIT, colonoscopy, pathological examination, and CRC treatment, while overheads related to programme administration, and individuals' out-of-pocket costs were excluded. Treatment costs were obtained from a multicentre, cross-sectional survey in 37 tertiary hospitals in 13 provinces across China between 2012 and 2014.[19] The costs associated with screening and diagnosis were based on TARGET-C.[6] Utility parameters were obtained from a cross-sectional questionnaire survey conducted in China's Heilongjiang province using the EQ-5D-5L.[20]

To ensure the robustness of the model, significant and invalid parameters were calibrated to the target data, including sex- and age-specific CRC incidence and mortality from population-based cancer registries. The simulated annealing algorithm searched for an optimum parameter solution by minimising the weighted sum of squared differences between the observed and simulated data.[21] Model outputs was further validated against incidence, mortality, and stage distribution data from nationwide cancer registries and the China Kadoorie Biobank (CKB) prospective cohort study.[2,9,22]

### Screening strategies and parameters

The current CRC screening guidelines and programmes in China are briefly introduced in Supplementary material p 5. Based on this, we evaluated four CRC screening strategies (Fig. 1 and Supplementary material pp. 6–7). The strategies included: (1) no screening; (2) colonoscopy screening (colonoscopy every 10 years between ages 45–74 years); (3) biennial FIT-based screening (FIT every two years between ages 45–74 years for all eligible participants, following by colonoscopy if the result is positive); and (4) roll-out FIT-based screening (FIT every two years between ages 45–74 years, with gradually increasing coverage from the oldest to youngest age groups between 45 and 74 years; additionally, the screening interval is extended to three years when five consecutive screening rounds are negative). The surveillance principle of colonoscopy was based on the guidelines from the US Multi-Society Task Force on Colorectal Cancer.[13] Screening parameters, including compliance rates, sensitivity, specificity, and costs, were derived from the published literature and expert opinions (Supplementary material pp. 7–8).[6,19,20,22]

### Single and multiple cohort analyses

Outcomes were evaluated using two approaches (Fig. 1): single-cohort analysis, which provides lifetime outcomes for a single birth cohort, and multiple-cohort analysis, which provides cross-sectional outcomes over time. The single-cohort analysis assessed the effect of the implemented CRC screening programme by comparing the lifetime outcomes of a single birth cohort of both sexes eligible to participate in CRC screening from the age of 45 years in 2020 with a birth cohort of 100,000 population that had never been screened (no screening strategy). This approach simulated the natural history of CRC in a cohort of individuals over their remaining lifetimes and compared the health and economic outcomes under different screening strategies. The study quantified the impact of different screening

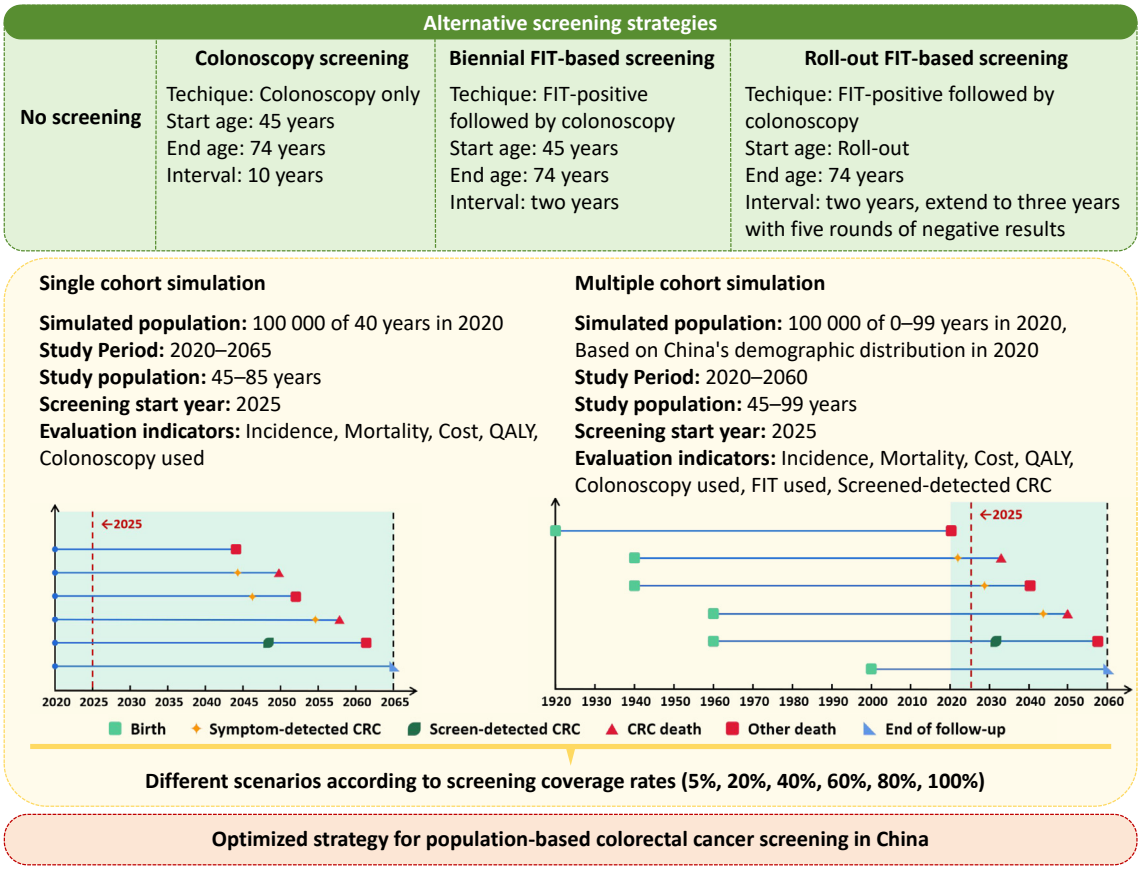


***Fig. 1:*** The alternative screening strategies and flowchart of the study. Abbreviations: FIT = faecal immunochemical testing; QALY = quality-adjusted life-year; CRC = colorectal cancer.

strategies on CRC incidence, mortality, quality-adjusted life-years (QALYs), costs, and resource utilisation in a single cohort. It provides insights into the lifetime benefits, costs, and resource implications of implementing various screening strategies at different screening invitation rates (5% [status quo],[23] 20%, 40%, 60%, 80%, and 100%).

