Cost-effectiveness analysis of different screening strategies for colorectal cancer in Guangzhou, southern China: a Markov simulation analysis based on natural community screening results

Qin Zhou,1 Hai-lin Li,1 Yan Li,1 Yu-ting Gu,2 Ying-ru Liang,1 Hua-zhang Liu,1 Ke Li,1 Hang Dong,1 Yuan-yuan Chen,1 Guo-zhen Lin1

ABSTRACT

Objectives To evaluate the cost-effectiveness of four different primary screening strategies: high-risk factor questionnaire (HRFQ) alone, single immunochemical faecal occult blood test (iFOBT), double iFOBT and HRFQ+double iFOBT for colorectal cancer (CRC) screening compared with no screening using the Markov model.

Methods TreeAge Pro V.2011 software was used to simulate the Markov model. The incremental cost-effectiveness ratio, which was compared with the willingness-to-pay (WTP) threshold, was used to reflect the cost-effectiveness of the CRC screening method. One-way sensitivity analysis and probabilistic sensitivity analysis were used for parameter uncertainty.

Results All strategies had greater effectiveness because they had more quality-adjusted life years (QALYs) than no screening. When the WTP was ¥435 762/QALY, all screening strategies were cost-effective compared with no screening. The double iFOBT strategy was the best-buy option compared with all other strategies because it had the most QALYs and the least cost. One-way sensitivity analysis showed that the sensitivity of low-risk adenoma, compliance with colonoscopy and primary screening cost were the main influencing factors comparing single iFOBT, double iFOBT and HRFQ+double iFOBT with no screening. However, within the scope of this study, there was no fundamental impact on cost-effectiveness. Probabilistic sensitivity analysis showed that when the WTP was ¥435 762/QALY, the probabilities of the cost-effectiveness acceptability curve with HRFQ alone, single iFOBT, double iFOBT and HRFQ+double iFOBT were 0.0%, 5.3%, 69.3% and 25.4%, respectively.

Conclusions All screening strategies for CRC were cost-effective compared with no screening strategy. Double iFOBT was the best-buy option compared with all other strategies. The significant influencing factors were the sensitivity of low-risk polyps, compliance with colonoscopy and cost of primary screening.

BACKGROUND

Globally, colorectal cancer (CRC) ranked third for cancer incidence but second for cancer death in 2018, with an estimate of 1 800 977 new cases and 861 663 deaths.1 In urban China, CRC ranked third in terms of incidence and fourth in terms of mortality.2 Both the crude incidence and the age-standardised rate have increased in recent years in the urban areas of China.3 4 The incidence and mortality were 41.77/10 5 and 18.76/10 5 in Guangzhou in 2015, ranking second and third of all the sites, respectively.5 The disease burden of CRC is severe in Guangzhou.6

CRC screening (CRCS) could significantly decrease the incidence and long-term mortality of CRC and increase the early detection rate.7 8 Many countries have carried out national CRCS programmes, such as the UK, the USA and Japan.9 10 11 Faecal occult blood tests (FOBTs) and colonoscopy are the most common screening methods worldwide.10 11 13 Cost-effectiveness analysis showed that all screening strategies were more cost-effective

Strengths and limitations of this study

► The Markov model was used to evaluate the cost-effectiveness of four different primary screening strategies for colorectal cancer (CRC) compared with no screening strategy, which was particular in China.

► Incremental cost-effectiveness ratios, which were compared with the willingness-to-pay threshold, were used to reflect the cost-effectiveness of the CRC screening method.

► Some parameters such as sensitivity and transition probability were from abroad or other early studies that may not be relevant to the Chinese population, particularly in Guangzhou.

► In the further study, it would be necessary to analyse the age-specific estimations of cost-effectiveness and obtain the accurate parameters.
than no screening, but there was uncertainty as to which strategy was optimal.\textsuperscript{14-17} Cost-effectiveness simulation of CRCS indicated that immunochemical FOBT (iFOBT) every year may be the most effective in the Hong Kong Chinese population compared with no screening, guaiac immunologic fecal occult blood testing (gFOBT) and biennial iFOBT.\textsuperscript{18} However, the results abroad and in Hong Kong may not be generalisable to the Chinese population.

