Optimising colorectal cancer screening in Shanghai, China: a modelling study

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ABSTRACT

Introduction To reduce the burden of colorectal cancer (CRC) in Shanghai, China, a CRC screening programme was commenced in 2013 inviting those aged 50–74 years to triennial screening with a faecal immunochemical test (FIT) and risk assessment. However, it is unknown whether this is the optimal screening strategy for this population.

We aimed to determine the optimal CRC screening programme for Shanghai in terms of benefits, burden, harms and cost-effectiveness.

Methods Using Microsimulation Screening Analysis-Colon (MISCAN-Colon), we estimated the costs and effects of the current screening programme compared with a situation without screening. Subsequently, we estimated the benefits (life years gained (LYG), burden (number of screening events, colonoscopies and false-positive tests), harms (number of colonoscopy complications and costs (Rennminbi (¥)) of screening for 324 alternative screening strategies. We compared several different age ranges, screening modalities, intervals and FIT cut-off levels. An incremental cost-effectiveness analysis determined the optimal strategy assuming a willingness-to-pay of ¥193 931 per LYG.

Results Compared with no screening, the current screening programme reduced CRC incidence by 40% (19 cases per 1000 screened individuals) and CRC mortality by 67% (7 deaths). This strategy gained 32 additional life years, increased colonoscopy demand to 1434 per 1000 individuals and cost an additional ¥199 652. The optimal screening strategy was annual testing using a validated one-sample FIT, with a cut-off of 10 μg haemoglobin per gram from ages 45 to 80 years (incremental cost-effectiveness ratio, ¥62 107). This strategy increased LYG by 0.18% and costs by 27%. Several alternative cost-effective strategies using a validated FIT offered comparable benefits to the current programme but lower burden and costs.

Conclusions Although the current screening programme in Shanghai is effective at reducing CRC incidence and mortality, the programme could be optimised using a validated FIT. When implementing CRC screening, jurisdictions with limited health resources should use a validated test.

INTRODUCTION

Colorectal cancer (CRC) is a global health issue with significant incidence and mortality, however, this burden is unevenly distributed. Due to its large population, China is a noteworthy contributor to the global burden of CRC and is expected to account for approximately 28% of CRC cases and deaths in 2018. Moreover, CRC incidence and mortality has been steadily increasing in China: between 2003 and 2011, incidence rose from 12.8 to 16.8 per 100 000, while mortality rose from 5.8 to 7.8. This, coupled with a steadily ageing population suggests the large burden of CRC is set to remain in the foreseeable future and represents a significant public health challenge for the country.

Although screening has long been established as an effective method to reduce CRC incidence and mortality, it has not yet been universally implemented. While a diverse range of CRC screening programmes have been established throughout Europe, North America and Australia, to date, very few countries in Asia have implemented such programmes. In an effort to reduce the
burden of CRC, there is a growing trend for lower incidence countries to implement organised population CRC screening, as is the case in China, where region-specific programmes are currently being implemented. However, despite the rising CRC incidence and mortality, the first consensus on organised CRC screening in China was not available until 2014.

Shanghai, one of the largest and most developed cities in China, experiences some of the highest CRC incidence and mortality in China. CRC incidence rates have increased significantly from 1973 to 2010, with the age-adjusted incidence rates increasing from 13.6 to 28.2 per 100 000 in men and 11.9 to 22.3 per 100 000 in women. To address this, the Shanghai Municipal Government implemented a community-based CRC screening programme in 2013. The programme invited individuals aged 50–74 to participate in CRC screening, offering triennial screening with a locally produced faecal immunochemical test (FIT) and a risk questionnaire. This strategy was decided on after comprehensive evaluation of the capacity of health resources of the region. The initial results of the screening programme in Shanghai and the Pudong New Area (the largest district of Shanghai) have recently been published. These results highlight several challenges for the implemented screening programme, including poor uptake of initial offer of screening, suboptimal attendance at diagnostic colonoscopy and low rates of cancer detection.

Such results call into question whether the implemented CRC screening programme is optimal for the population. Therefore, the aim of this research is to determine the optimal CRC screening programme for Shanghai in terms of benefits, burden, harms and costs. Using microsimulation modelling, we compared and assessed the performance of the current screening strategy against standardised and validated FITs, varying screening interval and screening start-age and stop-age.

METHODS
We used the Microsimulation Screening Analysis-Colon (MISCAN-Colon) model to simulate a cohort of citizens of Shanghai aged 45 years in 2013. We assessed 324 different screening strategies to determine the benefits, burden, harms and costs of screening compared with the same population without screening. Subsequently, we performed an incremental cost-effectiveness analysis to identify strategies that provide good value for money and to determine the optimal strategy from a cost-effectiveness perspective.

MISCAN-Colon
MISCAN-Colon is a well-established microsimulation model for CRC developed at the Department of Public Health, Erasmus University Medical Center. The model has been extensively described previously and is described in the model description (online supplemental file 1).

In brief, the model simulates the life-histories of a large population of individuals from birth to death, first without and then with screening for CRC. As each simulated person ages, one or more adenomas may arise and some can progress in size from small (<5 mm) to medium (6–9 mm) to large (>10 mm). Some adenomas develop into preclinical cancer and subsequently progress through cancer stages I to IV. At any time during the development of the disease, symptoms may present and CRC may be diagnosed. The introduction of screening may alter the simulated life-histories through detection and removal of adenomas or through detection of CRC at an earlier stage with a more favourable survival. By comparing the life-histories of a simulated population being screened to the corresponding life-histories in a simulated population not screened, MISCAN-Colon quantifies the effectiveness and the costs of screening.

MISCAN-Colon was adjusted to match age-specific incidence of CRC in China before the introduction of screening in 2013. Stage distribution, localisation of cancers in the colorectum and 5-year relative survival after clinical diagnosis of a cancer were based on Chinese literature (online supplemental file 2, table 1). Additional assumptions of the MISCAN-Colon model are presented in the Supplementary Methods (online supplemental file 2).

Screening strategies
In this analysis, we assessed four screening modalities: the FIT as currently offered in the Shanghai screening programme (Shanghai FIT), the Shanghai FIT coupled with the risk assessment (Shanghai FIT+RA) and a standardised and validated FIT taking either one-sample (FIT 1) or two-samples (FIT 2, at least one-sample positive). For the validated tests, we considered five different cut-off values—10, 15, 20, 30 and 40 micrograms of haemoglobin per gram faeces (µg Hb/g, table 1).

For each modality and cut-off value, we assessed multiple start ages (45, 50 or 55 years), stop ages (70, 75 or 80 years) and intervals (annual, biennial and triennial). Individuals with a positive screening test were invited to a diagnostic colonoscopy. Surveillance was based on findings at diagnostic colonoscopy in accordance with the European Society of Gastrointestinal Endoscopy Guidelines. We elected to simulated surveillance consistent with these guidelines because there is conflicting advice in China about the post diagnostic colonoscopy pathway (including when to return to screening and the surveillance pathway). and the Asia Pacific Consensus Group did not provide precise guidelines on surveillance intervals, other than to suggest that such intervals should be tailored to the risk level. In a sensitivity analysis, we assessed a surveillance pathway derived from Chinese literature (online supplemental file 2, figure 1).

We assumed 100% adherence to all screening, diagnostic and surveillance tests because this allows for the determination of the optimal benefit of CRC screening.
All strategies were compared with a situation without screening. In total, 324 unique strategies were evaluated. For each strategy, we simulated a population of 10 million 45-year-olds, with life expectancy as observed in China in 2010.26 It was assumed that no screening occurred before or after the screening start and stop ages. Individuals were followed for life, until a maximum age of 100 years, commencing in 2015.

**Test characteristics**

Although the Shanghai screening programme reports that it is using a qualitative FIT with a pre-set cut-off of 100 nanograms of haemoglobin per millilitre of faeces (equivalent to 20 µg Hb/g faeces),7 laboratory tests have shown that the quantity of faeces in samples and diluents of the test were not standardised, with the actual cut-off being lower than the pre-set cut-off.27 Consequently, the characteristics and actual cut-off of the Shanghai FIT remain unknown. Therefore, the test characteristics of the Shanghai FIT and the Shanghai FIT+RA (table 1 and online supplemental file 2, table 2) were fitted to the positivity and detection rates observed in the first three years of screening in Pudong New Area, the largest district of Shanghai (online supplemental file 2, table 3). Data were provided by the Pudong Centre for Disease Control (Pudong CDC).

The test characteristics of the validated FIT 1 and FIT 2 were fitted to the positivity and detection rates of advanced neoplasia observed in the first screening round of two Dutch randomised trials, which used the OC-Sensor micro (Eiken Chemical, Tokyo, Japan, table 1).28-31 To estimate the two-sample FIT test characteristics, we followed the approach described in Goede and colleagues.32 The characteristics differ to those previously presented as the natural history of the MISCAN-Colon model has been updated since this publication.33

In all instances, the sensitivity and specificity of the test characteristics were estimated so that simulated positivity rates and detection rates for (non-)advanced adenomas and cancer matched the observed rates to within 1%. The test characteristics were adjusted to take into account the effect of systematic false-positive and false-negative results.
(individuals who always test positive but do not have adenomas and/or who test negative because of adenomas which do not bleed).34

For colonoscopy, test characteristics were based on a systematic review of polyp miss rates in tandem colonoscopy studies.35 The lack of specificity of colonoscopy reflects the detection of benign hyperplastic polyps, which are not cancer precursors.36 Complications of colonoscopy were measured as the number of perforations arising from colonoscopy.37

Costs of screening, surveillance and CRC care
Costs associated with colonoscopy, polypectomy, complications from colonoscopy and costs of cancer treatment were obtained from Chinese literature (table 2).19 38–40 The costs of the Shanghai FIT, FIT 1, FIT 2 and the RA were provided by Pudong CDC. The costs of all of the FITs were based on the current reimbursement funding arrangement. These costs include the test kits, their distribution, return and analysis and expenses in marketing. We also included costs associated with colonoscopy, such as costs for following-up individuals with a positive screening test to encourage them to attend diagnostic colonoscopy and general outpatient costs.19 All costs are presented in Chinese Renminbi (RMB, ¥) and where necessary are standardised to 2019 prices using the Consumer Price Index.41

Outcomes
For all strategies, the model estimated CRC incidence, the number of CRC deaths and the number of screening, diagnostic and surveillance tests required between ages 45 and 80 years per 1000 individuals. The benefits of screening were measured as the reduction in CRC incidence and mortality and the number of life years gained (LYG) per 1000 individuals. The number of screening events and colonoscopies were taken as measures of the burden of screening and for colonoscopy, both diagnostic and surveillance colonoscopies were included. Harms of screening were measured as the number of perforations arising from colonoscopy and the number of false-positive tests (which is defined as a positive screening test followed by a colonoscopy with no clinical findings).

Cost-effectiveness analysis
We conducted a cost-effectiveness analysis from the healthcare sector perspective, and discounted both future costs and life-years using a standard annual rate of 3%.42 (undiscounted results and results discounted at 5% were also assessed). We plotted all of the screening strategies in a cost-effectiveness plane and performed an incremental cost-effectiveness analysis to see which strategies were efficient. The efficient strategy with the highest incremental cost-effectiveness ratio (ICER) below the willingness-to-pay (WTP) threshold was considered optimal. The WTP threshold was set at three times the Chinese gross domestic product per capita in 2018 (¥193 931 RMB which is equal to US$29 313)13 for one LYG.

| Table 2 Costs associated with colorectal cancer screening and treatment* |
|---------------------------------|------------------|------------------|
| Cost parameter                  | ¥                | Probabilistic sensitivity analysis, ranges† |
| Per quantitative FIT—one-sample‡, § | 15.00            | 7.50 to 30.00    |
| Per quantitative FIT—two-sample‡, § | 25.00            | 12.50 to 50.00   |
| Per qualitative FIT—one-sample‡, § | 13.00            | 6.50 to 26.00    |
| Per risk assessment‡           | 3.48             | 1.74 to 6.96     |
| Per positive screening test¶¶  | 15.00            | 7.50 to 30.00    |
| Per colonoscopy**              | 375.30           | 187.65 to 750.60 |
| Per polypectomy††              | 654.83           | 327.42 to 1309.66|
| Per perforation of colonoscopy†† | 19 761.04       | 9880.52 to 39 522.08 |
| Treatment by stage and location§§ |                 |                  |
| Stage I CRC                    | 35 227.92        | 17 613.96 to 70 455.84 |
| Stage II CRC                   | 37 342.58        | 18 617.29 to 74 685.58 |
| Stage III CRC                  | 37 481.16        | 18 740.58 to 74 962.32 |
| Stage IV CRC                   | 38 472.04        | 19 236.02 to 76 944.08 |
| General outpatient cost¶¶      | 23.30            | 11.65 to 46.60   |

*Costs are from a health system perspective and do not include patient time costs. All costs are presented in Chinese Renminbi (¥) and are indexed to 2019 prices.41
†Ranges of 95% CIs for the costs in the probabilistic sensitivity analysis were obtained by halving and doubling the base case values. Using these ranges, the shape parameter 𝜃 and the scale parameter 𝜆 are calculated as input for the gamma-distributions.
‡Costs provided by Pudong Centre for Disease Control and are based on the current reimbursement funding arrangement.
§Costs include the test kits, their distribution, return and analysis and expenses in marketing.
¶These costs are provided to encourage those with positive screening test to attend diagnostic colonoscopy, as well as support other activities related to colonoscopy.
**Costs for colonoscopy are based on sources from China38 and includes cost of bowel preparation.40
††Costs for polypectomy is based on sources from China38 and includes costs of biochemical and pathological testing.40 This cost is in addition to the cost for colonoscopy.
‡‡Costs for perforation during colonoscopy is based on sources from China.38
§§Costs of cancer treatment are taken from the Chinese setting.19 39
¶¶Co-payment made by patients when seeing a doctor and undergoing a colonoscopy.19 CRC, colorectal cancer; FIT, faecal immunochemical test.

Sensitivity analyses
We conducted a series of sensitivity analyses to assess the robustness of our assumptions. First, due to uncertainty about the performance of the validated FIT in the Chinese population, we conducted an analysis where we adjusted the characteristics such that the sensitivity and specificity were halfway between the calibrated Shanghai FIT and the validated FITs (online supplemental file 2, table 4). Second, due to uncertainty about the actual
cost of the validated FITs, we explored the impact of varying its cost by assuming a 50% reduction and a twofold increase. All other costs were held constant. Third, quality-adjusted life years were excluded from the main analysis because at present there is no available information on these measures in the Chinese setting. Therefore, we assessed the impact of using international quality of life measurements in a sensitivity analysis (online supplemental file 2, table 5).

Fourth, we assessed the impact of an alternative surveillance pathway, derived from Chinese literature (online supplemental file 2, figure 1). Finally, we assessed the impact of reducing the WTP threshold to the Chinese gross domestic product per capita in 2018 (¥64 644 RMB which is equal to US$9771) for one LYG.

Probabilistic sensitivity analysis

In the probabilistic sensitivity analysis, we assessed the uncertainty of the test characteristics and costs for four strategies: the current programme using the Shanghai FIT+RA, the current programme using a validated two-sample FIT, the strategy that was found to be cost-effective at the WTP threshold and the strategy on the efficient frontier with similar colonoscopy demand as the existing programme. For every strategy, we performed 1000 simulations each containing different parameter values drawn from corresponding probability distributions. The test characteristics were drawn from a beta distribution and costs from a gamma distribution (table 2 and online supplemental file 2, table 6).

RESULTS

Benefits of screening

MISCAN-Colon predicted that, compared with no screening, all screening strategies reduced CRC incidence and mortality (online supplemental file 3, table S1). Undiscounted results and results discounted to 3% are presented in (online supplemental file 3, table S2A,B) and (online supplemental file 4, figure S1A,B). In a situation without screening, CRC incidence was 49 per 1000 individuals while CRC mortality was 11 per 1000 individuals. Screening reduced CRC incidence by 16%–53% (8–26 cases) and CRC mortality by 41%–79% (4–9 deaths), depending on intensity of screening (online supplemental file 3, table S1). In addition, screening gained an additional 20–39 life years (LYs). The current screening programme (triennial screening with Shanghai FIT+RA from ages 50 to 75 years) reduced CRC incidence by 19 cases (40%) and mortality by 7 deaths (67%) and gained an additional 32 LYG.