The multiple-cohort analysis adopted a cross-sectional approach to estimate the aggregate year-by-year health outcomes, costs, and resource utilisation for the entire Chinese population eligible for CRC screening from 2025 to 2060. The cohorts were constructed to reflect the age and sex distributions of the Chinese population in 2020. This analysis simulated the natural history of CRC in multiple cohorts of 100,000 population, each associated with a different screening invitation rate (5% [status quo], 20%, 40%, 60%, 80%, or 100%). This approach allows for a comprehensive evaluation of the population-level impact of implementing nationwide screening programmes, accounting for dynamic changes in the population structure over time. By projecting cross-sectional outcomes, multiple-cohort analysis provides insights into long-term trends in CRC incidence, mortality, costs, and resource requirements associated with different screening strategies and coverage levels. The primary outcomes were CRC incidence, CRC-related mortality, cost, and QALYs of the different screening strategies compared with no screening. The number needed to screen (NNS) to prevent one CRC case was calculated by dividing the total number of FIT or colonoscopies used by the total number of CRC cases prevented during the study period. Period analysis was conducted to evaluate the aggregate year-by-year health outcomes, costs, and resource utilisation for the entire population eligible for CRC screening. In this analysis, study period is divided into three distinct periods: 2020–2030, 2020–2045, and 2020–2060. By segmenting the study period, we can observe the short-term, mid-term, and long-term impacts of different CRC screening strategies. We also calculated the incremental cost-effectiveness ratios (ICERs) by dividing the incremental costs by the incremental QALYs gained for each strategy and discounting them at a rate of 5% from 2020. We defined strategies with an ICER of 0.5 to 2 times China's gross domestic product per capita (CNY 35,446 and 141,784) per QALY gained as strongly and weakly cost-effective,

respectively. The median of the results of 1000 iterations of the best parameter set was used to represent the point estimates, and 95% uncertainty intervals (UI) were used to quantify the uncertainty.

### Nationwide benefit and budget analysis

A multiple-cohort analysis was performed to estimate the aggregate annual health outcomes, costs, and resource utilisation for the entire Chinese population eligible for CRC screening from 2020 to 2060 under an invitation rate of 100%. In this analysis, 100,000 individuals born from 1921 to 2020 (aged 0–99 in 2020 at the start of screening) based on China's demographic distribution were simulated. The cohorts were constructed to reflect the age and sex distributions of the Chinese population in 2020 based on census data. The population aged 40 and above was 591,387,828 in 2020. Based on model simulations of the population, we used a population adjusted index of 5917 to convert the model output into nationwide projection. For each screening strategy, the model projected the cumulative number of incident CRC cases, CRC deaths, screening-detected CRC cases, colonoscopies performed, FITs conducted, discounted total costs, and discounted total QALYs gained over a 40-year period. Costs were estimated from a health service perspective and discounted at 5% annually. The NNS for detect one CRC case was calculated.

### Sensitivity analyses

Univariate (one-way) and multivariate deterministic sensitivity analyses were conducted to assess the sensitivity of the results to changes in model input parameters, including utility, screening costs, diagnostic costs, discount rates, screening completion rates, screening sensitivity, and specificity. Additionally, we performed probabilistic sensitivity analyses under 1000 varied parameters sets to address joint uncertainties in the input parameter values. To generate the cost-effectiveness acceptability curve, a range of willingness-to-pay (WTP) thresholds was set (from 0 to 200,000 CNY per QALY, in increments of 1000 CNY). For each WTP threshold, the proportion of simulations where the intervention was cost-effective was calculated.

### Role of the funding source

The funding agency of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the manuscript.

## Results

### Single cohort analysis

In the single cohort analysis from 2020 to 2065, all screening strategies substantially reduced CRC incidence and mortality compared with no screening, and the colonoscopy screening strategy performed better than the biennial FIT-based screening and roll-out FIT-based screening under the same invitation rate scenario (Table 1). When assuming a 100% invitation rate, the colonoscopy strategy led to a 55.77% (95% UI 53.84–57.59%) reduction in CRC incidence and a 63.22% (95% UI 59.21–67.44%) reduction in CRC mortality compared with no screening. The biennial FIT-based screening and roll-out FIT-based screening strategies led to a 22.44% (95% UI 19.72–25.08) and 20.15% (95% UI 17.16–22.97) reduction in CRC incidence and a 41.03% (95% UI 34.99–46.73) and 37.66% (95% UI 31.28–43.62) reduction in CRC mortality, respectively, compared to no screening. However, screening strategies also led to significantly higher costs compared to no screening, with colonoscopy screening resulting in a 49.25% (95% UI 45.21–53.59) increase in discounted costs per person. When the same screening strategy was applied, scenarios assuming higher screening invitation rates were associated with lower CRC incidence and mortality, higher discounted costs, discounted QALY, and total number of colonoscopies used. When the screening invitation rate was the same, the effectiveness of colonoscopy screening, biennial FIT-based screening, and roll-out FIT-based screening decreased sequentially, whereas cost and colonoscopy use also decreased dramatically. For instance, when assuming a 100% invitation rate, the biennial FIT-based screening strategy resulted in a 0.10% decrease in QALY saved, but a 20.39% decrease in cost, and a 84.68% decrease in colonoscopy use compared to colonoscopy screening. Accordingly, when compared to roll-out FIT-based screening, it led to a 0.03% increase in QALY saved, but a 8.96% increase in cost, and a 19.09% increase in colonoscopy use.

Notably, when the colonoscopy screening invitation rate was set at 5% (assumed to be the status quo), the biennial FIT-based screening strategy would need to achieve an invitation rate of approximately 20%, and the roll-out FIT-based screening strategy would need to reach an invitation rate of more than 20% to attain comparable reductions in CRC incidence (Table 1). Under this assumption, biennial and roll-out FIT-based screening still cost slightly less than colonoscopy screening, and the number of colonoscopies used is only 43% and 34% of those for colonoscopy screening, respectively. In terms of mortality, biennial FIT-based screening and roll-out FIT-based screening only need to achieve an invitation rate of 10% and 15%, respectively, to achieve the same level of mortality reduction as colonoscopy screening and consume less cost and colonoscopy resources.