In China, a combination of the high-risk factor questionnaire (HRFQ) and FOBT is the most common screening strategy. Cost-effectiveness analysis on the urban Chinese population has shown that a combined use of FOBT and HRFQ is preferable in CRCS programmes as an initial screening instrument comparing FOBTs.\textsuperscript{19} Guangzhou has carried out the first-round screening of CRC in the community between 2015 and 2017. In this study, we evaluated the cost-effectiveness of four different primary screening strategies (HRFQ alone, single iFOBT, double iFOBT and HRFQ with double iFOBT) for CRC using the Markov model.

**MATERIALS AND METHODS**

**Patient and public involvement**

This study was part of the CRCS programme in Guangzhou 2015–2017. Participants were from the general community and hospitals. Written informed consent was obtained from all participants in the study. All the data collected in this study were coded. All names and personal information did not appear in the data or any publications.

**Study design**

Data for this study came from the CRCS programme in Guangzhou 2015–2017, Guangzhou Cancer Registry and published literature. The CRCS was undertaken from 1 January 2015 to 31 December 2017. A total of 371,046 residents aged 50–74 years who agreed to participate in the study were included as participants. Participants were asked to take an HRFQ and/or double iFOBT as primary screening. If either the results of the questionnaire or FOBT were positive, both would be considered as a positive result. A positive result was followed by a colonoscopy. Then the individuals with negative results or not involved in screening should continue to participate in the screening in the next year until they have positive results or have reached the age of 75 years. While the individuals were over 75 years old, they would stop screening.

We compared five initial screening protocols: (1) HRFQ alone; (2) single iFOBT; (3) double iFOBT; (4) double iFOBT and HRFQ; and (5) no screening. All screening protocols were conducted as a primary screening, followed by a colonoscopy if the result of the primary screening was positive.

**Markov model**

Five screening strategies for CRC were compared in terms of cost and effectiveness under Markov simulation. Treeage Pro V.2011 software was used to simulate the Markov model. A hypothetical cohort of 100,000 asymptomatic persons entered the model from 50 years old until death or 100 years old. In the model, each person had an initial health state. The natural history of colorectal adenomas and cancer is reflected in figure 1.

**History of disease**

The disease states were divided into eight sections in the model: ‘health’, ‘low-risk polyps’, ‘high-risk polyps’, ‘stage I CRC’, ‘stage II CRC’, ‘stage III CRC’, ‘stage IV CRC’ and ‘death’. Health status was defined as an asymptomatic state. According to the screening guidelines in Guangzhou, low-risk polyps were defined as adenomas that were <1 cm, while high-risk polyps were defined as adenomas where at least one was ≥1 cm or an adenoma with villous structure (≥25%). All states were simulated as Markov states with a 1-year cycle. A person could transition to a different state or remain at current state at the end of every 1-year period in the Markov process.

In the no screening model, it was hypothesised that the health state could change to low-risk polyps, and then to high-risk polyps. High-risk polyps could change to stage I CRC; health state could change directly to stage I, II, III or IV CRC; and only stage I, II, III or IV CRC in patients could lead to death due to CRC. All states could change to death for any other reason; all states could remain in the same state (figure 1).

The disease history of the model for CRCS was also shown in figure 1, assuming that people are divided into two groups: those who participated in the screening and those who did not. Those who did not participate in the screening group were the same as the history of disease. It was hypothesised that the positive population in primary screening was divided into two groups: those who participated in colonoscopy and those who did not participate in colonoscopy.

All the patients with low-risk polyps and high-risk polyps according to CRCS were treated and could return to the health state after treatment, assuming that the disease history of the positive population in primary screening without colonoscopy and negative population in primary screening was the same as that of the no screening population.