Annual screening with the Shanghai FIT+RA, from ages 45 to 80 years was the most effective strategy at reducing CRC incidence, while annual screening with the FIT 2 with a cut-off of 10 µg Hb/g from ages 45 to 80 years was the most effective at reducing CRC mortality.

Screening burden

In general, screening strategies with a shorter screening interval and a greater number of years of screening required more screening tests than strategies with longer interval for fewer years. For example, annual screening with FIT 1, with a cut-off of 40 µg Hb/g, from ages 45 to 80 years required the greatest number of screening tests (29 329 tests), while triennial screening with the Shanghai FIT+RA, from ages 55 to 70 years required the least number of screening tests (3706 tests). The current screening programme required 5346 tests.

This pattern did not hold for the number of required colonoscopies. Although triennial screening with FIT 1, with a cut-off of 40 µg Hb/g, from ages 55 to 70 years required the least number of colonoscopies (265 colonoscopies) and annual screening with the Shanghai FIT+RA, from 45 to 80 years required the greatest number of colonoscopies (2609 colonoscopies), the order of strategies between this varied greatly. The current screening programme required 1434 colonoscopies. In general, the screening strategies that used the Shanghai FIT had a substantially greater colonoscopy requirement than those using the validated tests.

Screening harms

Overall, the risk of screening related perforations was very low—ranging between 0.01 and 0.09 per 1000 individuals. Complications were proportional to the number of colonoscopies, such that those strategies with fewer colonoscopies had fewer complications. The number of false-positive tests ranged from 21 to 1971 and was generally highest for the Shanghai FITs, particularly with risk assessment.

Costs and cost-effectiveness

Without screening, the cost of diagnosing and treating colorectal cancer was ¥869 648 per 1000 individuals. Screening increased costs by 1%–66% (¥884 995–¥1 443 552). The current screening programme cost an additional ¥152 565, an increase of 18% (¥1 022 213).

Of the 324 screening strategies, 10 were on the efficient frontier (ie, considered to provide good value for money, table 3, figure 1). The efficient strategies all had a low cut-off (10–15 µg Hb/g), and were an even mix of validated one-sample and two-sample tests. Screening start age varied from a relatively short-time period (50–70) years to the longest assessed period (45–80) years, and the screening interval ranged from 1 to 3 years. All screening strategies using the Shanghai FIT, either with or without the risk assessment, were dominated.

Using a WTP threshold of ¥193 931 per LYG, the optimal screening strategy was annual testing with FIT 1, using a cut-off of 10 µg Hb/g from ages 45 to 80 years (ICER, ¥39 218). Annual screening with FIT 2, using a cut-off of 10 µg Hb/g from ages 45 to 80 years was also on the efficient frontier, but with an ICER, ¥739 677 per LYG, it would not be considered as cost-effective.
Table 3  Costs and effects (discounted at 3%) per 1000 simulated 45-year-olds for a situation without screening, the current screening programme in Shanghai and screening strategies on the efficient frontier

| Screening strategy | Start-stop age | Interval | FITs | Colonoscopies | False positives | Complications | CRC incidence | CRC mortality | Life years* | Total costs*† | ICER*† |
|--------------------|----------------|----------|------|----------------|----------------|--------------|--------------|--------------|-------------|--------------|---------|
| No screening       | 0              | 49       | 0    | 0.01           | 49             | 11           |              |              | 21 482      | 869 648      |         |
| Current screening programme in Shanghai |                  |          |      |                |                |              |              |              |            |              |         |
| Shanghai FIT+RA    | 50–75          | 3        | 5346 | 1434           | 890            | 0.07         | 30           | 4            | 21 514      | 1 022 213    | Dominated |
| Cost-effective screening strategies |                  |          |      |                |                |              |              |              |            |              |         |
| FIT-1–10           | 50–70          | 3        | 5901 | 514            | 151            | 0.03         | 36           | 5            | 21 509      | 874 095      | 164      |
| FIT-2–10           | 50–70          | 3        | 5645 | 652            | 239            | 0.04         | 33           | 5            | 21 511      | 884 484      | 4027     |
| FIT-2–10           | 50–75          | 3        | 6884 | 744            | 294            | 0.04         | 31           | 4            | 21 514      | 904 162      | 7778     |
| FIT-2–10           | 50–80          | 3        | 7768 | 795            | 327            | 0.05         | 30           | 3            | 21 515      | 917 846      | 14 254   |
| FIT-1–10           | 45–80          | 2        | 13 519 | 801           | 334            | 0.05         | 31           | 3            | 21 517      | 989 444      | 31 130   |
| FIT-1–10           | 50–80          | 1        | 20 134 | 986           | 476            | 0.05         | 28           | 3            | 21 518      | 1 007 490    | 31 660   |
| FIT-1–15           | 45–80          | 1        | 26 112 | 846           | 359            | 0.05         | 29           | 2            | 21 520      | 1 071 462    | 32 309   |
| FIT-1–10‡          | 45–80          | 1        | 24 054 | 1 104         | 572            | 0.06         | 27           | 2            | 21 520      | 1 101 071    | 59 218   |
| FIT-2–15           | 45–80          | 1        | 23 434 | 1 186         | 635            | 0.06         | 26           | 2            | 21 521      | 1 225 260    | 302 900  |
| FIT-2–10           | 45–80          | 1        | 21 214 | 1 456         | 867            | 0.07         | 24           | 2            | 21 521      | 1 254 847    | 739 677  |

*Results are discounted at an annual rate of 3%.
†Costs are presented in Chinese Renminbi (¥).
‡Optimal screening strategy at the willingness-to-pay threshold
 CRC, colorectal cancer; FIT, faecal immunochemical test; FIT-1–10, one sample faecal immunochemical test, 10 µg Hb/g cut-off value; FIT-1–15, one sample faecal immunochemical test, 15 µg Hb/g cut-off value; FIT-2–10, two sample faecal immunochemical test, 10 µg Hb/g cut-off value; FIT-2–15, two sample faecal immunochemical test, 15 µg Hb/g cut-off value; ICER, incremental cost-effectiveness ratio.
Sensitivity analyses

Our results were robust to changes in the validated FIT characteristics, costs, the use of international quality of life measurements and the adoption of a Chinese surveillance pathway. For all of these analyses, the validated FITs outperformed the Shanghai FIT, both with and without the risk assessment (online supplemental file 3, table S1A–E and online supplemental file 4, figure S2A–E). At the WTP threshold, the cost-effective strategies varied in terms of the test (FIT 1 and FIT 2) and cut-off, however all strategies required annual testing from ages 45 to 80 years (table 4). The Shanghai FIT+RA was on the efficient frontier when the Chinese surveillance pathway was assessed, however, with an ICER of ¥750 686, it would not be considered cost-effective.

Probabilistic sensitivity analysis

The probabilistic sensitivity analysis suggests that at the WTP threshold of ¥193 931, of the four considered strategies, the optimal screening strategy (annual screening with FIT 1, with a cut-off of 10 µg Hb/g from 45 to 80 years) is the cost-effective strategy in more than 50% of the simulations (online supplemental file 4, figure S3). Above the WTP threshold, a strategy with similar colonoscopy demand to the existing programme (annual screening with FIT 2, with a cut-off of 10 µg Hb/g from 45 to 80 years) has the highest likelihood of being cost-effective. The current programme was not cost-effective in any of the 1000 simulations.

**DISCUSSION**

This microsimulation analysis assessed the performance of the Shanghai FIT, with and without the use of a risk assessment, compared with the use of validated one-sample and two-sample FITs. Our results suggest that the screening tests currently used in the Shanghai screening programme are not the most cost-effective as in all instances they were outperformed by validated screening tests. Although the Shanghai tests performed similarly terms of reductions in incidence and mortality...
Table 4

| Screening strategy | Cost- effective strategy (discounted at 3%) for the sensitivity analyses. Outcomes are per 1000 45-year-olds |
|--------------------|----------------------------------------------------------------------------------|
| Test               | CRC incidence                     | CRC mortality | Life years* | QALYs* | Total costs*† | ICER*† |
|FIT-1–10 F1         | 1144                               | 144           | 26         | 3      | 21,519        | 60,319 |
|FIT-2–30 F1         | 26,476                             | 807           | 320        | 0.05   | 21,520        | 1,018,114 |
|FIT-1–10 F2         | 21,524                             | 1,477,922     | 934        | 0.07   | 21,521        | 2,027,847 |
|FIT-2–30 F2         | 21,524                             | 1,477,922     | 934        | 0.07   | 21,521        | 2,027,847 |

*Results are discounted at an annual rate of 3%.
†Costs are presented in Chinese Renminbi (¥).
CRC, colorectal cancer; FIT, faecal immunochemical test; FIT-1–10, one sample faecal immunochemical test, 10 µg Hb/g cut-off value; FIT-2–30, two sample faecal immunochemical test, 30 µg Hb/g cut-off value.

Shanghai is one of the only regions in the world to implement a triennial screening programme. This strategy was chosen after the completion of a comprehensive evaluation of the capacity of health resources of the region. This suggests that an alternative programme could be implemented if it did not exceed the demand of health services such as colonoscopy. According to our analysis, the current programme requires a colonoscopy capacity of 1434 per 1000 individuals, while our proposed cost-effective strategy reduces colonoscopy demand by approximately 30% (to 1104 colonoscopies). If colonoscopy demand was a key driver of the selection of a triennial screening programme, there are several alternatives that could be implemented. For example, while not considered to be cost-effective (ICER: ¥739,677), annual screening of individuals from 45 to 80 years with a validated, two-sample FIT, with a cut-off of 10 µg Hb/g results in a similar colonoscopy demand (1456 colonoscopies). The probabilistic sensitivity analysis shows that above the current WTP threshold, this strategy has the highest probability of being cost-effective. Alternatively, to achieve the same number of LYG (21,514 per 1000), a programme of triennial screening from 50 to 75 years with a validated, two-sample FIT, with a cut-off of 10 µg Hb/g could be implemented. This strategy would half the colonoscopy demand (to 744 colonoscopies) at an ICER of ¥7778. Other strategies could also be selected depending on desired outcomes, however, all of these alternatives use a validated FIT.

The suboptimal performance of the Shanghai screening tests is not surprising given their characteristics (Table 2). Although the sensitivity of the Shanghai screening tests is comparable to the validated screening tests, the specificity is considerably lower, especially when the risk assessment is included. Low specificity increases the rate of false-positive tests and consequently, greater numbers of individuals are unnecessarily sent for colonoscopy. This impacts the cost-effectiveness of the screening programme by increasing the burdens, harms and costs of screening. Shifting to a validated, quantitative FIT could help alleviate these issues while also providing an
opportunity to assess stool haemoglobin concentrations which have been demonstrated to be a strong predictor for future cancer risk.\textsuperscript{46}

The high rate of false positivity of the screening tests used in the Shanghai screening programme has been suggested as an explanation for the low uptake of diagnostic colonoscopy.\textsuperscript{7,13} Although failure to complete an appropriate follow-up test after a positive result further undermines the benefits of screening, the situation is not unique to the Shanghai screening programme - suboptimal compliance to diagnostic colonoscopy after a positive FIT has been noted in several screening programmes.\textsuperscript{47} Compliance to diagnostic colonoscopy is complex and multidimensional.\textsuperscript{28-30} In China, the results of primary screening test, perceived severity of the disease, personal or others experiences with colonoscopy and healthcare provider recommendation have also been shown to influence compliance.\textsuperscript{49} Cultural beliefs may also play a significant role.\textsuperscript{51} This suggests that health literacy related to CRC screening could be improved.

With compliance to diagnostic colonoscopy, and participation in screening in general, already demonstrated to be low in Shanghai and other locations in China,\textsuperscript{8} the optimal screening strategy suggested by this investigation may not be optimal in practice. Screening programmes have to consider their ‘real world’ application and as the effectiveness of a FIT screening programme relies heavily on participation, the implementation of an annual screening programme over an extended 35-year period may further diminish this already low participation rate. Participation may be further diminished as a result of ‘screening fatigue’—where motivation to participate is reduced due to a false perception of decreased CRC risk after several negative screening test results.\textsuperscript{52,53} As CRC risk increases with age\textsuperscript{1,2,54} participation of older individuals is important. With Shanghai being one of the most ageing cities in China,\textsuperscript{25} it has been suggested that offering screening to those aged 75–80 is potentially warranted. Therefore, it may be pertinent to consider an alternative cost-effective strategy such as annual screening from 50 to 80 years, using a validated, one-sample FIT, with a cut-off of 10 µg Hb/g (ICER: ¥31 660) or triennial screening from 50 to 80 years, using a validated, two-sample FIT, with a cut-off of 10 µg Hb/g (ICER: ¥14 254). Choosing either of these strategies would substantially reduce both the screening burden and costs, while still achieving comparable benefits.

There are four noteworthy limitations to our research. First, there remains some uncertainty about the accuracy of test characteristics and therefore the performance of the validated FITs in the Chinese population. We therefore conducted a sensitivity analysis where we reduced the performance of the validated FITs. Our results were robust to this change in test characteristics, although there was less difference in effectiveness, the analysis produced similar results as base case. Second, we simulated surveillance in our main analysis consistent with European Society of Gastrointestinal Endoscopy Guidelines,\textsuperscript{20} because there is conflicting advice in China about the post diagnostic colonoscopy pathway, (including when to return to screening and the surveillance pathway).\textsuperscript{15} 21-24 When we assumed surveillance guidelines derived from Chinese literature, our results did not change significantly. Although annual screening from 45 to 80 years with the Shanghai FIT+RA was on the efficient frontier, it was still not cost-effective. Third, we did not assess screening using colonoscopy. While colonoscopy screening could be considered advantageous over FIT screening, providing at least 10 years of screening coverage, compared with FIT, it is expensive, invasive and not without risk. Moreover, it is unlikely to become the test of choice in Shanghai for primary screening, given the very low colonoscopy uptake, even after a positive FIT, and the lack of colonoscopy capacity. Finally, there is limited information on complications arising from colonoscopy in China which likely means our results provide an underestimate of complications and their associated costs. However, given that the Shanghai FIT, both with and without the risk assessment, had higher numbers of colonoscopy, we do not feel that this would significantly alter our results. Fortunately, there is research underway to address this gap in knowledge.\textsuperscript{56}

Despite these limitations, our research has important implications. First, our results suggest that the CRC screening programme in Shanghai could achieve better outcomes and costs could be reduced if the programme was to switch to using a validated screening test. Based on our results the most cost-effective strategy is annual testing with the validated one-sample FIT, using a cut-off of 10 µg Hb/g and screening from ages 45 to 80 years. Second, although the current screening programme is not considered optimal based on our results, our findings support the implementation of screening in Shanghai; even the use of suboptimal screening tests result in a reduction of CRC incidence and mortality in a cost-effective way compared with no screening (cost-effectiveness ratio=¥4801). Given the recent trend of rising CRC incidence and mortality,\textsuperscript{10-12} coupled with the expectation that the burden is set to increase as the Chinese economy grows,\textsuperscript{5,57} efforts to reduce the impact of CRC are important. Moreover, despite the use of these tests, the programme already appears to be having an impact on survival—individuals diagnosed with CRC who participated in the screening programme and were compliant with the screening policy experienced better survival outcomes compared with those who did not participate.\textsuperscript{58} While this finding should be interpreted with caution given the short follow-up time and the potential for lead time and length bias,\textsuperscript{45} it adds support to the benefits of screening in this population. Finally, our results demonstrate that screening for CRC is a highly cost-effective method of reducing the burden of CRC in Shanghai. This is particularly salient in China where out-of-pocket expenses for treating cancer have been described as ‘catastrophic’ (defined as out-of-pocket expenditure in access of 40% of annual household income) for both
newly diagnosed and end stage cancer.\textsuperscript{50, 60} This finding may be relevant to other jurisdictions with limited health resources who are considering implementing CRC screening.