### Multiple cohort analysis

Table 2 shows the cost-effectiveness analyses of different screening strategies in multiple cohort analysis for 100,000 participants over the period 2020–2060. Over the study period (2020–2060) in the multiple cohort analysis, all screening strategies were more cost-effective than no screening, with an indicative threshold

| Strategy[a] | Colorectal cancer incidence rate per 100,000 individuals | | Colorectal cancer mortality rate per 100,000 individuals | | Discounted cost per person[b] | | Discounted QALY per person[b] | | Total number of colonoscopy used |
|---|---|---|---|---|---|---|---|---|---|
| | Base case (95% UI) | % reduction (95% UI) | Base case (95% UI) | % reduction (95% UI) | Base case (95% UI) | % increase (95% UI) | Base case (95% UI) | % increase (95% UI) | Base case (95% UI) |
| No screening | 4498 (4394–4608) | – | 798 (753–849) | – | 799 (778–819) | – | 14.579 (14.566–14.594) | – | – |
| Colonoscopy screening strategy | | | | | | | | | |
| Scenario 1 (5%) | 4158 (4064–4257) | 7.55% (4.39–10.62) | 730 (685–774) | 8.58% (0.77–16.23) | 831 (812–849) | 4.00% (0.51–7.73) | 14.584 (14.568–14.597) | 0.03% (−0.11 to 0.16) | 17,281 (17,072–17,482) |
| Scenario 2 (20%) | 3404 (3315–3499) | 24.28% (21.42–26.94) | 577 (539–617) | 27.65% (20.64–33.98) | 918 (900–936) | 14.92% (11.15–18.87) | 14.593 (14.578–14.607) | 0.10% (−0.05 to 0.23) | 58,111 (57,798–58,420) |
| Scenario 3 (40%) | 2789 (2703–2871) | 37.99% (35.60–40.31) | 455 (419–489) | 43.26% (37.32–48.63) | 1011 (994–1026) | 26.61% (22.76–30.54) | 14.602 (14.587–14.615) | 0.15% (0.02–0.28) | 95,672 (95,340–96,005) |
| Scenario 4 (60%) | 2404 (2325–2480) | 46.55% (44.47–48.68) | 377 (347–408) | 52.87% (47.97–57.41) | 1083 (1069–1099) | 35.78% (31.8–39.86) | 14.607 (14.592–14.621) | 0.19% (0.04–0.33) | 121,976 (121,644–122,310) |
| Scenario 5 (80%) | 2163 (2088–2231) | 51.93% (49.96–53.88) | 328 (299–360) | 58.88% (54.18–63.12) | 1145 (1129–1159) | 43.37% (39.42–47.54) | 14.611 (14.596–14.625) | 0.22% (0.07–0.35) | 141,298 (140,976–141,580) |
| Scenario 6 (100%) | 1988 (1922–2063) | 55.77% (53.84–57.59) | 293 (265–321) | 63.22% (59.21–67.44) | 1192 (1178–1206) | 49.25% (45.21–53.59) | 14.614 (14.598–14.628) | 0.24% (0.09–0.38) | 155,704 (155,380–156,023) |
| Biennial FIT-based screening strategy | | | | | | | | | |
| Scenario 1 (5%) | 4396 (4295–4498) | 2.20% (−0.77 to 5.46) | 765 (721–808) | 4.07% (−4.05 to 12.16) | 806 (787–825) | 0.94% (−2.53 to 4.61) | 14.581 (14.567–14.596) | 0.02% (−0.13 to 0.16) | 2096 (2023–2173) |
| Scenario 2 (20%) | 4156 (4052–4258) | 7.62% (4.41–10.68) | 689 (645–729) | 14.01% (6.06–21.15) | 832 (814–851) | 4.21% (0.89–8.10) | 14.586 (14.572–14.6) | 0.05% (−0.10 to 0.18) | 7487 (7342–7637) |
| Scenario 3 (40%) | 3914 (3825–4012) | 12.95% (10.01–15.91) | 610 (570–649) | 23.46% (16.51–30.35) | 865 (849–882) | 8.48% (4.90–11.98) | 14.59 (14.576–14.605) | 0.07% (−0.06 to 0.21) | 13,102 (12,914–13,293) |
| Scenario 4 (60%) | 3736 (3640–3830) | 16.88% (14.08–19.82) | 552 (512–590) | 31.14% (24.03–37.19) | 897 (879–911) | 12.29% (8.76–15.67) | 14.594 (14.579–14.608) | 0.10% (−0.05 to 0.23) | 17,484 (17,280–17,714) |
| Scenario 5 (80%) | 3600 (3500–3692) | 20.03% (17.00–22.94) | 507 (472–544) | 36.29% (30.48–42.32) | 924 (907–940) | 15.70% (12.02–19.54) | 14.596 (14.582–14.611) | 0.12% (−0.03 to 0.26) | 20,987 (20,750–21,208) |
| Scenario 6 (100%) | 3490 (3395–3580) | 22.44% (19.72–25.08) | 471 (436–507) | 41.03% (34.99–46.73) | 949 (933–964) | 18.84% (15.34–22.73) | 14.599 (14.585–14.612) | 0.13% (−0.01 to 0.26) | 23,856 (23,618–24,099) |
| Roll-out FIT-based screening strategy | | | | | | | | | |
| Scenario 1 (5%) | 4414 (4316–4512) | 1.95% (−1.39 to 4.91) | 772 (730–820) | 3.10% (−5.17 to 11.31) | 798 (780–818) | −0.10% (−3.18 to 3.73) | 14.582 (14.568–14.596) | 0.02% (−0.12 to 0.16) | 1597 (1539–1658) |
| Scenario 2 (20%) | 4213 (4110–4308) | 6.34% (3.27–9.40) | 701 (660–747) | 12.23% (4.44–19.38) | 805 (786–823) | 0.86% (−2.25 to 4.28) | 14.584 (14.571–14.6) | 0.03% (−0.10 to 0.18) | 5809 (5686–5925) |
| Scenario 3 (40%) | 3999 (3905–4097) | 11.16% (7.90–13.94) | 632 (590–673) | 20.81% (13.60–27.73) | 818 (800–836) | 2.46% (−0.90 to 6.03) | 14.588 (14.574–14.603) | 0.07% (−0.08 to 0.21) | 10,390 (10,208–10,548) |
| Scenario 4 (60%) | 3834 (3739–3933) | 14.72% (11.83–17.61) | 578 (538–617) | 27.45% (20.77–34.14) | 834 (816–852) | 4.47% (1.12–8.06) | 14.591 (14.577–14.605) | 0.08% (−0.05 to 0.21) | 14,121 (13,934–14,320) |
| Scenario 5 (80%) | 3704 (3612–3801) | 17.64% (14.70–20.47) | 534 (499–573) | 33.13% (26.98–38.88) | 852 (836–869) | 6.77% (3.40–10.25) | 14.594 (14.578–14.606) | 0.10% (−0.05 to 0.23) | 17,288 (17,080–17,500) |
| Scenario 6 (100%) | 3589 (3501–3691) | 20.15% (17.16–22.97) | 499 (460–537) | 37.66% (31.28–43.62) | 871 (856–888) | 9.19% (5.82–12.74) | 14.595 (14.58–14.61) | 0.10% (−0.04 to 0.24) | 20,032 (19,811–20,248) |