**Transitional parameters**

The CRC incidence in all age groups was from the Guangzhou Cancer Registry Center. All-cause mortality and CRC mortality were from the Guangzhou Death Cause Surveillance System. The CRCS data were obtained from the CRCS programme in Guangzhou. Previous studies have shown that colonoscopic polypectomy of adenomas can reduce CRC incidence by approximately 76%–95%.\textsuperscript{20} In this study, we assumed a conservative reduction of 75%. According to the suggestion of the WHO, the
The willingness-to-pay threshold was as three times as the gross domestic product, which was ¥145,254 in Guangzhou in 2016. Then, we assumed that the willingness-to-pay threshold was ¥435,762/quality-adjusted life year (QALY). The data on health utility, transition probability and sensitivity were derived from the literature. All parameters are shown in tables 1 and 2.

Cost and effectiveness estimates
All costs are shown as Chinese yuan in this study and were discounted until 2016. In this study, discount rates for both future costs and QALY were set at 3%. The costs for CRCs included direct and indirect costs. It was assumed that the organisational management costs of screening did not differ among different screening groups. The primary screening costs comprised the materials, reagents, investigation process, management costs and labour expenditure. Effectiveness was shown with QALYs. By discounting the cost and effectiveness, the cumulative cost and per capita cumulative effectiveness of different screening methods can be obtained. The incremental cost-effectiveness ratio (ICER) can be obtained by comparing it with the willingness-to-pay threshold. A smaller ICER indicated a lower cost for saving one QALY. The most cost-effective strategy was identified by efficiency frontiers that the most incremental QALYs and the least cost were the most cost-effective.

Sensitivity analysis
In the study, the one-way sensitivity analysis of variables in the model was carried out. The cost data took the base value (±30%) as the maximum and minimum value. The utility data of the screening method took the 95% CI as the maximum and minimum value. The sensitivity and compliance data took 10% and 100% as the minimum and maximum values, respectively. The discount rate took 7% and 0% as the maximum and minimum values, respectively. A Tornado map was drawn.

Finally, the probabilistic sensitivity analysis was used for multivariate analysis. The model was simulated 1000 times. The cost data were subject to a gamma distribution. Utility data followed a log-normal distribution. The sensitivity and compliance data followed the beta distribution. The cost-effectiveness scatterplot and acceptability curve were used to test the stability of the model results.

RESULTS
After simulation over 50 years, the cumulative cost and utility per capita of the unscreened group were ¥29,450 and 19.3983 QALYs, respectively. All strategies were more effective than no screening because they provided more QALYs. The total costs of single iFOBT, HRFQ+double iFOBT and double iFOBT were less than no screening which showed cost-saving (see table 3). When the willingness-to-pay threshold was ¥435,762/QALY, all screening strategies were cost-effective compared with no screening (see table 4). The ICERs of the screening group with HRFQ alone, single iFOBT, HRFQ+double iFOBT and double iFOBT were ¥11,480/QALY, −¥23,110/QALY, −¥27,564/QALY and −¥38,516/QALY, respectively, compared with that of the no screening group.

Figure 1 The CRC natural history of Markov simulation in screening and no screening status. CRC, colorectal cancer.
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double iFOBT strategy was the most cost-effective strategy compared with the other strategies (see table 3).

**Sensitivity analysis**

One-way sensitivity analysis showed that the most influential factors on the results were the sensitivity of low-risk polyps, primary screening cost and health utility value of low-risk polyps comparing the HRFQ alone screening strategy with no screening. The sensitivity of low-risk polyps, compliance with colonoscopy and primary screening cost compared single iFOBT, double iFOBT and HRFQ+double iFOBT screening strategy with no screening, respectively (see figure 2). However, within