CONCLUSION
Screening for CRC in Shanghai is an attractive and cost-effective option for reducing the burden of CRC. Although the current screening programme reduces both the incidence and mortality of CRC, a programme using a standardised, validated FIT could save more lives at a lower cost. In addition, addressing barriers to screening, such as poor health literacy and financial concerns, may increase participation and therefore improve the effectiveness of the screening programme.

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MISCAN-Colon Model Description

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Model Overview

The Microsimulation Screening Analysis-Colon (MISCAN-Colon) model is a stochastic, semi-Markov, microsimulation model that is useful in explaining and predicting trends in CRC incidence and mortality and to quantify the effects and costs of primary prevention of CRC, screening for CRC and surveillance.

The term ‘microsimulation’ implies that individuals are moved through the model one at a time (i.e. as individuals), rather than as proportions of a cohort. This allows future state transitions to depend on past transitions, giving the model a ‘memory’. Furthermore, unlike most traditional Markov models, MISCAN-Colon does not use yearly transition probabilities; instead it generates durations in states, thereby increasing model flexibility and computational performance. The term ‘stochastic’ implies that the model simulates sequences of events by drawing from distributions of probabilities/durations, rather than using fixed values. Hence, the results of the model are subject to random variation. Possible events are birth and death of a person, adenoma incidence and transitions from one state of disease to another.

At two expert meetings at the National Cancer Institute (Bethesda, Maryland, United States of America) held on June 5–7, 1996, and May 12–13, 1997, the structure of the model was devised in agreement with the currently accepted model of the adenoma–carcinoma sequence (Figure 1). MISCAN-Colon consists of 3 modules: a demography module, natural history module, and screening module (Figure 1). Although these parts are not physically separated in MISCAN-Colon, it is useful to consider them separately.

![Figure 1: Structure of MISCAN-Colon](image)

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Demography module

The demography module of MISCAN-Colon simulates individual life histories without colorectal cancer (CRC) to form a population. Using birth tables and life tables representative of the population under consideration, the model draws a date of birth and a date of non-CRC death for each simulated individual. The model restricts the maximum age a person can achieve to 100 years.

Natural history module

In the natural history module, MISCAN-Colon simulates the development of CRC in the population. It was assumed that all CRCs are preceded by adenomas. As each simulated individual ages, one or more adenomas may develop (Figure 2). These adenomas can be either progressive or non-progressive and both can grow in size from small (≤5 mm), to medium (6–9 mm), to large (≥10 mm). Only progressive adenomas can develop into preclinical cancer and these may progress through stages I to IV. In every stage there is a chance of the cancer being diagnosed because of symptoms. After clinical diagnosis, CRC survival is simulated using age-, stage-, and localisation-specific survival estimates for clinically diagnosed CRC obtained from a study by Rutter and colleagues. For individuals with synchronous CRCs at time of diagnosis, the survival of the most advanced cancer is used. The date of death for individuals with CRC is set to the earliest simulated death either because of CRC or because of another causes (Demography model).

The average duration between onset of a progressive adenoma and the transition to preclinical cancer was estimated based on the interval cancer rate after a once-only sigmoidoscopy in a randomized controlled trial from the United Kingdom. The duration of cancer in preclinical stages was estimated based on the results of three large randomised controlled screening trails. This resulted in the average duration of 2.5 years, 2.5 years, 3.7 years, and 1.5 years, for stages I-IV respectively, with a total average duration of 6.7 years because not every cancer reaches stage IV before clinical diagnosis. All durations were governed by an exponential probability distribution. Durations in each of the invasive cancer stages as well as durations in the stages of the non-invasive adenomas were assumed to be 100% associated with each other, but the durations in invasive stages as a whole were independent of durations in non-invasive adenoma stages that precede cancer. These assumptions resulted in an exponential distribution of the total duration of progressive non-invasive adenomas and of the total duration of preclinical cancer, which has also been used in other cancer screening models.
Figure 2: Schematic representation of the natural history module of the MISCAN-Colon model.

Abbreviations: CRC, colorectal cancer
The arrows between the states show which types of transitions can occur. In every state before death, a transition to “death from other causes” can occur (state and connect arrows not shown).

a. Cancer stages correspond to the American Joint Committee on Cancer / International Union Against Cancer staging system for CRC.

Based on expert opinion, it is assumed that 30% of the cancers arise from adenomas of 6–9 mm and that 70% arise from larger adenomas. The preclinical incidence of non-progressive adenomas that will never grow into cancer was varied until the simulated prevalence of all adenomas matched with data from autopsy studies. The size distribution of adenomas over all ages was assumed to be 73% for stages less than or equal to 5 mm, 15% for stages 6–9 mm, and 12% for stages greater than or equal to 10 mm.

An individual's risk of developing adenomas depends on the individual's age and a personal risk index. As a result most individuals will not develop adenomas, whilst others develop many.

The distribution of adenomas over the colon and rectum is assumed to equal the distribution of cancers observed before the introduction of screening. The age-specific onset of adenomas and the personal risk index were calibrated to data on the prevalence and multiplicity distribution of adenomas as observed in autopsy studies (Figure 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

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stages were simultaneously calibrated to SEER data on the age-, stage-, and localization-specific incidence of CRC as observed before the introduction of screening (Figure 4).

Figure 3: Adenoma prevalence observed in selected autopsy studies vs simulated by MISCAN-Colon (% of individuals with adenomas).*

*Observed results are shown only for the 2 largest studies on which the model has been calibrated. The model has additionally been calibrated to eight other autopsy studies.
The average durations of the preclinical cancer stages were calibrated to the rates of screen-detected and interval cancers observed in randomized controlled trials evaluating screening using guaiac faecal occult blood tests.\(^{17-19}\) This exercise has been described extensively in a publication by Lansdorp-Vogelaar and colleagues.\(^3\) The average duration from the emergence of an adenoma until progression into preclinical cancer (i.e., the adenoma dwell-time) was calibrated to the rates of interval cancers (including surveillance detected cancers) observed in a randomized controlled trial evaluating once-only sigmoidoscopy screening (Figure 5).\(^2\)
Furthermore, we assume: i) an equal overall dwell-time for adenomas developing into CRC from a medium size (30% of all CRCs) and from a large size (70% of all CRCs); exponential distribution for all durations in the adenoma and preclinical cancer phase; perfect correlation for the duration in the adenoma and preclinical cancer (meaning that if a small adenoma progresses rapidly to a medium-sized adenoma, it will also progress rapidly to a large adenoma or to a preclinical cancer stage I); and absence of correlation between durations in the adenoma phase and duration in the preclinical cancer phase.

The stage-specific survival of patients with screen-detected cancer is assumed to be the same as the survival of patients with cancers clinically diagnosed in the same stage, except if screen-detection occurs in the same stage as the cancer would have been diagnosed without screening. In that case, survival is assumed to be similar to survival of one stage more favourable (i.e. stage II cancer gets stage I survival). Only if screen-detected in stage IV, we assume no possibility for within-stage shift and stage IV screen detected cancers always have the same survival as clinically diagnosed cancers in stage IV. Removal of an adenoma always prevents development of any subsequent cancer that may have arisen from this adenoma.
Figure 5: Distal CRC incidence observed in the intervention group of the UK Flexible Sigmoidoscopy Trial vs simulated by MISCAN-Colon (per year of follow-up (A), cumulative (B); cases per 100,000 person years).
**Screening module**

Screening interrupts the development of CRC and therefore alters some of the simulated life histories. With screening, some cancers will be prevented by the detection and removal of adenomas; other cancers will be detected in an earlier stage than with clinical diagnosis which offers a more favourable survival. In this way, screening prevents CRC incidence or CRC death. The life-years gained by screening are calculated by comparing the model-predicted life-years lived in the population with and without screening. The effects of different screening policies can be compared by applying them to identical natural histories. As seen in RCTs on guaiac faecal occult blood testing, the stage-specific survival of screen-detected CRC was more favourable compared with clinically detected CRC, even after the lead-time bias correction. We therefore assign screen-detected cancers that would have been clinically detected in the same stage the survival corresponding to a cancer that is one stage less progressive. For example, a cancer which is screen-detected in stage II, that would also have been clinically diagnosed in stage II, is assigned the survival of a clinically diagnosed stage I cancer. The only exceptions were screen-detected stage IV cancers. These cancers were always assigned the survival of a clinically diagnosed stage IV cancer.

In addition to modelling positive health effects of screening, we also model colonoscopy-related complications, over-diagnosis and over-treatment of CRC (ie, the detection and treatment of cancers that would not have been diagnosed without screening).

**Integration of the model components**

For each individual, the demography module of MISCAN-Colon simulates a date of birth and a date of death of other causes than CRC, creating a life history without adenomas or CRC.

In patient A in Figure 6, the natural history module generates an adenoma. This adenoma progresses into preclinical cancer (diagnosed as stage II CRC because of symptoms) and results in CRC death before non-CRC death would have occurred. However, in the screening module, a screening examination is introduced (indicated by the blue arrow). During this examination, the adenoma is detected and then removed, and both CRC and CRC death prevented. Hence, in Patient A, the positive effect of the screening intervention is indicated by the green arrow and represents the increased LYG for this patient because of screening.

Patient B also develops an adenoma, and although this adenoma does progress into preclinical cancer, Patient B would never have been diagnosed with CRC in a scenario without screening (see life history 2). However, during the simulated screening examination (blue arrow) CRC is screen-detected in stage I and for this patient, the screening results in over-diagnosis and overtreatment of CRC: in this situation, screening does not prolong life, but it
does result in additional LYs with CRC care (over-treatment) as indicated by the red arrow.

**Figure 6: Integrating modules: two example individuals (A and B).**
Model Outputs

The model generates the following output, both undiscounted and discounted:

Demography

1. Life-years lived in the population by calendar year and age
2. Deaths from other causes than CRC by calendar year and age

Natural history

1. CRC cases by calendar year, stage and age
2. CRC deaths by calendar year and age
3. Life-years lived with CRC by calendar year, stage and age
4. Total number of life years with surveillance for adenoma patients
5. Total number of life years with initial therapy after screen-detected or clinical invasive cancer by stage
6. Total number of life years with continuing therapy after screen-detected or clinical invasive cancer by stage
7. Total number of life years with terminal care before death from other causes by stage
8. Total number of life years with terminal care before death from CRC by stage

Screening

1. Number of invitations for screen-tests, screen-tests, diagnostic tests, surveillance and opportunistic screen tests by calendar year
2. Number of positive and negative test results per preclinical state and per year
3. Total number of life years lived, life years lost due to cancer, number of specific deaths and non-specific deaths
4. Number of screenings that prevented cancer by year of screening
5. Number of screenings that detected cancer early by year of screening
6. Number of surveillance tests that prevented cancer by year of surveillance
7. Number of surveillance tests that detected cancer early by year of surveillance
8. Number of life years gained due to screening by year of screening
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Supplementary Methods

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MISCAN-Colon Model Quantification

Model parameters

The quantification of the demography and natural history parameters in the model may vary depending on the population simulated. The following data is the description of the model quantification used in the present analysis.

Demography parameters

In these analyses, a cohort of 45 year old males or females was modelled. Life tables and birth tables were based on data from China's 6th population census in 2010 (most recent available data). Although there was no organised screening in Shanghai at this time, there was a small screening pilot project in communities of Qibao Town in Shanghai from 2008-2011. These life tables include CRC mortality and the demography part simulates mortality from causes other than CRC. However, no adjustment was made to the life tables because the percentage of CRC mortality in overall mortality is small and the data on CRCs deaths by age and sex in this setting are sparse.

Natural history parameters

Colorectal cancer incidence and mortality data was derived from data sourced from Shanghai Municipal Center for Disease Control and Prevention. The incidence of progressive adenomas was chosen to reproduce the CRC incidence by age, stage, and localisation in Shanghai. Stage-specific survival was based on data from 2015 in Shanghai. As the survival data was divided into colon and rectal cancer and MISCAN-Colon uses survival for CRC, the data was transformed into a weighted CRC survival.

The anatomic site distribution of both progressive and non-progressive adenomas and thus of preclinical and clinical cancers is assumed to be equal to the site distribution of CRCs as reported by the Shanghai Municipal Center for Disease Control and Prevention.

Table 1 contains a detailed summary of the natural history input values and data sources.
Table 1: Main natural history assumptions in the MISCAN-Colon model

| Model parameter                                      | Value                                                                 | Source                                                                 |
|------------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------------------------------|
| Heterogeneity of risk for adenomas over the general population | Gamma distributed, mean 1, variance sex dependent                      | Fit to multiplicity distribution of adenomas in autopsy studies<sup>6-15</sup> and cancer incidence from Shanghai in 2015<sup>3</sup> |
| Adenoma incidence per year                           | Age and sex dependent.                                                | Fit to adenoma prevalence in autopsy studies<sup>6-15</sup> Cancer incidence from Shanghai in 2015<sup>3</sup> |
| Probability that a new adenoma is progressive         |                                                                       | Fit to adenoma prevalence in autopsy studies<sup>6-15</sup> Cancer incidence from Shanghai in 2015<sup>3</sup> |
| Regression of adenomas                               | No significant regression of adenomas                                 | Expert opinion                                                         |
| Mean duration of development of progressive adenomas to preclinical cancer | 14 years                                                             | Estimated from randomized controlled trial of once-only sigmoidoscopy<sup>16</sup> |
| Average duration of preclinical cancer by stage       | Stage I: 2.5 years                                                    | Estimated from FOBT trials<sup>17</sup>                                 |
|                                                      | Stage II: 2.5 year                                                    |                                                                        |
|                                                      | Stage III: 3.7 years                                                 |                                                                        |
|                                                      | Stage IV: 1.5 year                                                  |                                                                        |
| Mean duration of preclinical cancer                  | 6.7 years                                                            | Estimated from FOBT trials<sup>17</sup>                                 |
| Per cent of non-progressive adenomas that stay 6-9mm | 25%                                                                  | Fit to size distribution of adenomas in colonoscopy trial (corrected for colonoscopy sensitivity)<sup>18</sup> |
| Per cent of non-progressive adenomas that become 10mm or larger | 75%                                                                  |                                                                        |
| Per cent of cancers that develops from 6-9mm adenoma and from 10+mm adenoma | 30% develop from 6-9mm 70% develop from 10+mm | Expert opinion                                                         |
| Localisation distribution of adenomas and cancer      | Cecum: 5.41% Ascending colon: 16.67% Transverse colon: 8.33% Descending colon: 4.62% sigmoid: 20.54% Rectosigmoid junction: 0.00% rectum: 44.43% unknown: 0.00% | Estimated from Shanghai cancer incidence in 2015<sup>3</sup> |
| 5-year survival after clinical diagnosis of CRC       | Dependent on age and stage at diagnosis, and localization            |                                                                        |

Abbreviations: CRC, colorectal cancer; FOBT, faecal occult blood test
Screening parameters

Data and assumptions for occult blood screening

We estimated the test characteristics of the Shanghai FIT and the Shanghai FIT+RA (Table 2) so that the model predicted positivity and detection rates for advanced neoplasia are similar to those observed in the first three years of screening in Pudong (2013-2015). These observed rates were provided by the Pudong Centre for Disease Control (Table 3). The algorithm used for this estimation is the Nelder-Mead Simplex method.19 This iterative parameter search method constructs a simplex consisting of a number of sets of potential test characteristics equal to the number of test characteristics plus 1. For each set, the goodness-of-fit (GOF) is computed and a better set (in terms of GOF) replaces the worst set.20 Since the data consists of rates, the Poisson likelihood was used as the GOF during the calibration.