CNY = Chinese Yuan. [a]Scenario 1 represents the screening is conducted assuming screening invitation rate of 5%; Scenario 2 represents the screening is conducted assuming screening invitation rate of 20%; Scenario 3 represents the screening is conducted assuming screening invitation rate of 40%; Scenario 4 represents the screening is conducted assuming screening invitation rate of 60%; Scenario 5 represents the screening is conducted assuming screening invitation rate of 80%; Scenario 6 represents the screening is conducted assuming screening invitation rate of 100%. [b]Discounted at 5% per year since 2020.

***Table 1:*** **Single cohort analysis findings of health outcomes, cost and health resources used over the study period.**

| Screening strategy[a] | Discounted cost per person (CNY, 95% UI)[b] | Discounted QALY per person (95% UI)[b] | Incremental cost per person (CNY, 95% UI) | Incremental QALY per person (95% UI) | ICER (median, CNY/QALY) |
|---|---|---|---|---|---|
| No screening | 555 (539–574) | 8.181 (8.170–8.192) | Ref | Ref | Ref |
| Colonoscopy screening strategy | | | | | |
| Scenario 1 (5%) | 577 (560–593) | 8.183 (8.173–8.194) | 21 (−3 to 44) | 0.002 (−0.013 to 0.018) | 9173 |
| Scenario 2 (20%) | 629 (614–645) | 8.190 (8.180–8.202) | 74 (50–97) | 0.009 (−0.006 to 0.024) | 8070 |
| Scenario 3 (40%) | 684 (670–699) | 8.196 (8.186–8.207) | 128 (105–151) | 0.015 (0.000–0.030) | 8385 |
| Scenario 4 (60%) | 727 (713–741) | 8.200 (8.190–8.211) | 171 (149–193) | 0.020 (0.004–0.034) | 8860 |
| Scenario 5 (80%) | 761 (749–774) | 8.203 (8.192–8.214) | 206 (183–227) | 0.023 (0.007–0.037) | 9232 |
| Scenario 6 (100%) | 790 (777–803) | 8.206 (8.195–8.217) | 234 (213–255) | 0.025 (0.010–0.041) | 9449 |
| Biennial FIT-based screening strategy | | | | | |
| Scenario 1 (5%) | 558 (540–573) | 8.182 (8.172–8.193) | 2 (−23 to 24) | 0.001 (−0.014 to 0.017) | 1617 |
| Scenario 2 (20%) | 563 (548–579) | 8.185 (8.174–8.196) | 7 (−16 to 29) | 0.004 (−0.011 to 0.019) | 1733 |
| Scenario 3 (40%) | 574 (558–587) | 8.189 (8.177–8.200) | 18 (−6 to 40) | 0.008 (−0.009 to 0.023) | 2363 |
| Scenario 4 (60%) | 584 (571–600) | 8.191 (8.180–8.202) | 29 (6–49) | 0.010 (−0.005 to 0.026) | 2746 |
| Scenario 5 (80%) | 596 (583–609) | 8.193 (8.181–8.203) | 40 (18–60) | 0.012 (−0.004 to 0.027) | 3466 |
| Scenario 6 (100%) | 607 (593–620) | 8.194 (8.183–8.205) | 52 (29–71) | 0.013 (−0.002 to 0.029) | 3912 |
| Roll-out FIT-based screening strategy | | | | | |
| Scenario 1 (5%) | 554 (537–569) | 8.182 (8.171–8.193) | −2 (−25 to 21) | 0.001 (−0.015 to 0.016) | dominate |
| Scenario 2 (20%) | 550 (534–567) | 8.185 (8.175–8.196) | −5 (−28 to 16) | 0.004 (−0.011 to 0.019) | dominate |
| Scenario 3 (40%) | 552 (537–566) | 8.187 (8.176–8.198) | −4 (−26 to 18) | 0.006 (−0.009 to 0.021) | dominate |
| Scenario 4 (60%) | 557 (544–571) | 8.189 (8.178–8.200) | 1 (−20 to 23) | 0.009 (−0.007 to 0.023) | 200 |
| Scenario 5 (80%) | 564 (551–578) | 8.191 (8.180–8.201) | 8 (−13 to 28) | 0.010 (−0.005 to 0.026) | 848 |
| Scenario 6 (100%) | 573 (559–586) | 8.193 (8.182–8.203) | 17 (−5 to 36) | 0.012 (−0.003 to 0.028) | 1508 |

CNY = Chinese Yuan. QALY = quality adjusted life year. ICER = incremental cost-effectiveness ratio. [a]Scenario 1 represents the screening is conducted assuming screening invitation rate of 5%; Scenario 2 represents the screening is conducted assuming screening invitation rate of 20%; Scenario 3 represents the screening is conducted assuming screening invitation rate of 40%; Scenario 4 represents the screening is conducted assuming screening invitation rate of 60%; Scenario 5 represents the screening is conducted assuming screening invitation rate of 80%; Scenario 6 represents the screening is conducted assuming screening invitation rate of 100%. [b]Discounted at 5% per year since 2020.