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Parameters in the Markov model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Values (range)</td>
</tr>
<tr>
<td>40-</td>
<td>14.90</td>
</tr>
<tr>
<td>45-</td>
<td>24.02</td>
</tr>
<tr>
<td>50-</td>
<td>42.00</td>
</tr>
<tr>
<td>55-</td>
<td>71.28</td>
</tr>
<tr>
<td>60-</td>
<td>105.62</td>
</tr>
<tr>
<td>65-</td>
<td>146.38</td>
</tr>
<tr>
<td>70-</td>
<td>207.13</td>
</tr>
<tr>
<td>75-</td>
<td>270.62</td>
</tr>
<tr>
<td>80-</td>
<td>265.61</td>
</tr>
<tr>
<td>85-</td>
<td>248.57</td>
</tr>
<tr>
<td>Mortality of all causes other than CRC (1/10^5)</td>
<td>Death cause surveillance in Guangzhou (2014–2015)</td>
</tr>
<tr>
<td>40-</td>
<td>120.65</td>
</tr>
<tr>
<td>45-</td>
<td>201.37</td>
</tr>
<tr>
<td>50-</td>
<td>323.81</td>
</tr>
<tr>
<td>55-</td>
<td>489.62</td>
</tr>
<tr>
<td>60-</td>
<td>694.20</td>
</tr>
<tr>
<td>65-</td>
<td>1091.64</td>
</tr>
<tr>
<td>70-</td>
<td>1973.18</td>
</tr>
<tr>
<td>75-</td>
<td>3388.49</td>
</tr>
<tr>
<td>80-</td>
<td>6261.38</td>
</tr>
<tr>
<td>85-</td>
<td>13657.21</td>
</tr>
<tr>
<td>Cost of screening (CNY: ¥)</td>
<td>Follow-up cost of positive result in primary screening</td>
</tr>
<tr>
<td>CRC</td>
<td>10</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>340</td>
</tr>
<tr>
<td>Pathology examination</td>
<td>172</td>
</tr>
<tr>
<td>Colonoscopic polypectomy</td>
<td>500</td>
</tr>
</tbody>
</table>

CRC, colorectal cancer; CRCS, CRC screening.
the scope of this study, there was no fundamental impact on cost-effectiveness. The ICERs were still lower than the willingness-to-pay threshold, and with cost-effectiveness, screening was better than no screening.

With increasing compliance of colonoscopy and sensitivity of low-risk polyps, the ICERs decreased in all screening strategies (see figure 3), while with increasing primary screening cost, the ICERs increased in all screening strategies.

Probabilistic sensitivity analysis showed the difference of cost and effectiveness distribution which was significant among the five strategies (see figure 4). Furthermore, when the willingness-to-pay threshold was ¥435 762/QALY, the probabilities of the cost-effectiveness acceptability curve with HRFQ alone, single iFOBT, double iFOBT and HRFQ+double iFOBT were 0.0%, 5.3%, 69.3% and 25.4%, respectively (see figure 5).

**DISCUSSION**

The Markov model simulation showed that any screening strategy was more cost-effective than no screening strategy in Guangzhou. Globally, most population screening programmes for CRC are carried out by FOBTs, flexible sigmoidoscopy or colonoscopy.21 The economic evaluation showed that CRCS was more cost-effective than other strategies, including newer technologies such as CT colonography (CTC), faecal DNA test and PillCam COLON compared with no screening. However, no strategy, whether alone or combined, has

### Table 2 Parameters for different screening strategies in the Markov model: (1) single iFOBT; (2) double iFOBT; (3) HRFQ alone; (4) double iFOBT and HRFQ