The test characteristics of the validated FIT 1 and FIT 2 were fitted to the positivity and detection rates of advanced neoplasia observed in the first screening round of two Dutch randomised trials, which utilised the OC-Sensor micro (Eiken Chemical, Tokyo, Japan, Table 2).21-24 To estimate the two-sample FIT test characteristics we followed the approach described in Goede and colleagues.25 The characteristics differ to those previously presented as the natural history of the MISCAN-Colon model has been updated since this publication.26

The sensitivity of the stool tests for cancer was split to take into account the variance in test sensitivity at different time points before clinical diagnosis (shortly before and longer before). It was assumed that the probability a CRC bleeds, and thus the sensitivity of stool tests for CRC, depends on the time until clinical diagnosis, hence the distinction between ‘early’ and ‘late’ preclinical CRC. This is to be expected when cancers that bleed do so increasingly over time, starting with occult blood loss and progressing to clinically visible bleeding.17 In addition, the effect of systematic false negative FIT (that is, adenomas that do not bleed) and systematic false positive (individuals who always test positive but do not have adenomas) results were taken into account.27
Table 2: Test characteristics of the faecal immunochemical tests and colonoscopy

| Test                      | Sensitivity (%) | Specificity (%) |
|---------------------------|-----------------|-----------------|
|                           | Adenoma ≤5mm    | Adenoma 6-9mm   | Adenoma ≥10mm | CRC early preclinical | CRC late preclinical |
| Shanghai FIT b            | 0.0             | 8.7             | 20.3          | 44.6                | 78.9                | 87.4                |
| Shanghai FIT + RA b       | 0.0             | 9.4             | 33.0          | 74.2                | 93.1                | 79.3                |
| One-sample FIT10 c        | 0.0             | 11.0            | 39.4          | 65.5                | 90.0                | 96.1                |
| One-sample FIT15 c        | 0.0             | 6.5             | 33.3          | 58.5                | 87.0                | 97.3                |
| One-sample FIT20 c        | 0.0             | 5.0             | 29.3          | 52.0                | 83.5                | 97.9                |
| One-sample FIT30 c        | 0.0             | 3.3             | 26.6          | 50.5                | 83.0                | 98.4                |
| One-sample FIT40 c        | 0.0             | 2.6             | 22.1          | 50.0                | 82.5                | 98.7                |
| Two-sample FIT10 c,d      | 0.0             | 16.2            | 63.3          | 75.0                | 93.5                | 94.1                |
| Two-sample FIT15 c,d      | 0.0             | 8.9             | 52.7          | 71.0                | 92.0                | 95.7                |
| Two-sample FIT20 c,d      | 0.0             | 7.1             | 46.9          | 66.0                | 90.0                | 98.7                |
| Two-sample FIT30 c,d      | 0.0             | 4.6             | 42.5          | 66.5                | 90.5                | 97.4                |
| Two-sample FIT40 c,d      | 0.0             | 4.9             | 12.5          | 66.0                | 90.0                | 97.7                |
| Colonoscopy e,f           | 75.0            | 85.0            | 95.0          | 95.0                | 95.0                | 86.0                |

Abbreviations: CRC, colorectal cancer; FIT10, faecal immunochemical test; RA, risk assessment; 10 µg Hb/g faeces cut-off value; FIT15, faecal immunochemical test, 15 µg Hb/g cut-off value; FIT20, faecal immunochemical test, 20 µg Hb/g faeces cut-off value; FIT30, faecal immunochemical test, 30 µg Hb/g cut-off value; FIT40, faecal immunochemical test, 40 µg Hb/g cut-off value; µg Hb/g, micrograms of haemoglobin per gram faeces.

a. It was assumed that the probability a CRC bleeds and thus the sensitivity of a FIT for CRC depends on the time until clinical diagnosis.17

b. Specificity and sensitivity based on the positivity rates and detection rates of advanced neoplasia observed in the first screening round in Pudong, Shanghai. This data for this was provided by Pudong Centre for Disease Control. Sensitivity for adenomas smaller than 5 mm was assumed to be 0% for all tests.

c. Specificity and sensitivity based on the positivity rates and detection rates of advanced neoplasia observed in the first screening round of two Dutch randomised trials.21-24 Sensitivity for adenomas smaller than 5 mm was assumed to be 0% for all tests, at any cut-off level.

d. A two-sample FIT is considered positive when at least one-sample contains detectable blood at the specified cut-off value.

e. Specificity for colonoscopy is based on Schroy et al, 2013.28 The lack of specificity with endoscopy reflects the detection of non-adenomatous lesions, which, in the case of colonoscopy, leads to unnecessary polypectomy, which is associated with an increased risk complications.

f. Sensitivity of colonoscopy for the detection of adenomas and CRC within the reach of the endoscope was obtained from a systematic review on miss rates observed in tandem colonoscopy studies.29
Table 3: Positive and detection rate per 1,000 obtained by estimation and provided by Pudong CDC for the first three years of screening.

|                  | Positivity rate | Detection rate for non-advanced adenomas | Detection rate for advanced adenomas | Detection rate for CRC |
|------------------|-----------------|------------------------------------------|-------------------------------------|------------------------|
|                  | Observed (95% CI) | Estimated b | Observed (95% CI) | Estimated b | Observed (95% CI) | Estimated b | Observed (95% CI) | Estimated b |
| Shanghai FIT     | 145.26 (144.06–146.47) | 145.32 | 25.05 (24.15–25.98) | 25.07 | 17.51 (16.76–18.29) | 17.52 | 3.63 (3.29–4.00) | 3.63 |
| Shanghai FIT+RA  | 231.37 (229.94–232.82) | 231.37 | 38.32 (37.06–39.61) | 38.32 | 25.82 (24.79–26.88) | 25.82 | 4.80 (4.36–5.27) | 4.79 |

Abbreviations: CRC, colorectal cancer; FIT, faecal immunochemical test; RA, risk assessment; CI, confidence interval.

a. The observed positivity rate is determined as the total number of positive tests divided by the total number of participants using the specific screening test. In case of the Shanghai FIT+RA, this screening test was considered positive when both Shanghai FIT and the risk assessment were positive. The total number of participants consists of only participants for the Shanghai FIT or only participants for both the Shanghai FIT and the risk assessment.

b. The estimated positivity and detection rates are obtained by the Nelder-Mead Simplex method as explained in the methods section.

c. The observed detection rates were determined by multiplying the observed positivity rate with the positive predictive value to correct for the assumed 100% adherence in the model estimation.
Data and assumptions for colonoscopy

For colonoscopy procedures the caecal intubation rate was assumed to be 95%.\textsuperscript{30-32} The percentage of the population without adenomas or cancer but with hyperplastic polyps, lipomas, or other lesions that lead to polypectomy and pathology after colonoscopy (colonoscopy lack of specificity) has been estimated as 16%.\textsuperscript{28} This percentage was assumed to be independent of the screening round. The sensitivity for each lesion within reach was based on back-to-back colonoscopy studies increasing from 75% for small adenomas (≤5 mm) to 85% for medium-sized adenomas (6-9 mm) and to 95% for large adenomas (≥10 mm) and CRC.\textsuperscript{29} At detection, lesions are removed immediately.

Risks of complications reported in organised screening programs\textsuperscript{33-35} are lower than those reported for general practice colonoscopies.\textsuperscript{36,37} The major complications of colonoscopy are perforations (which can occur with or without polypectomy), serosal burns, bleeds requiring transfusion and bleeds not requiring transfusion.\textsuperscript{33-37} For the purposes of this analysis, complications are conditional on polypectomy,\textsuperscript{38} and we assume that polypectomy is only performed if colonoscopy is positive.

Information on complications arising from colonoscopy are scarce in China. One study reported 14 perforations associated with polypectomy out of 110,785 colonoscopies over a 12 year period (rate of perforation equals 0.012%).\textsuperscript{39} Another found 99 bleeding events associated with 15,553 polypectomies performed in 5,600 patients.\textsuperscript{40} Unfortunately this research did not report how many individuals experienced bleeding and therefore it could not be used in our analysis. We were unable to find any information of deaths associated with colonoscopy. Therefore we did not report rates of death or bleeding. Fortunately, there is research underway to address this gap in knowledge.\textsuperscript{41} Complications of colonoscopy were based on hospital admissions within 30 days of index colonoscopy.

Follow-up and surveillance

For all strategies, it was assumed that after a positive stool test result, a diagnostic colonoscopy was offered. Adenomas identified at diagnostic colonoscopies were removed and the individual entered colonoscopy surveillance at intervals dependent on adenoma findings consistent with European Society of Gastrointestinal Endoscopy Guidelines.\textsuperscript{42} Individuals with low risk findings (less than 3 low risk (i.e. less than 10mm) adenomas at primary screening) did not receive any surveillance while individuals with high-risk findings were offered surveillance with colonoscopy after three years, and thereafter repeated colonoscopies with
intervals of three to five years depending on the findings. It was assumed that surveillance stopped at 80 years of age.

**Parameters for the Sensitivity Analyses**

**Changes to test characteristics**

We conducted a series of sensitivity analyses to assess the robustness of our assumptions. Due to uncertainty about the performance of the validated FIT in the Chinese population, we conducted an analysis where we adjusted the characteristics such that the sensitivity and specificity were halfway between calibrated Shanghai FIT and validated FITs (Table 4).

**Table 4: Test characteristics of the validated faecal immunochemical tests used in the sensitivity analysis**

| Test               | Adenoma ≤5mm | Adenoma 6-9mm | Adenoma ≥10mm | CRC early preclinical | CRC late preclinical | Specificity (%) |
|--------------------|--------------|---------------|---------------|-----------------------|---------------------|-----------------|
| One sample FIT10   | 12.4         | 9.9           | 29.9          | 54.8                  | 84.5                | 91.7            |
| One sample FIT15   | 8.8          | 7.6           | 26.8          | 51.6                  | 83.0                | 92.3            |
| One sample FIT20   | 7.9          | 6.8           | 24.8          | 48.3                  | 81.2                | 92.7            |
| One sample FIT30   | 6.6          | 6.0           | 23.4          | 47.6                  | 81.0                | 92.9            |
| One sample FIT40   | 6.1          | 5.6           | 9.9           | 47.3                  | 80.7                | 93.1            |
| Two sample FIT10   | 12.4         | 12.4          | 41.8          | 59.8                  | 86.2                | 90.8            |
| Two sample FIT15   | 8.8          | 8.8           | 36.5          | 57.8                  | 85.5                | 91.6            |
| Two sample FIT20   | 7.9          | 7.9           | 33.6          | 55.3                  | 84.5                | 92.0            |
| Two sample FIT30   | 6.6          | 6.6           | 31.4          | 55.6                  | 84.7                | 92.4            |
| Two sample FIT40   | 6.1          | 6.1           | 12.4          | 55.3                  | 84.5                | 92.6            |

Abbreviations: CRC = colorectal cancer; FIT10 = faecal immunochemical test, 10 µg Hb/g faeces cut-off value; FIT15 = faecal immunochemical test, 15 µg Hb/g cut-off value; FIT20 = faecal immunochemical test, 20 µg Hb/g faeces cut-off value; FIT30 = faecal immunochemical test, 30 µg Hb/g cut-off value; FIT40 = faecal immunochemical test, 40 µg Hb/g cut-off value; µg Hb/g = micrograms of haemoglobin per gram faeces

**a.** It was assumed that the probability a CRC bleeds and thus the sensitivity of a FIT for CRC depends on the time until clinical diagnosis.17

**b.** Original specificity and sensitivity based on the positivity rates and detection rates of advanced neoplasia observed in the first screening round of two Dutch randomised trials.21,24 This was then adjusted so that it was halfway between this and the specificity and sensitivity of the Shanghai FIT. Sensitivity for adenomas smaller than 5 mm was assumed to be 0% for all tests, at any cut-off level.

**c.** A two sample FIT is considered positive when at least one sample contains detectable blood at the specified cut-off value.
Quality-adjusted life years

As information on quality-adjusted life years is scarce in the Chinese setting, they were excluded from the main analysis. Therefore, we assessed the impact of utilising international quality of life measurements in a sensitivity analysis (Table 5).

Table 5: International utility losses associated with colorectal cancer screening and treatment

| Per FIT | 0 |
|---|---|
| Per colonoscopy | 0.00274 |
| Per perforation during colonoscopy | 0.00548 |
| Per LY with CRC Care d,e | Initial Care | Continuing Care | Terminal care (Death CRC) | Terminal care (Death OC) |
| Stage I | 0.12 | 0.05 | 0.70 | 0.05 |
| Stage II | 0.18 | 0.05 | 0.70 | 0.05 |
| Stage III | 0.24 | 0.24 | 0.70 | 0.24 |
| Stage IV | 0.70 | 0.70 | 0.70 | 0.70 |

Abbreviations: CRC, Colorectal Cancer; FIT, faecal immunochemical test; OC, Other Cause; LY, Life Year
a. The loss of quality of life associated with a particular event.
b. Equal to 2 days per colonoscopy at a utility of 0.5.
c. Perforations associated with colonoscopy were assumed to be equal to 4 days at a utility of 0.5.
d. Care for CRC was divided in three clinically relevant phases: the initial, continuing, and terminal care phase. The initial care phase was defined as the first 12 months after diagnosis; the terminal care phase was defined as the final 12 months of life; the continuing care phase was defined as all months in between. In the terminal care phase, we distinguished between CRC patients dying from CRC and CRC patients dying from another cause. For patients surviving less than 24 months, the final 12 months were allocated to the terminal care phase and the remaining months were allocated to the initial care phase.
e. Utility losses for LYs with initial care were derived from a study by Ness and colleagues. For LYs with continuing care for stage III and IV CRC, we assumed the corresponding utility losses for LYs with initial care. For LYs with terminal care for CRC, we assumed the utility loss for LYs with initial care for stage IV CRC. For LYs with terminal care for another cause, we assumed the corresponding utility losses for LYs with continuing care.

Chinese surveillance pathway

Although there is conflicting advice in China about the post diagnostic colonoscopy pathway (including when to return to screening and the surveillance pathway), we assessed the impact of following a surveillance pathway derived from Chinese literature (Figure 1).
Figure 1: Screening pathway as reported by Gong\textsuperscript{44} and surveillance pathway as reported in Chinese clinical practice guidelines\textsuperscript{45}

Note: In the sensitivity analysis, the surveillance interval used after finding a low risk adenoma is 3 years and after finding a middle risk adenoma is 2 years.
### Parameters for the Probabilistic Sensitivity Analyses

Table 6: Test characteristics including mean and ranges used in the probabilistic sensitivity analysis.

|                     | Shanghai FIT + RA Mean | One-sample FIT10 Mean | Two-sample FIT10 Mean | Two-sample FIT20 Mean |
|---------------------|-------------------------|------------------------|------------------------|------------------------|
|                     | Range                   | Range                  | Range                  | Range                  |
| **Sensitivity (%)** |                         |                        |                        |                        |
| Adenoma 6-9mm       | 9.4 [9.2; 9.5]          | 11.0 [10.2; 11.9]      | 16.2 [15.1; 17.3]      | 7.1 [6.4; 7.7]         |
| Adenoma ≥10mm       | 33.0 [32.4; 33.5]       | 39.4 [37.5; 41.4]      | 63.3 [61.1; 65.6]      | 46.9 [44.6; 49.1]      |
| CRC early preclinical | 74.2 [72.4; 76.0]     | 65.5 [59.2; 70.8]      | 75.0 [69.9; 80.1]      | 66.0 [60.5; 71.5]      |
| CRC late preclinical | 93.1 [91.9; 94.2]      | 90.0 [85.7; 94.3]      | 93.5 [90.3; 96.7]      | 90.0 [86.0; 94.0]      |
| **Specificity (%)** |                         |                        |                        |                        |
|                     | 79.3 [79.3; 79.4]       | 96.1 [95.9; 96.3]      | 94.1 [93.9; 94.4]      | 96.7 [96.5; 96.9]      |
| **Probability of systematic test result for (%)**a |                     |                        |                        |                        |
| False positive      | 1.27 [1.27; 1.27]       | 1.27 [1.22; 1.32]      | 1.27 [1.23; 1.31]      | 1.27 [1.22; 1.32]      |
| Adenoma 6-9mm       | 73.1 [73.0; 73.2]       | 73.1 [72.7; 73.5]      | 73.1 [72.7; 73.5]      | 73.1 [72.7; 73.5]      |
| Adenoma ≥10mm       | 26.0 [26.0; 26.0]       | 26.0 [25.8; 26.2]      | 26.0 [25.8; 26.2]      | 26.0 [25.8; 26.2]      |

**Abbreviations:** CRC, colorectal cancer; FIT, faecal immunochemical test; RA, risk-assessment; FIT10, faecal immunochemical test, 10 µg Hb/g faeces cut-off value; FIT20, faecal immunochemical test, 20 µg Hb/g faeces cut-off value; µg Hb/g, micrograms of haemoglobin per gram faeces.