*Table 2:* **Cost-effectiveness analyses of different screening strategies in multiple cohort analysis for 100,000 participants over the period 2020–2060.**

of CNY 141,784 per QALY saved. For instance, colonoscopy screening at a 100% invitation rate with the highest discounted QALY per person of 8.206 (8.195–8.217) gained an ICER of 9449 CNY/QALY compared to no screening. Most biennial and roll-out FIT-based screening strategies were dominant (more effective and less costly) compared to no screening. Colonoscopy screening was the most cost-effective strategy when screening invitation rates were the same. Assuming a 100% invitation rate, colonoscopy screening gained an ICER of 15,250, and 16,692 CNY/QALY compared with biennial and roll-out FIT-based screening, respectively. Compared to colonoscopy screening with a 5% invitation rate, biennial and roll-out FIT-based screening strategies require a 20% invitation rate to be dominant.

## Period analysis

Figs. 2 and 3 depicts the year- and period-specific health outcomes, costs, and resource use of the selected screening strategies for 100,000 simulated individuals from 2020 to 2060. Under the no-screening assumption, approximately 4287 incident CRC cases and 750 CRC deaths are predicted in 2060. A lower number of incident CRC cases and CRC-related deaths over time was predicted for the screening scenarios. For colonoscopy screening at 5%, 40% and 100% screening coverage rate, the starting year of incidence lower than no screening would be 2033, 2032, and 2032, respectively. For biennial FIT-based screening at 5%, 40% and 100% screening coverage rate, the starting year of incidence lower than no screening would be 2037, 2038, and 2037, respectively. For the roll-out FIT-based screening at 5%, 40% and 100% screening coverage rate, the starting year of incidence lower than no screening would be 2043, 2042, and 2041 (Fig. 2a). Over the period from 2020 to 2030 (Fig. 3), colonoscopy screening, biennial FIT-based screening, and roll-out FIT-based screening, with a 100% screening invitation rate, were predicted to detect an additional 5, 14, and 8 CRC cases and prevent 0, 0, and 1 CRC-related deaths per 100,000 population, compared with no screening. An additional 1628, 594, and 550 CRC and 335, 261, and 248 CRC-related deaths, respectively, were predicted to be prevented per 100,000 population by the end of the study period. With the continuous implementation of screening, the reduction in mortality is greater. However, the incidence benefits lagged and became more

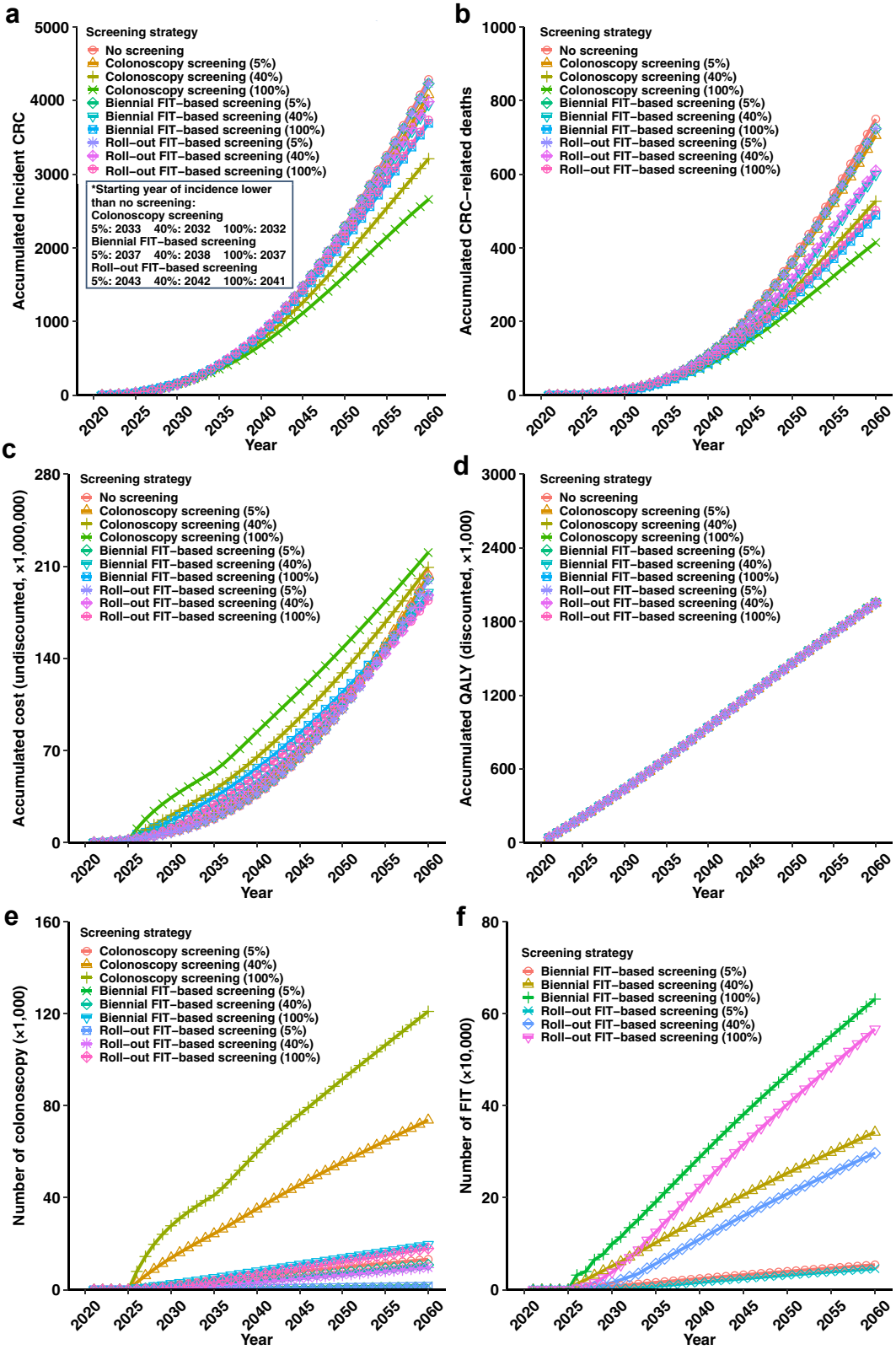


*Fig. 2:* Predicted year-specific health outcomes, costs, and health resource use in multiple cohort analysis over the period 2020–2060 among alternative screening strategies. (a) Accumulated incident CRC; (b) Accumulated CRC-related deaths; (c) Accumulated cost; (d) Accumulated QALY; (e) Number of colonoscopy used; (f) Number of FIT used. Abbreviations: CRC = colorectal cancer; QALY = quality-adjusted life-year; FIT = faecal immunochemical testing.