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HRFQ alone (range)</th>
<th>Single iFOBT (range)</th>
<th>Double iFOBT (range)</th>
<th>HRFQ +double iFOBT (range)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uptake in primary screening</td>
<td>0.17 (0.1–1.0)</td>
<td>0.15 (0.1–1.0)</td>
<td>0.14 (0.1–1.0)</td>
<td>0.14 (0.1–1.0)</td>
<td>CRCS</td>
</tr>
<tr>
<td>Positive result ratio in primary screening</td>
<td>0.10</td>
<td>0.06</td>
<td>0.08</td>
<td>0.16</td>
<td>CRCS</td>
</tr>
<tr>
<td>Uptake of colonoscopy</td>
<td>0.16 (0.1–1.0)</td>
<td>0.25 (0.1–1.0)</td>
<td>0.26 (0.1–1.0)</td>
<td>0.19 (0.1–1.0)</td>
<td>CRCS</td>
</tr>
<tr>
<td>Sensitivity of low-risk polyps</td>
<td>0.13a (0.1–1.0)</td>
<td>0.16b (0.1–1.0)</td>
<td>0.27a (0.1–1.0)</td>
<td>0.37b(0.1–1.0)</td>
<td>a: China reference b: Hong Kong reference</td>
</tr>
<tr>
<td>Sensitivity of high-risk polyps</td>
<td>0.14a (0.1–1.0)</td>
<td>0.47b (0.1–1.0)</td>
<td>0.47a (0.1–1.0)</td>
<td>0.58b (0.1–1.0)</td>
<td>a: China reference b: Hong Kong reference</td>
</tr>
<tr>
<td>Sensitivity of CRC</td>
<td>0.10a (0.1–1.0)</td>
<td>0.56c (0.1–1.0)</td>
<td>0.70a (0.1–1.0)</td>
<td>0.70a (0.1–1.0)</td>
<td>a: China reference c: Chinese reference</td>
</tr>
<tr>
<td>Cost in primary screening (CNY: ¥)</td>
<td>9.7 (6.79–25.61)</td>
<td>9.7 (6.79–25.61)</td>
<td>14.7 (6.79–25.61)</td>
<td>19.7 (6.79–25.61)</td>
<td>CRCS</td>
</tr>
</tbody>
</table>

Uptake in primary screening means number of primary screening participators divided by target population; uptake of colonoscopy means number of colonoscopy participants divided by positive result of primary screening.

CRC, colorectal cancer; CRCS, CRC screening; HRFQ, high-risk factor questionnaire; iFOBT, immunochemical faecal occult blood test.

### Table 3 Cost and QALYs per person for each screening strategy, and the incremental cost and QALYs of a screening strategy

<table>
<thead>
<tr>
<th>Strategy</th>
<th>No screening</th>
<th>HRFQ alone</th>
<th>Single iFOBT</th>
<th>HRFQ +double iFOBT</th>
<th>Double iFOBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per person</td>
<td>29 450.02675</td>
<td>29 454.04466</td>
<td>29 431.30783</td>
<td>29 418.87898</td>
<td>29 404.19321</td>
</tr>
<tr>
<td>Incremental cost compared with next best alternative</td>
<td>4.01791</td>
<td>−22.73683</td>
<td>−12.42885</td>
<td>−14.68577</td>
<td></td>
</tr>
<tr>
<td>Expected QALYs per person</td>
<td>19.39483</td>
<td>19.39518</td>
<td>19.39564</td>
<td>19.39596</td>
<td>19.39602</td>
</tr>
<tr>
<td>Incremental QALYs compared with next best alternative</td>
<td>0.00035</td>
<td>0.00046</td>
<td>0.00032</td>
<td>0.00006</td>
<td></td>
</tr>
<tr>
<td>ICERs</td>
<td>11 479.74286</td>
<td>−38840.15625</td>
<td>−38840.15625</td>
<td>−38840.15625</td>
<td>−38840.15625</td>
</tr>
<tr>
<td>Interpretation</td>
<td>Dominated*</td>
<td>Cost-saving†</td>
<td>Dominated‡</td>
<td>Cost-saving§ (best-buy option)</td>
<td></td>
</tr>
</tbody>
</table>

* Dominated by single iFOBT, HRFQ+double iFOBT and double iFOBT as they provide more QALYs and less cost.
† Cost-saving when compared with no screening and HRFQ alone.
‡ Dominated by double iFOBT as it provided more QALYs and required less cost.
§ Cost-saving when compared with no screening, HRFQ alone, single iFOBT and HRFQ +double iFOBT.