- a. The test characteristics were adjusted to take into account the effect of systematic false-positive and false-negative results (individuals who always test positive but do not have adenomas or who test negative because of adenomas which do not bleed). Ranges of the 95% confidence intervals differ between the tests due to different numbers of positive/negative tests and adenomas and/or CRCs detected.
- b. Ranges of the 95% confidence intervals for the test characteristics in the probabilistic sensitivity analyses are approximated using the binomial distribution, with p the probability of success (i.e. finding a lesion, or a positive/negative result) and n, the number of experiments (i.e. total number of lesions available, or total number of positive/negative tests). Using the formula \( \sigma = \sqrt{npr} \), we were able to compute ranges for the test characteristics and using these ranges, the two shape parameters \( \alpha \) and \( \beta \) for the beta-distribution.
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Supplementary Results Tables

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Table S1: Costs and effects (discounted at 3%) of 324 screening scenarios and a scenario without screening, per 1,000 simulated 45-year-olds, assuming perfect adherence

| Screening Strategy | Test | Start-Stop Age | Interval | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years<sup>a</sup> | Total Costs<sup>b</sup> | ICER<sup>ab</sup> |
|--------------------|------|----------------|----------|------|---------------|----------------|---------------|--------------|---------------|----------------|----------------|---------------|
| No Screening       |      |                |          | 0    | 49            | 0              | 0.01          | 49           | 11            | 21,482         | 869,648        |               |
| FIT-1-10           | 50-70| 3              |          | 5,901| 514           | 151            | 0.03          | 36           | 5             | 21,509         | 874,095        | 164           |
| FIT-1-15           | 50-70| 3              |          | 6,065| 425           | 96             | 0.03          | 38           | 6             | 21,507         | 880,303        | Dominated     |
| FIT-1-20           | 50-70| 3              |          | 6,163| 369           | 64             | 0.03          | 39           | 6             | 21,506         | 883,159        | Dominated     |
| FIT-2-10           | 50-70| 3              |          | 5,645| 652           | 239            | 0.04          | 33           | 5             | 21,511         | 884,484        | 4,027         |
| FIT-1-30           | 50-70| 3              |          | 6,246| 321           | 37             | 0.02          | 40           | 6             | 21,505         | 888,156        | Dominated     |
| FIT-1-10           | 50-75| 3              |          | 7,208| 583           | 188            | 0.04          | 34           | 4             | 21,511         | 889,841        | Dominated     |
| FIT-2-15           | 50-70| 3              |          | 5,844| 551           | 169            | 0.04          | 35           | 5             | 21,510         | 891,807        | Dominated     |
| FIT-2-20           | 50-70| 3              |          | 5,973| 484           | 123            | 0.03          | 36           | 5             | 21,509         | 893,295        | Dominated     |
| FIT-1-15           | 50-75| 3              |          | 7,419| 480           | 121            | 0.03          | 36           | 5             | 21,510         | 896,283        | Dominated     |
| FIT-1-40           | 50-70| 3              |          | 6,301| 282           | 22             | 0.02          | 42           | 6             | 21,504         | 897,592        | Dominated     |
| FIT-2-30           | 50-70| 3              |          | 6,081| 426           | 87             | 0.03          | 38           | 6             | 21,508         | 898,845        | Dominated     |
| FIT-1-20           | 50-75| 3              |          | 7,547| 415           | 82             | 0.03          | 38           | 5             | 21,508         | 898,949        | Dominated     |
| FIT-1-10           | 50-80| 3              |          | 8,171| 620           | 209            | 0.04          | 34           | 4             | 21,512         | 902,544        | Dominated     |
| FIT-2-10           | 50-75| 3              |          | 6,884| 744           | 294            | 0.04          | 31           | 4             | 21,514         | 904,162        | 7,778         |
| FIT-1-30           | 50-75| 3              |          | 7,656| 359           | 49             | 0.03          | 39           | 5             | 21,507         | 904,505        | Dominated     |
| FIT-1-20           | 55-70| 2              |          | 6,778| 379           | 66             | 0.03          | 38           | 6             | 21,505         | 904,663        | Dominated     |
| FIT-1-20           | 50-70| 2              |          | 9,424| 445           | 95             | 0.03          | 37           | 5             | 21,510         | 904,771        | Dominated     |
| FIT-1-15           | 55-70| 2              |          | 6,642| 436           | 101            | 0.03          | 37           | 5             | 21,506         | 905,330        | Dominated     |
| FIT-1-30           | 50-70| 2              |          | 9,599| 381           | 54             | 0.03          | 38           | 5             | 21,509         | 906,163        | Dominated     |
| FIT-1-15           | 50-70| 2              |          | 9,221| 519           | 144            | 0.03          | 36           | 5             | 21,511         | 906,225        | Dominated     |
| FIT-1-30           | 55-70| 2              |          | 6,895| 328           | 37             | 0.03          | 39           | 6             | 21,504         | 906,607        | Dominated     |
| FIT-1-10           | 55-70| 2              |          | 6,415| 527           | 160            | 0.03          | 35           | 5             | 21,507         | 906,973        | Dominated     |
| FIT-1-10           | 50-70| 2              |          | 8,887| 636           | 226            | 0.04          | 34           | 5             | 21,512         | 907,172        | Dominated     |
| FIT-2-40           | 50-70| 3              |          | 6,147| 385           | 67             | 0.03          | 39           | 6             | 21,508         | 908,998        | Dominated     |
| FIT-1-15 | 50-80  | 3    | 8,434 | 507   | 133  | 0.04 | 36  | 4    | 21,511 | 909,297 | Dominated |
| FIT-2-15 | 50-75  | 3    | 7,136 | 625   | 209  | 0.04 | 33  | 4    | 21,513 | 911,585 | Dominated |
| FIT-1-20 | 50-80  | 3    | 8,595 | 436   | 89   | 0.03 | 37  | 4    | 21,509 | 912,196 | Dominated |
| FIT-2-20 | 50-75  | 3    | 7,301 | 546   | 154  | 0.04 | 34  | 4    | 21,512 | 912,631 | Dominated |
| FIT-1-20 | 55-70  | 3    | 5,111 | 343   | 55   | 0.03 | 39  | 6    | 21,503 | 913,143 | Dominated |
| FIT-1-40 | 50-70  | 2    | 6,971 | 289   | 21   | 0.02 | 41  | 6    | 21,503 | 913,621 | Dominated |
| FIT-1-15 | 55-70  | 3    | 5,033 | 392   | 81   | 0.03 | 38  | 6    | 21,504 | 913,967 | Dominated |
| FIT-1-10 | 55-70  | 3    | 4,900 | 469   | 126  | 0.03 | 36  | 5    | 21,506 | 914,303 | Dominated |
| FIT-1-30 | 55-70  | 3    | 5,178 | 300   | 33   | 0.02 | 41  | 6    | 21,502 | 914,926 | Dominated |
| FIT-1-40 | 50-70  | 2    | 9,709 | 334   | 31   | 0.03 | 39  | 5    | 21,508 | 915,395 | Dominated |
| FIT-1-20 | 50-75  | 2    | 10,756 | 472  | 104  | 0.03 | 36  | 4    | 21,511 | 915,809 | Dominated |
| FIT-1-40 | 50-75  | 3    | 7,728 | 316   | 31   | 0.03 | 41  | 5    | 21,507 | 916,198 | Dominated |
| FIT-1-30 | 50-75  | 2    | 10,962 | 401  | 57   | 0.03 | 37  | 5    | 21,511 | 917,261 | Dominated |
| FIT-1-15 | 50-75  | 3    | 5,033 | 392   | 81   | 0.03 | 38  | 6    | 21,504 | 913,967 | Dominated |
| FIT-1-20 | 55-70  | 3    | 8,570 | 489   | 125  | 0.03 | 35  | 4    | 21,508 | 930,189 | Dominated |
| FIT-1-15 | 55-70  | 3    | 5,788 | 359   | 59   | 0.03 | 39  | 5    | 21,504 | 930,341 | Dominated |
| FIT-1-40 | 45-70  | 3    | 8,179 | 317   | 33   | 0.02 | 41  | 6    | 21,506 | 931,352 | Dominated |
| FIT-2-40 | 50-75  | 3    | 7,526 | 432   | 85   | 0.03 | 37  | 5    | 21,510 | 931,470 | Dominated |
| FIT-1-10  | 55-75  | 3  | 5,538  | 497  | 140  | 0.03 | 36 | 4  | 21,511 | 932,621 | Dominated |
| FIT-1-15  | 50-80  | 2  | 12,040 | 588  | 178  | 0.04 | 34 | 3  | 21,514 | 933,801 | Dominated |
| FIT-2-10  | 55-70  | 2  | 8,250  | 599  | 200  | 0.04 | 33 | 4  | 21,510 | 934,461 | Dominated |
| FIT-2-20  | 50-70  | 2  | 9,043  | 588  | 184  | 0.04 | 34 | 5  | 21,513 | 934,635 | Dominated |
| FIT-2-50  | 55-70  | 3  | 17,295 | 544  | 150  | 0.04 | 34 | 4  | 21,513 | 934,892 | Dominated |
| FIT-2-55  | 50-70  | 3  | 4,956  | 445  | 103  | 0.03 | 36 | 5  | 21,506 | 934,914 | Dominated |
| FIT-2-60  | 50-70  | 2  | 9,265  | 511  | 129  | 0.03 | 35 | 5  | 21,512 | 935,176 | Dominated |
| FIT-2-70  | 50-80  | 2  | 11,549 | 733  | 284  | 0.04 | 31 | 3  | 21,515 | 935,694 | Dominated |
| FIT-2-80  | 55-70  | 3  | 5,042  | 394  | 73   | 0.03 | 38 | 5  | 21,505 | 936,274 | Dominated |
| FIT-2-90  | 45-75  | 3  | 9,323  | 453  | 97   | 0.03 | 37 | 5  | 21,510 | 936,538 | Dominated |
| FIT-3-10  | 55-70  | 2  | 6,341  | 562  | 178  | 0.04 | 34 | 5  | 21,508 | 937,236 | Dominated |
| FIT-3-15  | 45-75  | 3  | 9,460  | 388  | 56   | 0.03 | 39 | 5  | 21,509 | 937,374 | Dominated |
| FIT-3-20  | 55-70  | 1  | 13,375 | 387  | 53   | 0.03 | 36 | 5  | 21,508 | 937,778 | Dominated |
| FIT-3-25  | 55-70  | 3  | 4,853  | 503  | 141  | 0.03 | 35 | 5  | 21,507 | 937,878 | Dominated |
| FIT-3-30  | 50-80  | 2  | 9,817  | 436  | 87   | 0.03 | 36 | 4  | 21,508 | 938,268 | Dominated |
| FIT-3-35  | 50-80  | 3  | 8,778  | 680  | 252  | 0.04 | 32 | 4  | 21,513 | 938,906 | Dominated |
| FIT-3-40  | 55-70  | 3  | 5,923  | 275  | 21   | 0.02 | 41 | 6  | 21,503 | 939,136 | Dominated |
| FIT-3-45  | 50-70  | 1  | 18,335 | 377  | 32   | 0.03 | 37 | 5  | 21,512 | 999,709 | Dominated |
| FIT-3-50  | 55-70  | 3  | 4,692  | 592  | 198  | 0.04 | 33 | 5  | 21,508 | 999,920 | Dominated |
| FIT-1-15 | 45-75 | 3 | 9,162 | 529 | 146 | 0.04 | 36 | 4 | 21,512 | 939,969 | Dominated |
| FIT-1-30 | 55-80 | 2 | 10,026 | 370 | 45 | 0.03 | 38 | 4 | 21,508 | 940,088 | Dominated |
| FIT-1-20 | 55-70 | 1 | 12,923 | 467 | 109 | 0.03 | 35 | 5 | 21,509 | 940,333 | Dominated |
| FIT-1-15 | 55-80 | 2 | 9,576 | 512 | 137 | 0.04 | 35 | 4 | 21,509 | 940,475 | Dominated |
| FIT-1-30 | 45-70 | 2 | 11,616 | 402 | 61 | 0.03 | 38 | 5 | 21,511 | 940,633 | Dominated |
| FIT-1-15 | 50-70 | 1 | 16,557 | 659 | 236 | 0.04 | 33 | 4 | 21,514 | 940,866 | Dominated |
| FIT-1-20 | 45-70 | 2 | 11,401 | 477 | 112 | 0.03 | 37 | 5 | 21,511 | 941,639 | Dominated |
| FIT-2-10 | 50-70 | 2 | 8,380 | 814 | 354 | 0.05 | 31 | 4 | 21,514 | 942,307 | Dominated |
| SH-FIT | 50-70 | 3 | 5,054 | 906 | 491 | 0.05 | 35 | 5 | 21,507 | 942,515 | Dominated |
| FIT-2-40 | 55-70 | 3 | 5,097 | 357 | 57 | 0.03 | 39 | 6 | 21,505 | 942,926 | Dominated |
| FIT-1-40 | 55-70 | 1 | 13,648 | 335 | 22 | 0.03 | 38 | 5 | 21,508 | 942,965 | Dominated |
| FIT-2-10 | 55-70 | 2 | 6,070 | 665 | 251 | 0.04 | 32 | 5 | 21,509 | 943,029 | Dominated |
| FIT-1-20 | 45-80 | 3 | 9,867 | 462 | 101 | 0.03 | 37 | 4 | 21,511 | 943,151 | Dominated |
| FIT-2-40 | 50-70 | 2 | 9,398 | 460 | 99 | 0.03 | 36 | 5 | 21,511 | 943,650 | Dominated |
| FIT-1-10 | 45-75 | 3 | 8,897 | 649 | 230 | 0.04 | 34 | 4 | 21,514 | 944,174 | Dominated |
| FIT-1-30 | 45-80 | 3 | 10,017 | 394 | 57 | 0.03 | 39 | 5 | 21,510 | 944,223 | Dominated |
| FIT-1-10 | 55-80 | 2 | 9,183 | 631 | 220 | 0.04 | 33 | 4 | 21,510 | 944,505 | Dominated |
| FIT-1-15 | 45-70 | 2 | 11,150 | 562 | 172 | 0.04 | 35 | 5 | 21,513 | 945,081 | Dominated |
| FIT-1-20 | 55-80 | 3 | 6,905 | 382 | 67 | 0.03 | 38 | 5 | 21,505 | 945,763 | Dominated |
| FIT-1-40 | 50-80 | 2 | 12,766 | 362 | 32 | 0.03 | 38 | 4 | 21,511 | 946,182 | Dominated |
| FIT-1-40 | 45-75 | 3 | 9,549 | 339 | 34 | 0.03 | 40 | 5 | 21,508 | 946,385 | Dominated |
| FIT-1-15 | 45-80 | 3 | 9,691 | 541 | 153 | 0.04 | 36 | 4 | 21,512 | 946,541 | Dominated |
| FIT-1-15 | 55-70 | 1 | 12,409 | 557 | 173 | 0.04 | 34 | 5 | 21,509 | 947,045 | Dominated |
| FIT-1-40 | 45-70 | 2 | 11,749 | 350 | 33 | 0.03 | 39 | 6 | 21,510 | 947,433 | Dominated |
| FIT-1-30 | 55-80 | 3 | 7,009 | 329 | 38 | 0.03 | 40 | 5 | 21,505 | 947,443 | Dominated |
| FIT-1-15 | 55-80 | 3 | 6,783 | 442 | 102 | 0.03 | 37 | 4 | 21,507 | 947,731 | Dominated |
| FIT-2-40 | 50-80 | 3 | 8,569 | 453 | 93 | 0.03 | 37 | 4 | 21,511 | 948,558 | Dominated |
| FIT-1-10 | 55-80 | 3 | 6,582 | 538 | 163 | 0.04 | 35 | 4 | 21,508 | 949,512 | Dominated |
| FIT-1-40 | 55-80 | 2 | 10,159 | 322 | 22 | 0.03 | 39 | 4 | 21,507 | 950,435 | Dominated |
| FIT-1-10 | 45-80 | 3 | 9,402 | 667 | 241 | 0.04 | 33 | 4 | 21,514 | 950,599 | Dominated |
| FIT-2-20 | 50-75 | 2 | 10,308 | 631 | 206 | 0.04 | 32 | 4 | 21,514 | 950,649 | Dominated |
| FIT-2-30 | 50-75 | 2 | 10,569 | 544 | 143 | 0.04 | 34 | 4 | 21,514 | 951,052 | Dominated |
| FIT-1-10 | 50-70 | 1 | 15,401 | 834 | 372 | 0.05 | 31 | 4 | 21,515 | 951,596 | Dominated |
| FIT-1-10 | 45-70 | 2 | 10,739 | 697 | 273 | 0.04 | 34 | 5 | 21,514 | 952,510 | Dominated |
| FIT-1-40 | 45-80 | 3 | 10,115 | 343 | 34 | 0.03 | 40 | 5 | 21,509 | 954,258 | Dominated |
| FIT-2-30 | 45-70 | 3 | 7,886 | 485 | 118 | 0.03 | 37 | 5 | 21,511 | 955,616 | Dominated |
| FIT-2-15 | 50-70 | 2 | 9,997 | 733 | 283 | 0.04 | 31 | 4 | 21,515 | 956,251 | Dominated |
| FIT-1-40 | 55-80 | 3 | 7,080 | 289 | 21 | 0.02 | 41 | 5 | 21,504 | 956,745 | Dominated |
| FIT-2-20 | 45-70 | 3 | 7,740 | 555 | 166 | 0.04 | 35 | 5 | 21,512 | 956,870 | Dominated |
| FIT-2-20 | 55-75 | 3 | 5,605 | 469 | 114 | 0.03 | 36 | 5 | 21,507 | 958,261 | Dominated |
| FIT-2-30 | 55-75 | 3 | 5,707 | 414 | 80 | 0.03 | 37 | 5 | 21,507 | 958,887 | Dominated |
| FIT-1-30 | 50-75 | 1 | 21,270 | 473 | 83 | 0.03 | 34 | 4 | 21,515 | 958,984 | Dominated |
| FIT-1-10 | 55-70 | 1 | 11,590 | 694 | 275 | 0.04 | 32 | 4 | 21,510 | 959,511 | Dominated |
| FIT-2-40 | 50-75 | 2 | 10,724 | 488 | 109 | 0.03 | 35 | 4 | 21,513 | 960,696 | Dominated |
| FIT-2-10 | 50-75 | 2 | 9,533 | 882 | 398 | 0.05 | 29 | 3 | 21,516 | 961,132 | Dominated |
| FIT-2-40 | 45-70 | 3 | 7,973 | 437 | 92 | 0.03 | 38 | 5 | 21,510 | 962,292 | Dominated |
| FIT-2-15 | 55-75 | 3 | 5,483 | 533 | 156 | 0.04 | 34 | 5 | 21,508 | 962,404 | Dominated |
| FIT-1-20 | 50-75 | 1 | 20,462 | 591 | 171 | 0.04 | 32 | 3 | 21,516 | 963,312 | Dominated |
| FIT-1-30 | 45-75 | 2 | 13,657 | 431 | 66 | 0.03 | 37 | 4 | 21,513 | 963,951 | Dominated |
| FIT-2-15 | 45-70 | 3 | 7,566 | 637 | 226 | 0.04 | 34 | 5 | 21,513 | 964,178 | Dominated |
| FIT-1-30 | 55-75 | 1 | 16,694 | 418 | 61 | 0.03 | 35 | 4 | 21,510 | 964,751 | Dominated |
| FIT-1-20 | 45-75 | 2 | 13,392 | 516 | 125 | 0.04 | 35 | 4 | 21,514 | 965,533 | Dominated |
| FIT-2-10 | 55-75 | 3 | 5,295 | 630 | 221 | 0.04 | 32 | 4 | 21,509 | 965,721 | Dominated |
| FIT-2-40 | 55-75 | 3 | 5,771 | 374 | 62 | 0.03 | 38 | 5 | 21,506 | 966,173 | Dominated |
| FIT-2-30 | 50-75 | 2 | 8,610 | 481 | 111 | 0.03 | 35 | 4 | 21,509 | 966,183 | Dominated |
| FIT-1-40 | 50-75 | 1 | 21,753 | 397 | 33 | 0.03 | 35 | 4 | 21,515 | 966,993 | Dominated |
| FIT-2-20 | 55-75 | 2 | 8,397 | 554 | 162 | 0.04 | 33 | 4 | 21,510 | 967,096 | Dominated |
| FIT-1-20 | 55-75 | 1 | 16,084 | 514 | 130 | 0.04 | 33 | 4 | 21,511 | 968,995 | Dominated |
| FIT-2-30 | 45-75 | 3 | 9,192 | 525 | 132 | 0.04 | 35 | 4 | 21,513 | 970,158 | Dominated |
| FIT-1-15 | 45-75 | 2 | 13,084 | 613 | 196 | 0.04 | 34 | 4 | 21,515 | 970,183 | Dominated |
| FIT-1-40 | 55-75 | 1 | 17,061 | 356 | 22 | 0.03 | 36 | 4 | 21,510 | 970,593 | Dominated |
| FIT-2-20 | 45-75 | 3 | 9,016 | 604 | 187 | 0.04 | 34 | 4 | 21,514 | 970,860 | Dominated |
| Value   | 984,636 | 983,251 | 982,901 | 982,797 | 979,085 | 978,320 | 978,146 | 977,790 | 977,533 | 979,085 | 979,247 | 979,418 | 979,997 | 980,248 | 981,127 | 982,049 | 982,797 | 982,901 | 983,237 | 983,251 | 984,636 |
|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
|       |       |       |       |       |       |       |
|-------|-------|-------|-------|-------|-------|-------|
| FIT-2-10 | 55-80 | 3 | 6,272 | 688 | 258 | 0.04 | 31 | 4 | 21,510 | 984,859 | Dominated |
| FIT-2-10 | 45-75 | 3 | 8,490 | 838 | 362 | 0.05 | 30 | 3 | 21,516 | 985,512 | Dominated |
| FIT-2-15 | 45-80 | 3 | 9,303 | 717 | 269 | 0.04 | 32 | 3 | 21,515 | 986,059 | Dominated |