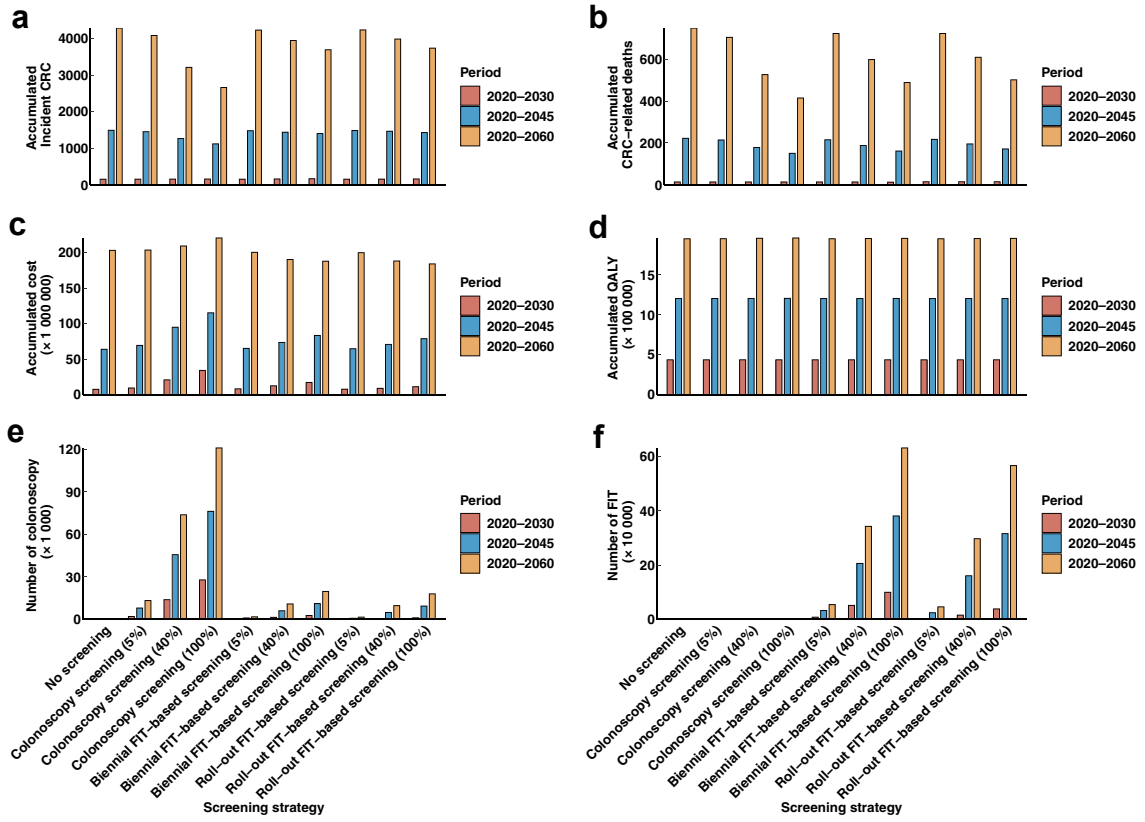


*Fig. 3:* Predicted health outcomes, costs, and health resource use in multiple cohort analysis over the periods 2020–2030, 2020–2045, and 2025–2060 among alternative screening strategies. (a) Accumulated incident CRC; (b) Accumulated CRC-related deaths; (c) Accumulated cost; (d) Accumulated QALY; (e) Number of colonoscopy used; (f) Number of FIT used. Abbreviations: CRC = colorectal cancer; QALY = quality-adjusted life-year; FIT = faecal immunochemical testing.

apparent over the longer term. For example, assuming a 100% invitation rate, colonoscopy screening detected five additional CRC cases per 100,000 population between 2020 and 2030, while 1628 incidents were prevented by 2060.

Cumulative costs and resource requirements also increased significantly over time (Figs. 2 and 3). By 2060, colonoscopy screening would utilise over 120,000 colonoscopies per 100,000 population, whereas biennial FIT-based screening would require nearly 20,000 colonoscopies and 631,000 FIT tests. The roll-out FIT-based screening strategy had a similar but lower resource profile, with approximately 18,000 colonoscopies and 570,000 FITs per 100,000 population. As noted earlier, biennial and roll-out FIT-based screening with 20% invitation rates are close to the effectiveness of colonoscopy screening at a 5% invitation rate and are effective in reducing costs and colonoscopy use during 2020–2060. Interestingly, biennial FIT-based screening will still cost more than colonoscopy screening between 2020 and 2045, but less than colonoscopy screening after that. In contrast, the cost of roll-out FIT-based screening is lower than that of colonoscopy screening in 2020–2030 and remains the lowest (Supplementary material pp. 17–20). In terms of colonoscopy use, biennial FIT-based screening and roll-out FIT-based screening only use 10% and 4% of the colonoscopies, respectively, compared to colonoscopy screening in 2020–2030. This figure increases to 16% and 12% in the period 2020–2045 and continues to grow to 16% and 15% in the period 2020–2060, respectively, indicating more significant resource savings in the early period of screening.

### Nationwide benefit and budget analysis

With nationwide screening among populations above 45 years of age with a 100% invitation rate (Table 3), all screening strategies led to substantial reductions in incident CRC cases and deaths. With no screening, there will be 25.4 million CRCs and 4.4 million CRC-related deaths in the Chinese population over 40 years of age from 2020 to 2060, resulting in CNY 324,081 million costs. The colonoscopy screening strategy averted approximately 9.7 million incident CRC cases and 1.9 million CRC deaths, while the biennial FIT-based screening strategy prevented 3.5 million incident cases and 1.5 million deaths compared to no screening.