| FIT-2-40 | 55-80 | 3 | 6,883 | 397 | 70 | 0.03 | 38 | 4 | 21,507 | 986,287 | Dominated |
| FIT-1-40 | 50-80 | 1 | 24,514 | 408 | 33 | 0.03 | 35 | 3 | 21,516 | 986,462 | Dominated |
| FIT-1-10 | 50-75 | 1 | 18,132 | 925 | 433 | 0.05 | 29 | 3 | 21,517 | 987,112 | Dominated |
| FIT-2-40 | 55-80 | 2 | 9,785 | 450 | 91 | 0.03 | 35 | 4 | 21,510 | 987,262 | Dominated |
| FIT-2-15 | 55-80 | 2 | 9,055 | 675 | 246 | 0.04 | 31 | 3 | 21,511 | 987,391 | Dominated |
| FIT-2-40 | 45-80 | 3 | 9,840 | 481 | 105 | 0.03 | 36 | 4 | 21,513 | 987,618 | Dominated |
| FIT-1-20 | 55-80 | 1 | 18,561 | 544 | 147 | 0.04 | 33 | 3 | 21,512 | 987,882 | Dominated |
| FIT-1-10 | 45-80 | 2 | 13,519 | 801 | 334 | 0.05 | 31 | 3 | 21,517 | 989,444 | 31,130 |
| FIT-1-40 | 55-80 | 1 | 19,818 | 367 | 23 | 0.03 | 36 | 3 | 21,511 | 990,233 | Dominated |
| FIT-1-15 | 50-80 | 1 | 21,842 | 766 | 301 | 0.05 | 30 | 3 | 21,517 | 991,409 | Dominated |
| FIT-2-30 | 45-70 | 2 | 11,208 | 551 | 154 | 0.04 | 35 | 5 | 21,514 | 991,845 | Dominated |
| FIT-2-10 | 45-80 | 3 | 8,958 | 863 | 380 | 0.05 | 30 | 3 | 21,517 | 992,642 | Dominated |
| SH-FIT | 55-70 | 2 | 5,267 | 939 | 504 | 0.05 | 33 | 5 | 21,506 | 994,525 | Dominated |
| FIT-2-20 | 45-70 | 2 | 10,934 | 641 | 222 | 0.04 | 34 | 5 | 21,514 | 994,905 | Dominated |
| FIT-1-10 | 55-75 | 1 | 14,316 | 786 | 334 | 0.05 | 30 | 4 | 21,512 | 994,922 | Dominated |
| FIT-2-10 | 55-80 | 2 | 8,592 | 810 | 347 | 0.05 | 29 | 3 | 21,512 | 996,526 | Dominated |
| SH-FIT | 55-70 | 3 | 4,238 | 795 | 405 | 0.04 | 35 | 5 | 21,504 | 997,304 | Dominated |
| FIT-1-15 | 55-80 | 1 | 17,680 | 664 | 237 | 0.04 | 31 | 3 | 21,512 | 997,705 | Dominated |
| FIT-2-40 | 45-70 | 2 | 11,370 | 493 | 117 | 0.03 | 36 | 5 | 21,513 | 998,393 | Dominated |
| FIT-1-30 | 45-70 | 1 | 22,637 | 476 | 89 | 0.03 | 35 | 4 | 21,515 | 998,625 | Dominated |
| SH-FIT | 50-80 | 3 | 6,824 | 1,144 | 663 | 0.06 | 32 | 4 | 21,510 | 999,827 | Dominated |
| FIT-1-40 | 45-70 | 1 | 23,144 | 398 | 34 | 0.03 | 36 | 5 | 21,515 | 1,001,944 | Dominated |
| FIT-2-15 | 45-70 | 2 | 10,605 | 748 | 305 | 0.04 | 33 | 4 | 21,515 | 1,004,414 | Dominated |
| FIT-2-30 | 55-70 | 1 | 12,547 | 538 | 154 | 0.04 | 34 | 5 | 21,510 | 1,004,668 | Dominated |
| FIT-2-30 | 50-70 | 1 | 16,758 | 634 | 211 | 0.04 | 32 | 4 | 21,515 | 1,004,976 | Dominated |
| FIT-2-40 | 55-70 | 1 | 12,875 | 479 | 114 | 0.03 | 35 | 5 | 21,509 | 1,006,756 | Dominated |
| FIT-1-20 | 45-70 | 1 | 21,782 | 600 | 185 | 0.04 | 33 | 4 | 21,516 | 1,007,233 | Dominated |
| FIT-1-10 | 50-80 | 1 | 20,134 | 986 | 476 | 0.05 | 28 | 3 | 21,518 | 1,007,490 | 31,660 |
|     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|
| FIT-2-20 | 50-70 | 1  | 15,965 | 754 | 304 | 0.04 | 31 | 4 | 21,515 | 1,009,036 | Dominated |
| FIT-2-40 | 50-70 | 1  | 17,224 | 560 | 157 | 0.04 | 33 | 4 | 21,515 | 1,009,612 | Dominated |
| FIT-2-20 | 55-70 | 1  | 11,988 | 632 | 224 | 0.04 | 32 | 4 | 21,510 | 1,010,209 | Dominated |
| FIT-2-10 | 45-70 | 2  | 10,114 | 904 | 429 | 0.05 | 31 | 4 | 21,516 | 1,015,357 | Dominated |
| FIT-1-10 | 55-80 | 1  | 16,312 | 846 | 378 | 0.05 | 29 | 3 | 21,513 | 1,015,619 | Dominated |
| FIT-2-15 | 50-70 | 1  | 15,051 | 891 | 413 | 0.05 | 30 | 4 | 21,515 | 1,018,164 | Dominated |
| FIT-2-15 | 55-70 | 1  | 11,340 | 739 | 305 | 0.04 | 31 | 4 | 21,511 | 1,020,540 | Dominated |
| FIT-1-15 | 45-70 | 1  | 20,815 | 739 | 295 | 0.04 | 32 | 4 | 21,517 | 1,021,111 | Dominated |
| SH-FIT-RA | 50-75 | 3  | 5,346 | 1,434 | 890 | 0.07 | 30 | 4 | 21,514 | 1,022,213 | Dominated |
| FIT-2-30 | 45-75 | 2  | 13,155 | 599 | 175 | 0.04 | 33 | 4 | 21,516 | 1,025,466 | Dominated |
| FIT-1-30 | 45-75 | 1  | 25,966 | 506 | 97  | 0.04 | 33 | 3 | 21,518 | 1,025,486 | Dominated |
| SH-FIT | 50-70 | 2  | 7,163 | 1,196 | 702 | 0.06 | 31 | 4 | 21,511 | 1,027,590 | Dominated |
| FIT-2-10 | 50-70 | 1  | 13,775 | 1,078 | 566 | 0.06 | 28 | 4 | 21,516 | 1,028,721 | Dominated |
| FIT-2-20 | 45-75 | 2  | 12,819 | 703 | 253 | 0.04 | 32 | 3 | 21,517 | 1,029,542 | Dominated |
| FIT-1-40 | 45-75 | 1  | 26,566 | 418 | 35  | 0.03 | 35 | 4 | 21,517 | 1,029,716 | Dominated |
| SH-FIT | 55-75 | 3  | 4,762 | 863 | 454 | 0.05 | 34 | 5 | 21,505 | 1,033,501 | Dominated |
| FIT-2-40 | 45-75 | 2  | 13,354 | 534 | 132 | 0.04 | 35 | 4 | 21,516 | 1,033,662 | Dominated |
| FIT-2-10 | 55-70 | 1  | 10,419 | 887 | 420 | 0.05 | 30 | 4 | 21,511 | 1,035,548 | Dominated |
| FIT-1-20 | 45-75 | 1  | 24,955 | 646 | 206 | 0.04 | 32 | 3 | 21,518 | 1,035,902 | Dominated |
| FIT-2-30 | 45-80 | 2  | 14,176 | 621 | 186 | 0.04 | 32 | 3 | 21,517 | 1,038,484 | Dominated |
| FIT-2-15 | 45-75 | 2  | 12,417 | 826 | 350 | 0.05 | 30 | 3 | 21,517 | 1,041,086 | Dominated |
| FIT-2-20 | 45-80 | 2  | 13,792 | 730 | 270 | 0.04 | 31 | 3 | 21,517 | 1,042,339 | Dominated |
| FIT-1-30 | 45-80 | 1  | 28,627 | 524 | 103 | 0.04 | 32 | 3 | 21,519 | 1,043,702 | Dominated |
| SH-FIT-RA | 50-80 | 3  | 5,860 | 1,539 | 973 | 0.07 | 29 | 3 | 21,514 | 1,045,156 | Dominated |
| FIT-1-10 | 45-70 | 1  | 19,306 | 952 | 468 | 0.05 | 30 | 4 | 21,517 | 1,045,692 | Dominated |
| FIT-2-40 | 45-80 | 2  | 14,403 | 551 | 139 | 0.04 | 34 | 3 | 21,517 | 1,047,603 | Dominated |
| FIT-1-40 | 45-80 | 1  | 29,329 | 429 | 35  | 0.03 | 34 | 3 | 21,518 | 1,049,078 | Dominated |
| FIT-2-30 | 55-75 | 1  | 15,580 | 598 | 186 | 0.04 | 32 | 4 | 21,512 | 1,050,769 | Dominated |
| FIT-2-30 | 50-75 | 1  | 19,799 | 693 | 243 | 0.04 | 30 | 3 | 21,517 | 1,051,216 | Dominated |
| SH-FIT | 55-75 | 2  | 6,636 | 1,113 | 633 | 0.06 | 31 | 4 | 21,508 | 1,052,112 | Dominated |
| FIT-1-15 | 45-75 | 1  | 23,816 | 803 | 331 | 0.05 | 30 | 3 | 21,519 | 1,052,274 | Dominated |
| Group   | Value Range | Value 1 | Value 2 | Value 3 | Value 4 | Value 5 | Value 6 | Value 7 | Value 8 | Value 9 | Value 10 | Ratio | Dominated |
|---------|-------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|--------|-----------|
| FIT-2-40 | 55-75       | 16,018  | 528     | 137     | 0.04    | 33      | 4       | 21,512  | 1,052,886| Dominated|
| FIT-2-15 | 45-80       | 13,331  | 861     | 373     | 0.05    | 29      | 3       | 21,518  | 1,053,960| Dominated|
| FIT-1-20 | 45-80       | 27,443  | 677     | 223     | 0.04    | 31      | 3       | 21,519  | 1,054,448| Dominated|
| FIT-2-10 | 45-75       | 11,820  | 1,004   | 494     | 0.05    | 28      | 3       | 21,518  | 1,055,227| Dominated|
| FIT-2-40 | 50-75       | 20,373  | 608     | 180     | 0.04    | 32      | 3       | 21,517  | 1,055,675| Dominated|
| SH-FIT-RA| 55-70       | 3,706   | 1,071   | 603     | 0.05    | 32      | 5       | 21,508  | 1,056,505| Dominated|
| FIT-2-20 | 50-75       | 18,824  | 831     | 353     | 0.05    | 29      | 3       | 21,517  | 1,057,255| Dominated|
| SH-FIT   | 50-75       | 8,105   | 1,314   | 792     | 0.06    | 30      | 4       | 21,512  | 1,057,526| Dominated|
| FIT-2-20 | 55-75       | 14,840  | 710     | 272     | 0.04    | 30      | 4       | 21,512  | 1,058,372| Dominated|
| SH-FIT-RA| 55-70       | 4,457   | 1,239   | 729     | 0.06    | 30      | 4       | 21,509  | 1,059,262| Dominated|
| SH-FIT   | 55-80       | 5,576   | 965     | 529     | 0.05    | 34      | 4       | 21,506  | 1,064,117| Dominated|
| SH-FIT   | 45-70       | 6,481   | 1,098   | 647     | 0.05    | 34      | 5       | 21,509  | 1,067,597| Dominated|
| FIT-2-10 | 45-80       | 12,651  | 1,049   | 526     | 0.06    | 27      | 3       | 21,519  | 1,068,267| Dominated|
| SH-FIT   | 55-80       | 7,201   | 1,182   | 686     | 0.06    | 31      | 4       | 21,509  | 1,068,421| Dominated|
| FIT-2-15 | 50-75       | 17,703  | 990     | 480     | 0.05    | 28      | 3       | 21,517  | 1,069,207| Dominated|
| SH-FIT   | 55-70       | 7,868   | 1,275   | 755     | 0.06    | 30      | 4       | 21,510  | 1,069,910| Dominated|
| FIT-1-15 | 45-80       | 26,112  | 846     | 359     | 0.05    | 29      | 3       | 21,520  | 1,071,462| 32,309  |
| FIT-2-15 | 55-75       | 13,989  | 839     | 372     | 0.05    | 29      | 3       | 21,512  | 1,071,578| Dominated|
| SH-FIT   | 50-70       | 10,250  | 1,577   | 1,008   | 0.07    | 28      | 4       | 21,514  | 1,074,395| Dominated|
| FIT-2-30 | 50-80       | 17,917  | 637     | 211     | 0.04    | 31      | 3       | 21,513  | 1,078,966| Dominated|
| FIT-2-30 | 50-80       | 22,142  | 732     | 268     | 0.05    | 29      | 3       | 21,518  | 1,079,189| Dominated|
| FIT-1-10 | 45-75       | 22,046  | 1,043   | 528     | 0.06    | 28      | 3       | 21,519  | 1,080,650| Dominated|
| FIT-2-40 | 55-80       | 18,475  | 560     | 155     | 0.04    | 32      | 3       | 21,513  | 1,081,598| Dominated|
| FIT-2-10 | 50-75       | 16,149  | 1,205   | 658     | 0.06    | 26      | 3       | 21,518  | 1,083,434| Dominated|
| FIT-2-40 | 50-80       | 22,837  | 640     | 198     | 0.04    | 31      | 3       | 21,518  | 1,084,351| Dominated|
| FIT-2-20 | 50-80       | 20,966  | 884     | 389     | 0.05    | 28      | 3       | 21,518  | 1,085,373| Dominated|
| SH-FIT   | 50-80       | 9,016   | 1,423   | 877     | 0.07    | 29      | 3       | 21,513  | 1,085,652| Dominated|
| FIT-2-20 | 55-80       | 16,976  | 763     | 308     | 0.05    | 29      | 3       | 21,513  | 1,086,709| Dominated|
| SH-FIT-RA| 50-70       | 6,002   | 1,574   | 1,006   | 0.07    | 28      | 4       | 21,514  | 1,087,581| Dominated|
| FIT-2-10 | 55-75       | 12,800  | 1,014   | 512     | 0.05    | 28      | 3       | 21,513  | 1,090,473| Dominated|
| FIT-2-15 | 50-80       | 19,618  | 1,055   | 528     | 0.06    | 27      | 3       | 21,518  | 1,097,581| Dominated|
| SH-FIT  | 45-75 | 3   | 7,513 | 1,233 | 743 | 0.06 | 32  | 4   | 21,511 | 1,098,318 | Dominated |
| FIT-2-15 | 55-80 | 1   | 15,900 | 904  | 420 | 0.05 | 28  | 3   | 21,513 | 1,100,195 | Dominated |
| SH-FIT  | 45-70 | 2   | 8,575 | 1,366 | 854 | 0.06 | 31  | 5   | 21,513 | 1,100,494 | Dominated |
| SH-FIT-RA | 55-75 | 3   | 4,158 | 1,167 | 676 | 0.06 | 31  | 4   | 21,509 | 1,100,988 | Dominated |
| FIT-1-10 | 45-80 | 1   | 24,054 | 1,104 | 572 | 0.06 | 27  | 2   | 21,520 | 1,101,071 | 59,218 |
| SH-FIT  | 45-80 | 3   | 7,888 | 1,278 | 777 | 0.06 | 32  | 4   | 21,512 | 1,110,020 | Dominated |
| FIT-2-10 | 50-80 | 1   | 17,765 | 1,286 | 720 | 0.06 | 25  | 2   | 21,518 | 1,111,829 | Dominated |
| FIT-2-30 | 45-70 | 1   | 21,081 | 708  | 263 | 0.04 | 32  | 4   | 21,517 | 1,114,413 | Dominated |
| SH-FIT-RA | 50-70 | 1   | 7,715 | 1,920 | 1,303 | 0.08 | 26  | 4   | 21,515 | 1,115,459 | Dominated |
| FIT-4-0  | 45-70 | 1   | 21,688 | 619  | 195 | 0.04 | 33  | 4   | 21,517 | 1,115,466 | Dominated |
| FIT-2-10 | 55-80 | 1   | 14,414 | 1,095 | 574 | 0.06 | 27  | 3   | 21,513 | 1,119,186 | Dominated |
| SH-FIT-RA | 50-75 | 2   | 6,768 | 1,733 | 1,134 | 0.08 | 27  | 3   | 21,515 | 1,126,386 | Dominated |
| FIT-2-20 | 45-70 | 1   | 20,045 | 854  | 381 | 0.05 | 30  | 4   | 21,518 | 1,126,396 | Dominated |
| SH-FIT-RA | 55-75 | 2   | 5,534 | 1,463 | 907 | 0.07 | 28  | 3   | 21,511 | 1,129,147 | Dominated |
| SH-FIT  | 55-75 | 1   | 9,542 | 1,478 | 918 | 0.07 | 28  | 3   | 21,511 | 1,130,051 | Dominated |
| SH-FIT  | 50-75 | 1   | 11,862 | 1,771 | 1,164 | 0.08 | 26  | 3   | 21,516 | 1,133,633 | Dominated |
| SH-FIT-RA | 55-80 | 3   | 4,810 | 1,301 | 782 | 0.06 | 30  | 3   | 21,510 | 1,138,803 | Dominated |
| SH-FIT-RA | 55-80 | 2   | 5,890 | 1,535 | 965 | 0.07 | 28  | 3   | 21,511 | 1,144,689 | Dominated |
| FIT-2-15 | 45-70 | 1   | 18,851 | 1,021 | 520 | 0.05 | 29  | 4   | 21,518 | 1,146,170 | Dominated |
| SH-FIT-RA | 55-70 | 1   | 6,074 | 1,577 | 1,003 | 0.07 | 27  | 4   | 21,511 | 1,151,265 | Dominated |
| SH-FIT  | 50-80 | 1   | 10,381 | 1,576 | 998 | 0.07 | 27  | 3   | 21,511 | 1,153,884 | Dominated |
| SH-FIT-RA | 50-80 | 2   | 7,394 | 1,858 | 1,237 | 0.08 | 26  | 3   | 21,516 | 1,155,841 | Dominated |
| SH-FIT  | 50-80 | 1   | 12,721 | 1,872 | 1,247 | 0.08 | 26  | 3   | 21,516 | 1,157,678 | Dominated |
| SH-FIT  | 45-75 | 2   | 9,946 | 1,537 | 984 | 0.07 | 29  | 4   | 21,515 | 1,157,820 | Dominated |
| FIT-2-30 | 45-75 | 1   | 24,128 | 767  | 295 | 0.05 | 30  | 3   | 21,519 | 1,160,623 | Dominated |
| FIT-2-40 | 45-75 | 1   | 24,842 | 667  | 218 | 0.04 | 31  | 3   | 21,519 | 1,161,608 | Dominated |
| SH-FIT-RA | 45-70 | 3   | 5,648 | 1,490 | 959 | 0.07 | 31  | 4   | 21,514 | 1,164,269 | Dominated |
| FIT-2-10 | 45-70 | 1   | 17,201 | 1,248 | 712 | 0.06 | 28  | 4   | 21,518 | 1,172,422 | Dominated |
| SH-FIT  | 45-80 | 2   | 10,516 | 1,606 | 1,037 | 0.07 | 29  | 3   | 21,515 | 1,174,222 | Dominated |
| FIT-2-20 | 45-75 | 1   | 22,910 | 932  | 430 | 0.05 | 28  | 3   | 21,520 | 1,174,611 | Dominated |
| FIT-2-30 | 45-80 | 1   | 26,476 | 807  | 320 | 0.05 | 29  | 2   | 21,520 | 1,188,375 | Dominated |
| Screening Strategy | Interval (Years) | Test Cut-off | Test Results | Success Rate | Total Test Cost (¥) | ICER (¥/QALY) | Notes |
|--------------------|-----------------|--------------|--------------|--------------|---------------------|----------------|-------|
| SH-FIT-RA          | 50-75           | 1            | 8,898        | 2,159        | 1,504               | 0.09           | 24    | 3    | 21,517 | 1,188,421 | Dominated |
| FIT-2-40           | 45-80           | 1            | 27,310       | 699          | 235                 | 0.04           | 30    | 3    | 21,520 | 1,190,044 | Dominated |
| FIT-2-15           | 45-75           | 1            | 21,512       | 1,120        | 587                 | 0.06           | 27    | 3    | 21,520 | 1,196,983 | Dominated |
| FIT-2-20           | 45-80           | 1            | 25,058       | 984          | 466                 | 0.05           | 27    | 2    | 21,520 | 1,202,507 | Dominated |
| SH-FIT-RA          | 45-70           | 2            | 7,160        | 1,804        | 1,220               | 0.08           | 28    | 4    | 21,516 | 1,203,877 | Dominated |
| SH-FIT-RA          | 45-70           | 3            | 6,527        | 1,677        | 1,102               | 0.07           | 29    | 3    | 21,516 | 1,205,624 | Dominated |
| SH-FIT-RA          | 50-80           | 1            | 9,379        | 2,255        | 1,585               | 0.09           | 24    | 3    | 21,516 | 1,210,308 | Dominated |
| SH-FIT-RA          | 55-75           | 1            | 7,174        | 1,800        | 1,189               | 0.08           | 26    | 3    | 21,512 | 1,211,069 | Dominated |
| SH-FIT-RA          | 45-80           | 3            | 6,816        | 1,734        | 1,149               | 0.08           | 29    | 3    | 21,516 | 1,218,569 | Dominated |
| FIT-2-15           | 45-80           | 1            | 23,434       | 1,186        | 635                 | 0.06           | 26    | 2    | 21,521 | 1,225,260 | 302,900 |
| FIT-2-10           | 45-75           | 1            | 19,588       | 1,375        | 804                 | 0.07           | 25    | 3    | 21,520 | 1,226,525 | Dominated |
| SH-FIT-RA          | 55-80           | 1            | 7,529        | 1,871        | 1,248               | 0.08           | 25    | 3    | 21,512 | 1,227,673 | Dominated |
| SH-FIT             | 45-70           | 1            | 12,622       | 1,852        | 1,259               | 0.08           | 28    | 4    | 21,516 | 1,235,011 | Dominated |
| FIT-2-10           | 45-80           | 1            | 21,214       | 1,456        | 867                 | 0.07           | 24    | 2    | 21,521 | 1,254,847 | 739,677 |
| SH-FIT-RA          | 45-75           | 2            | 8,256        | 2,030        | 1,402               | 0.08           | 26    | 3    | 21,518 | 1,275,517 | Dominated |
| SH-FIT-RA          | 45-80           | 2            | 8,626        | 2,104        | 1,463               | 0.09           | 26    | 3    | 21,518 | 1,291,208 | Dominated |
| SH-FIT             | 45-75           | 1            | 14,305       | 2,054        | 1,423               | 0.09           | 26    | 3    | 21,518 | 1,295,685 | Dominated |
| SH-FIT             | 45-80           | 1            | 15,186       | 2,157        | 1,508               | 0.09           | 25    | 3    | 21,518 | 1,320,127 | Dominated |
| SH-FIT-RA          | 45-70           | 1            | 9,490        | 2,265        | 1,629               | 0.09           | 26    | 4    | 21,517 | 1,350,956 | Dominated |
| SH-FIT-RA          | 45-75           | 1            | 10,746       | 2,519        | 1,841               | 0.10           | 24    | 3    | 21,519 | 1,422,729 | Dominated |
| SH-FIT-RA          | 45-80           | 1            | 11,197       | 2,609        | 1,917               | 0.10           | 23    | 3    | 21,519 | 1,443,352 | Dominated |