| Screening strategy[a] | Incident CRC (×100,000) | CRC death (×100,000) | Screen-detected CRC (×100,000) | Colonoscopy used (×100,000) | FIT used (×100,000) | NNS | Discounted total cost (CNY × 1,000,000)[b] | Discounted total QALY (×1,000,000)[b] |
|---|---|---|---|---|---|---|---|---|
| No screening | 254 | 44 | – | – | – | – | 324,081 | 4802 |
| Colonoscopy screening strategy | | | | | | | | |
| Scenario 1 (5%) | 242 | 42 | 3 | 781 | – | 260 | 335,908 | 4803 |
| Scenario 2 (20%) | 214 | 36 | 9 | 2639 | – | 293 | 367,843 | 4805 |
| Scenario 3 (40%) | 190 | 31 | 13 | 4364 | – | 336 | 399,778 | 4807 |
| Scenario 4 (60%) | 175 | 28 | 16 | 5572 | – | 348 | 425,208 | 4808 |
| Scenario 5 (80%) | 165 | 26 | 18 | 6465 | – | 359 | 445,906 | 4809 |
| Scenario 6 (100%) | 157 | 25 | 19 | 7156 | – | 377 | 462,465 | 4810 |
| Biennial FIT-based screening strategy | | | | | | | | |
| Scenario 1 (5%) | 250 | 43 | 4 | 103 | 3200 | 26 | 324,081 | 4804 |
| Scenario 2 (20%) | 242 | 39 | 15 | 367 | 11,441 | 24 | 327,629 | 4808 |
| Scenario 3 (40%) | 233 | 35 | 26 | 641 | 20,260 | 25 | 333,543 | 4811 |
| Scenario 4 (60%) | 227 | 33 | 34 | 854 | 27,160 | 25 | 340,639 | 4814 |
| Scenario 5 (80%) | 223 | 31 | 40 | 1024 | 32,744 | 26 | 347,736 | 4815 |
| Scenario 6 (100%) | 219 | 29 | 45 | 1163 | 37,357 | 26 | 354,241 | 4817 |
| Roll-out FIT-based screening strategy | | | | | | | | |
| Scenario 1 (5%) | 251 | 43 | 4 | 90 | 2717 | 23 | 321,715 | 4803 |
| Scenario 2 (20%) | 243 | 39 | 15 | 323 | 9857 | 22 | 320,532 | 4804 |
| Scenario 3 (40%) | 236 | 36 | 25 | 570 | 17,572 | 23 | 321,124 | 4806 |
| Scenario 4 (60%) | 230 | 33 | 33 | 766 | 23,829 | 23 | 324,672 | 4807 |
| Scenario 5 (80%) | 225 | 31 | 39 | 927 | 29,050 | 24 | 328,812 | 4808 |
| Scenario 6 (100%) | 221 | 30 | 44 | 1062 | 33,508 | 24 | 334,134 | 4809 |

CRC = colorectal cancer. FIT = faecal immunochemical test. NNS = Colonoscopy number needed to scope one screen-detected CRC. CNY = Chinese Yuan. QALY = quality adjusted life year. [a]Scenario 1 represents the screening is conducted assuming screening invitation rate of 5%; Scenario 2 represents the screening is conducted assuming screening invitation rate of 20%; Scenario 3 represents the screening is conducted assuming screening invitation rate of 40%; Scenario 4 represents the screening is conducted assuming screening invitation rate of 60%; Scenario 5 represents the screening is conducted assuming screening invitation rate of 80%; Scenario 6 represents the screening is conducted assuming screening invitation rate of 100%. [b]Discounted at 5% per year since 2020.

*Table 3:* **Predicted overall health outcomes, costs, and health resource use in China over the period 2020–2060.**

The roll-out FIT-based screening strategy showed similar benefits, averting 3.3 million incident cases and 1.4 million deaths. However, the enhanced effectiveness of screening has increased costs and resource utilisation. Adopting the colonoscopy screening strategy at 100% participation would require over 0.7 billion colonoscopies and lead to a total discounted cost of 462 billion CNY over 40 years. In contrast, the biennial FIT-based screening strategy only requires approximately 0.1 billion colonoscopies and 3.7 billion FIT tests, with a total cost of 354 billion CNY. The roll-out FIT-based screening strategy has a comparable resource profile, requiring 0.1 million colonoscopies, 3.3 billion FITs, and a cost of 334 billion CNY. Notably, the NNS to prevent one CRC case ranged from 377 for colonoscopy screening to 26 for biennial FIT-based screening and 24 for roll-out FIT-based screening, highlighting the potential efficiency gains from combining FIT and colonoscopy.

### Sensitivity analysis

In the sensitivity analysis, one-way analyses revealed that the ICERs of the screening strategies were sensitive to changes in the cost of FIT, utility of CRC patients diagnosed of TNM stage I, sensitivity of FIT, and transition rates of different disease states (Supplementary material pp. 10–15). The rankings of the strategies were relatively robust to variations in the parameters. Probabilistic sensitivity analyses and cost-effectiveness acceptability curve showed that colonoscopy screening had the highest probability of being cost-effective under the WTP of 141,784 CNY/QALY (Supplementary material pp. 16–17).

## Discussion

In this modelling study, we evaluated the long-term health outcomes, costs, and cost-effectiveness of implementing various CRC screening strategies in China over the next 40 years. Our findings suggest that all screening strategies were cost-effective compared to no screening, and screening strategies with higher invitation rates can substantially reduce CRC incidence and mortality. Direct colonoscopy screening is the most cost-effective strategy but requires significant colonoscopy resources. Screening with FIT combined with colonoscopy saves significant resources, although it is slightly less effective. The expenditures of roll-out FIT-based screening are predicted to be substantially lower

than those of colonoscopy screening and biennial FIT-based screening, due to savings in cancer treatment costs and reasonable allocation of upfront screening costs. Overall, these findings underscore the substantial upfront investments required for nationwide screening implementation in China as well as the potential long-term health benefits and cost-effectiveness of roll-out FIT-based screening strategies.