Note: Screening strategies: screening test - screening interval – test cut-off. Grey shading highlights screening scenarios on the efficient frontier.
Abbreviations: CRC, colorectal cancer; FIT, faecal immunochemical test; ICER, incremental cost-effectiveness ratio.

a. Results are discounted at an annual rate of 3%.
b. Costs are presented in Chinese Renminbi Yuan (¥).
### Table S2: Costs and effects per 1,000 simulated 45-year-olds for screening scenarios on the efficient frontier.

**a) Results are undiscounted**

| Screening Strategy | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years | Total Costs* | ICER* |
|--------------------|------|---------------|-----------------|---------------|---------------|--------------|------------|--------------|-------|
| No Screening       | 0    | 49            | 0               | 0.01          | 49            | 11           | 35,247     | 1,860,008    |       |
| FIT-1-10           | 55-75| 3             | 5,538           | 497           | 140           | 0.03         | 36         | 5            | 35,316 |
| FIT-1-10           | 55-75| 2             | 8,250           | 599           | 200           | 0.04         | 33         | 4            | 35,233 |
| FIT-1-10           | 50-80| 2             | 11,549          | 733           | 284           | 0.04         | 31         | 3            | 35,335 |
| FIT-1-10           | 45-80| 2             | 13,519          | 801           | 334           | 0.05         | 31         | 3            | 35,339 |
| FIT-1-10           | 45-80| 1             | 26,112          | 846           | 359           | 0.05         | 29         | 3            | 35,346 |
| FIT-1-10           | 45-80| 1             | 24,054          | 1,104         | 572           | 0.06         | 27         | 2            | 35,347 |
| FIT-1-15           | 45-80| 1             | 26,112          | 846           | 359           | 0.05         | 29         | 3            | 35,346 |
| FIT-2-10           | 45-80| 1             | 24,054          | 1,104         | 572           | 0.06         | 27         | 2            | 35,347 |
| FIT-1-10           | 45-80| 1             | 24,054          | 1,104         | 572           | 0.06         | 27         | 2            | 35,347 |

**Note:** Screening strategies: screening test - screening interval – test cut-off. Grey shading highlights optimal screening scenario at the willingness-to-pay threshold.

**Abbreviations:** CRC, colorectal cancer; FIT, faecal immunochemical test; ICER, incremental cost-effectiveness ratio.

**a.** Costs are presented in Chinese Renminbi (¥).

**b.** Results are discounted at an annual rate of 5%.

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### Table S2: Costs and effects per 1,000 simulated 45-year-olds for screening scenarios on the efficient frontier.

**b) Results are discounted at 5%**

| Screening Strategy | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years* | Total Costsab | ICERab |
|--------------------|------|---------------|-----------------|---------------|---------------|--------------|------------|--------------|--------|
| No Screening       | 0    | 49            | 0               | 0.01          | 49            | 11           | 16,550     | 561,215 |
| FIT-1-10           | 50-70| 3             | 5,901           | 514           | 151           | 0.03         | 36         | 5            | 16,565 |
| FIT-2-10           | 50-70| 3             | 5,645           | 652           | 239           | 0.04         | 33         | 4            | 16,568 |
| FIT-1-10           | 50-75| 3             | 6,884           | 744           | 294           | 0.04         | 31         | 3            | 16,568 |
| FIT-2-10           | 50-80| 3             | 7,768           | 795           | 327           | 0.05         | 30         | 3            | 16,568 |
| FIT-1-15           | 45-80| 1             | 26,112          | 846           | 359           | 0.05         | 29         | 3            | 16,572 |
| FIT-2-10           | 45-80| 1             | 24,054          | 1,104         | 572           | 0.06         | 27         | 2            | 16,572 |
| FIT-2-15           | 45-80| 1             | 23,434          | 1,186         | 635           | 0.06         | 26         | 2            | 16,572 |
| FIT-2-10           | 45-80| 1             | 21,214          | 1,456         | 867           | 0.07         | 24         | 2            | 16,572 |

**Note:** Screening strategies: screening test - screening interval – test cut-off. Grey shading highlights optimal screening scenario at the willingness-to-pay threshold.

**Abbreviations:** CRC, colorectal cancer; FIT, faecal immunochemical test; ICER, incremental cost-effectiveness ratio.

**a.** Costs are presented in Chinese Renminbi (¥).

**b.** Results are discounted at an annual rate of 5%.
Table S3: Costs and effects (discounted at 3%) per 1,000 simulated 45-year-olds for screening scenarios on the efficient frontier

a) Assuming adjusted FIT characteristic’s

| Screening Strategy | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years\(^a\) | Total Costs\(^ab\) | ICER\(^ab\) |
|--------------------|------|---------------|-----------------|--------------|--------------|--------------|----------------|-----------------|--------|
| No Screening       |      |               |                 |              |              |              | 21,482         | 869,648         |        |
| FIT-1-10           | 50-70| 3             | 5,443           | 729          | 335          | 0.04         | 35             | 21,508          | 914,230 | 1,700 |
| FIT-2-10           | 50-70| 3             | 5,324           | 797          | 373          | 0.04         | 34             | 21,509          | 928,340 | 9,344 |
| FIT-2-10           | 50-75| 3             | 6,473           | 920          | 456          | 0.05         | 32             | 21,512          | 959,707 | 13,124 |
| FIT-1-10           | 45-70| 3             | 7,250           | 991          | 506          | 0.06         | 29             | 21,515          | 1,031,672 | 27,739 |
| FIT-1-10           | 45-70| 1             | 15,621          | 1,538        | 949          | 0.07         | 26             | 21,517          | 1,107,699 | 42,153 |
| FIT-1-10           | 45-70| 1             | 18,630          | 1,758        | 1,144        | 0.08         | 26             | 21,519          | 1,242,210 | 60,319 |
| FIT-1-10           | 45-80| 1             | 17,690          | 1,873        | 1,240        | 0.08         | 24             | 21,520          | 1,344,893 | 256,708 |

b) Assuming a 50% reduction in the costs of the validated FITs.

| Screening Strategy | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years\(^a\) | Total Costs\(^ab\) | ICER\(^ab\) |
|--------------------|------|---------------|-----------------|--------------|--------------|--------------|----------------|-----------------|--------|
| No Screening       |      |               |                 |              |              |              | 21,482         | 869,648         |        |
| FIT-2-10           | 50-70| 3             | 5,645           | 652          | 239          | 0.04         | 33             | 21,511          | 852,337 | 4,635 |
| FIT-2-10           | 50-70| 3             | 6,884           | 744          | 294          | 0.04         | 31             | 21,514          | 864,063 | 9,769 |
| FIT-2-10           | 50-80| 3             | 7,768           | 795          | 327          | 0.05         | 30             | 21,515          | 873,441 | 14,376 |
| FIT-1-30           | 50-80| 1             | 23,928          | 491          | 89           | 0.04         | 33             | 21,516          | 892,706 | 16,383 |
| FIT-1-30           | 45-80| 1             | 28,627          | 524          | 103          | 0.04         | 32             | 21,519          | 933,826 | 36,773 |
| FIT-1-15           | 45-80| 1             | 26,112          | 846          | 359          | 0.05         | 29             | 21,520          | 970,599 | 66,922 |
| FIT-2-30           | 45-80| 1             | 26,476          | 807          | 320          | 0.05         | 29             | 21,520          | 1,018,114 | 66,922 |
| FIT-2-15           | 45-80| 1             | 23,434          | 1,186        | 635          | 0.06         | 26             | 21,521          | 1,073,151 | 275,187 |
| FIT-2-10           | 45-80| 1             | 21,214          | 1,456        | 867          | 0.07         | 24             | 21,521          | 1,115,972 | 1,070,518 |
### c) Assuming a 200% increase in the costs of the validated FITs.

| Screening Strategy | Test | Start-Stop Interval | Age | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years | Total Costs | ICER |
|--------------------|------|---------------------|-----|------|---------------|-----------------|---------------|---------------|--------------|------------|-------------|------|
| No Screening       |      |                     |     | 0    | 49            | 0               | 0.01          | 49            | 11           | 21,482     | 869,648     |      |
| FIT-1-10           | 50-70| 3                   | 49  | 5,901| 514           | 151             | 0.03          | 36            | 5            | 21,509     | 914,585     | 1,662 |
| FIT-1-10           | 50-75| 3                   | 49  | 7,208| 583           | 188             | 0.04          | 34            | 4            | 21,511     | 940,484     | 10,078 |
| FIT-2-10           | 50-75| 3                   | 49  | 6,884| 744           | 294             | 0.04          | 31            | 4            | 21,514     | 984,361     | 17,274 |
| FIT-2-10           | 50-80| 3                   | 49  | 7,768| 795           | 327             | 0.05          | 30            | 3            | 21,515     | 1,006,655   | 23,223 |
| FIT-1-10           | 45-80| 2                   | 49  | 13,519| 801          | 334             | 0.05          | 31            | 3            | 21,517     | 1,098,355   | 39,869 |
| FIT-1-10           | 45-80| 1                   | 49  | 24,054| 1,104       | 572             | 0.06          | 27            | 2            | 21,520     | 1,288,058   | 62,198 |
| FIT-2-10           | 45-80| 1                   | 49  | 21,214| 1,456       | 867             | 0.07          | 24            | 2            | 21,521     | 1,532,598   | 543,423 |

### d) Assuming Chinese surveillance guidelines.

| Screening Strategy | Test | Start-Stop Interval | Age | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years | Total Costs | LY ICER |
|--------------------|------|---------------------|-----|------|---------------|-----------------|---------------|---------------|--------------|------------|-------------|--------|
| No Screening       |      |                     |     | 0    | 49            | 0               | 0.01          | 49            | 11           | 21,482     | 869,648     |        |
| FIT-1-10           | 50-70| 3                   | 49  | 6,572| 638           | 343             | 0.03          | 39            | 6            | 21,509     | 932,920     | 2,357  |
| FIT-2-10           | 50-70| 3                   | 49  | 6,563| 801           | 449             | 0.04          | 35            | 5            | 21,512     | 946,907     | 4,632  |
| FIT-1-10           | 50-75| 3                   | 49  | 8,108| 949           | 561             | 0.04          | 32            | 4            | 21,515     | 980,771     | 10,924 |
| FIT-2-10           | 50-80| 3                   | 49  | 9,185| 1,008         | 601             | 0.05          | 31            | 3            | 21,516     | 995,748     | 11,432 |
| FIT-1-15           | 50-80| 1                   | 49  | 25,386| 967          | 570             | 0.05          | 31            | 3            | 21,519     | 1,073,331   | 27,808 |
| FIT-1-10           | 50-80| 1                   | 49  | 25,130| 1,291       | 815             | 0.06          | 28            | 2            | 21,520     | 1,112,751   | 34,579 |
| FIT-1-15           | 45-80| 1                   | 49  | 30,333| 1,113       | 695             | 0.05          | 30            | 2            | 21,522     | 1,173,484   | 35,516 |
| FIT-1-15           | 45-80| 1                   | 49  | 30,063| 1,499       | 993             | 0.06          | 27            | 2            | 21,523     | 1,232,248   | 46,638 |
| FIT-2-10           | 45-80| 1                   | 49  | 29,675| 2,123       | 1,499           | 0.08          | 22            | 2            | 21,524     | 1,487,932   | 164,958 |
| SH-FIT-RA          | 45-80| 1                   | 49  | 27,798| 6,290       | 5,290           | 0.18          | 16            | 1            | 21,526     | 2,433,797   | 750,886 |
### e) Assuming international quality of life estimates.

| Screening Strategy | Test | Start-Stop Age | FITs | Colonoscopies | False Positives | Complications | CRC Incidence | CRC Mortality | Life Years* | Total QALYs* | Total Costsab | ICERab |
|--------------------|------|----------------|------|----------------|-----------------|---------------|---------------|--------------|-------------|--------------|---------------|----------|
| No Screening       |      | 0              | 49   | 0              | 0.01            | 49            | 11            | 21,482       | 19,035      | 869,648      |               |          |
| FIT-1-10           | 50-70| 3              | 5,901| 514            | 151             | 0.03          | 36            | 5            | 21,509      | 19,768       | 874,095      | 6        |
| FIT-2-10           | 50-70| 3              | 5,645| 652            | 239             | 0.04          | 33            | 5            | 21,511      | 19,892       | 884,484      | 84       |
| FIT-2-10           | 50-75| 3              | 6,884| 744            | 294             | 0.04          | 31            | 4            | 21,514      | 19,959       | 904,162      | 298      |
| FIT-2-10           | 45-75| 3              | 8,490| 838            | 362             | 0.05          | 30            | 3            | 21,516      | 20,085       | 985,512      | 642      |
| FIT-2-10           | 45-80| 3              | 8,958| 863            | 380             | 0.05          | 30            | 3            | 21,517      | 20,096       | 992,642      | 652      |
| FIT-1-10           | 45-75| 1              | 22,046| 1,043        | 528             | 0.06          | 28            | 3            | 21,519      | 20,213       | 1,080,650    | 754      |
| FIT-1-10           | 45-80| 1              | 24,054| 1,104        | 572             | 0.06          | 27            | 2            | 21,520      | 20,232       | 1,101,071    | 1,092    |
| FIT-2-10           | 45-80| 1              | 21,214| 1,456        | 867             | 0.07          | 24            | 2            | 21,521      | 20,277       | 1,254,847    | 3,374    |

Note: Screening strategies: screening test - screening interval – test cut-off. Grey shading highlights optimal screening scenario at the willingness-to-pay threshold.

Abbreviations: CRC, colorectal cancer; FIT, faecal immunochemical test; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life-years.

a. Results are discounted at an annual rate of 3%.

b. Costs are presented in Chinese Renminbi (¥).
Supplementary Results Figures

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Figure S1: Costs and life years gained (per 1,000 45-year-olds for all 324 colorectal cancer screening scenarios and a scenario without screening, assuming perfect adherence. The efficient frontier connects the economically efficient strategies.  
a) Results are undiscounted.
b) Results are discounted at 5%.

Abbreviations: FIT, faecal immunochemical test; ICER, incremental cost-effectiveness ratio, LYs, life years; µg Hb/g, micrograms of haemoglobin per gram faeces

a. Discounted costs and life years gained reflect total costs and life years gained of a screening program, accounting for time preference for present over future outcomes. Life years gained are plotted on the y-axis, and total costs are plotted on the x-axis. Each possible screening strategy is represented by a point. Strategies that form the solid line connecting the points lying left and upward are the economically rational subset of choices. This line is called the efficient frontier. The inverse slope of the line represents the incremental cost-effectiveness ratio of the connected strategies. Points lying to the right and beneath the line represent the dominated strategies.
Figure S2: Costs and life years gained (discounted at 3%) per 1,000 45-year-olds for all 324 colorectal cancer screening scenarios and a scenario without screening. The efficient frontier connects the economically efficient strategies.

a) Assuming perfect adherence and adjusted FIT characteristic's.
b) Assuming perfect adherence and a 50% decrease in the costs of the validated FITs.

Supplemental material

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c) Assuming perfect adherence and a 200% increase in the costs of the validated FITs.

- Screening test
  - No Screening
  - Shanghai FIT
  - Shanghai FIT and Risk Assessment
  - One sample FIT 10μg Hgb
  - One sample FIT 15μg Hgb
  - One sample FIT 20μg Hgb
  - One sample FIT 30μg Hgb
  - One sample FIT 40μg Hgb
  - Two sample FIT 10μg Hgb
  - Two sample FIT 15μg Hgb
  - Two sample FIT 20μg Hgb
  - Two sample FIT 30μg Hgb
  - Two sample FIT 40μg Hgb

- Screening start and stop ages
  - 45-70 years
  - 45-75 years
  - 50-80 years
  - 50-70 years
  - 50-75 years
  - 55-70 years
  - 55-75 years
  - 55-80 years

| Screen leaf | No/different FIT | FIT-1-10 | FIT-1-10 | FIT-2-10 | FIT-2-10 | FIT-1-10 | FIT-1-10 |
|-------------|-----------------|----------|----------|----------|----------|----------|----------|
| Screen ages | 50-70 | 50-75 | 50-75 | 50-80 | 45-80 | 45-80 | 45-80 |
| Screen frequency | 3 | 3 | 3 | 3 | 2 | 1 | 1 |
| #CER (k) | 1662 | 10078 | 17274 | 23023 | 38669 | 62198 | 543423 |
d) Assuming perfect adherence and Chinese surveillance guidelines.
e) Assuming perfect adherence and international quality of life estimates.

Abbreviations: FIT, faecal immunochemical test; ICER, incremental cost-effectiveness ratio, LY, life years; QALY, quality adjusted life years; µg Hb/g, micrograms of haemoglobin per gram faeces

- Discounted costs and life years gained reflect total costs and life years gained of a screening program, accounting for time preference for present over future outcomes. Life years gained are plotted on the y-axis, and total costs are plotted on the x-axis. Each possible screening strategy is represented by a point. Strategies that form the solid line connecting the points lying left and upward are the economically rational subset of choices. This line is called the efficient frontier. The inverse slope of the line represents the incremental cost-effectiveness ratio of the connected strategies. Points lying to the right and beneath the line represent the dominated strategies.
Figure S3: Cost-effectiveness acceptability curve from the probabilistic sensitivity analysis

The vertical dashed line represents the willingness-to-pay threshold in China (this threshold was set at three times the Chinese gross domestic product per capita in 2018 (¥193,931 RMB which is equal to $29,313 US) for one LYG.)