The updated MIMIC-CRC micro-simulation model offers a robust platform for evaluating CRC screening and prevention strategies tailored to the Chinese population.[11] The natural history parameters of the model were synthesised from high-quality contemporary data sources, including large, pooled analyses and meta-analyses of studies conducted in China, whenever possible. Extensive calibration and validation against nationwide cancer registry data and the prospective CKB cohort study further ensured that the model accurately captured the unique epidemiology and natural history of CRC in Chinese individuals. A reliable modelling framework allows for comprehensive projections of the long-term comparative effectiveness, costs, and resource utilisation implications of different screening strategies. Current guidelines worldwide generally recommend CRC screening with stool-based tests, such as FIT, or colonoscopy. Many countries have implemented organised population-based screening programmes applying these evidence-based modalities.[24] In China, the guidelines recommend CRC screening with colonoscopy every 5–10 years or FIT every year (Supplementary material p 5). However, considering the potentially huge cost and resource burden for China, this analysis focused on evaluating colonoscopy screening every 10 years and a biennial FIT screening strategy, aiming to balance effectiveness with programmatic resource utilisation in the Chinese context. Recent studies have evaluated the cost-effectiveness of CRC screening in various regions of China using different modelling approaches. These studies consistently show that CRC screening reduces incidence and mortality and can be cost-effective, particularly with strategies like FIT.[25–27] Ren et al. evaluates the cost-effectiveness of CRC screening in China using a 13-state Markov model to compare annual and biennial FIT and electronic colonoscopy every 5 or 10 years. The results indicate that both FIT and colonoscopy are cost-effective, with FIT being cost-saving. In addition, Wang et al. evaluated the cost-effectiveness of CRC screening in Shanghai using the MISCAN-Colon microsimulation model. All screening strategies (including current Shanghai FIT, Shanghai FIT plus risk assessment, and a validated FIT) reduced CRC incidence and mortality, with the validated FIT being the most cost-effective. However, these studies have limitations, including their focus on specific regions that may not represent the national population, lack of China-specific data, and insufficient research on the impact of varying screening coverage rates. Despite these limitations, the findings provide valuable insights for developing CRC screening strategies in China.

The findings from this modelling study are mainly consistent with previous modelling analyses from other countries.[28] For example, modelling studies from the United States have shown that most common screening strategies are cost effective (and even cost saving) compared to no screening. In addition, colonoscopy screening strategies were more effective but less costly compared to FIT-based screening, with more inefficient use of colonoscopy resources.[14] A strength of this analysis was the construction of multiple birth cohorts reflecting sex and age structure in the Chinese population. This enabled comprehensive projections of not only screening effectiveness, but also the associated resource utilisation and costs required for nationwide implementation. These results suggest that while a colonoscopy screening strategy could achieve the greatest reduction in CRC incidence and mortality, it would necessitate immense investment in colonoscopy resources and costs. Conversely, a stepwise roll-out approach initiating biennial FIT screening among older age groups and gradually extending to younger cohorts after negative rounds could provide a resource-efficient alternative that is better aligned with China's diverse regional contexts. However, further research is warranted to optimise specific roll-out parameters such as age ranges and interval extension criteria to maximise the effectiveness of this approach while minimising upfront resource investments. Modelling analyses from Australia[29] and Germany[30] and have highlighted the favourable performance of FIT-based screening in nationwide implementation programmes when factoring in constraints on colonoscopy capacity and overall programmatic costs. An optimised nationwide CRC screening programme will be highly cost-effective, and there will be reduced annual health system expenditure on CRC control.

As innovations in CRC screening emerge, their integration into population-based screening programmes must be explored. Blood-based biomarker tests and stool DNA assays have shown promise in increasing screening participation rates and sensitivity for precancerous lesions. Recent modelling studies have evaluated how multi-target blood tests could impact screening effectiveness and cost-effectiveness.[31–33] Most studies have shown that new blood-based testing is not cost-effective compared to FIT; however, for those who refuse to participate in FIT testing, expanding the screening population using a blood-based screening method may improve the overall screening effectiveness. For instance, even with higher screening uptake, triennial blood-based screening, with a sensitivity of 74% and specificity of 90%, was not projected to be cost-effective compared with established strategies for CRC screening.[31] To further improve the cost-effectiveness of

blood-based testing, the diagnosis efficacy of the test for precancerous lesions needs to be further improved and the costs reduced. Modelling studies have been used to evaluate the cost-effectiveness of artificial intelligence-assisted and computer-assisted detection CRC screening techniques.[34,35] These new cross-disciplinary technologies currently have insufficient evidence for population-based applications.

This study has several limitations. First, although the micro-simulation model was calibrated and validated using the best available data, some parameter estimates, particularly those related to the natural history of CRC and region-dependent parameters, may have been subject to uncertainty. Second, the model did not account for potential changes in screening modalities, costs, or adherence rates over time, which may influence the long-term cost-effectiveness of the evaluated strategies. Third, the analysis focused solely on the health system perspective and did not consider the broader societal costs or productivity losses associated with CRC. Fourth, cost of polyp surveillance colonoscopies following the diagnosis of adenoma were not included in this study. Surveillance colonoscopies are an essential part of post-screening management to monitor and prevent the progression of pre-malignant lesions to CRC. This omission may lead to an underestimation of the total costs associated with the different screening strategies. Future research should incorporate these surveillance costs to provide a more comprehensive evaluation of the long-term economic impact of CRC screening. Fifth, although we evaluated various screening strategies under different screening coverage scenarios, the costs of increasing the screening invitation rate were not included, which may have affected the interpretation of the results. Sixth, this cost-effectiveness analysis of CRC screening was limited to colonoscopy and FIT-based screening and did not consider emerging screening technologies. Seventh, this study did not account for the potential harms associated with screening, particularly the risk of complications of colonoscopy. Future research should aim to incorporate these risks to provide a more balanced evaluation of the overall impact of CRC screening strategies. Eighth, this study does not account for potential improvements in CRC treatment over time, which could affect both mortality rates and treatment costs as projected by the model. Future studies should consider these dynamic factors to provide a more comprehensive evaluation.

In summary, organised population-based CRC screening has great potential for reducing the overall incidence and mortality. Our comprehensive modelling study indicates that the roll-out FIT-based approach could contribute to the prevention of CRC in China for the next 40 years, and is also cost-effective compared to colonoscopy and biennial FIT screening strategies in terms of QALYs and resource demands. To reduce the burden of CRC in China, the implementation of appropriate nationwide CRC screening strategies and further enhancement of the participation and compliance rates of CRC screening are imperative.

#### Contributors

HDC, MD and BL conceptualized and designed the study. BL led the model development, natural history calibration, and was responsible for the collation and integration of data into the model, performed model analysis. BL, YYK, YHZ, NL, and YYZ participated in the sourcing of model data. BL and JHL participated in model development and natural history calibration. BL and HDC drafted the manuscript. HDC, MD and DW supervised the analysis output. All authors reviewed and edited subsequent drafts. All authors read and approved the final report and made the decision to submit for publication.

#### Data sharing statement

The raw data collected during the descriptions of the model structure, and the parameters included in the model are available in the appendix. The analysis code is available on request to chenhongda@pumch.cn or daimin2002@hotmail.com.

#### Declaration of interests

We declare no competing interests.

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101172.

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