HRFQ, high-risk factor questionnaire; ICERs, incremental cost-effectiveness ratios; iFOBT, immunochemical faecal occult blood test; QALYs, quality-adjusted life years.
be the main influences on cost-the screening cost was, the better the cost-

**Table 4** Cost and QALYs per person for each screening strategy, and the incremental cost and QALYs of a screening strategy compared with no screening

<table>
<thead>
<tr>
<th>Strategy</th>
<th>No screening</th>
<th>HRFQ alone</th>
<th>Single iFOBT</th>
<th>HRFQ +double iFOBT</th>
<th>Double iFOBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per person</td>
<td>29,450.02675</td>
<td>29,454.04666</td>
<td>29,431.30783</td>
<td>29,418.87988</td>
<td>29,404.19321</td>
</tr>
<tr>
<td>Incremental cost compared with no screening</td>
<td>4.01791</td>
<td>−18.71892</td>
<td>−31.14777</td>
<td>−45.83354</td>
<td></td>
</tr>
<tr>
<td>Expected QALYs per person</td>
<td>19.39483</td>
<td>19.39518</td>
<td>19.39564</td>
<td>19.39596</td>
<td>19.39602</td>
</tr>
<tr>
<td>Incremental QALYs compared with no screening</td>
<td>0.00035</td>
<td>0.00081</td>
<td>0.00113</td>
<td>0.00119</td>
<td></td>
</tr>
<tr>
<td>ICERs (when compared with no screening)</td>
<td>Cost-effective</td>
<td>Cost-saving</td>
<td>Cost-saving</td>
<td>Cost-saving</td>
<td></td>
</tr>
</tbody>
</table>

HRFQ, high-risk factor questionnaire; ICERs, incremental cost-effectiveness ratios; iFOBT, immunochemical faecal occult blood test; QALYs, quality-adjusted life years.

been indicated definitively to be the most cost-effective method or has had a better ICER than the rest.\(^1\)\(^-\)\(^4\)\(^-\)\(^7\) Sarfati et al showed that faecal immunochemical test (FIT)-based screening was more cost-effective than one-off sigmoidoscopy screening. The combination of one-off sigmoidoscopy with the FIT was more cost-effective in saving lives than either modality alone.\(^4\)\(^-\)\(^7\) Some studies favoured FITs over gFOBTs concerning effectiveness and cost-effectiveness.\(^2\)\(^-\)\(^4\)\(^-\)\(^7\) Hybrid faecal testing/colonoscopy appeared superior to plasma methylated Septin 9 DNA (mSEPT9) based screening in Germany.\(^2\)\(^-\)\(^7\) There was agreement among studies that the newly developed screening tests of stool DNA testing, CTC and capsule endoscopy were not yet cost-effective compared with the established screening options such as FIT screening.\(^2\)\(^-\)\(^7\) Phisalprapa et al indicated that the colonoscopy screening every 10 years was cost-effective compared with annual FIT in Thailand.\(^2\)\(^-\)\(^7\) However, in terms of human resources and budgetary burden, screening by annual FIT was more feasible. This also applies to China because of its large population and shortage of medical resources.

In this study, the double iFOBT was the most cost-effective strategy compared with single iFOBT, HRFQ + double iFOBT and HRFQ alone. This result was not consistent with Huang et al’s finding that combined use of FOBT and HRFQ as an initial step for CRCS was a better strategy than FOBT alone.\(^1\)\(^-\)\(^9\) The compliance with colonoscopy both in the single iFOBT strategy and double iFOBT strategy was higher than that in the HRFQ + double iFOBT strategy. Analysis showed that the initial screening cost and compliance with colonoscopy significantly influenced the cost-effectiveness of CRCS. The higher the compliance of colonoscopy was, the better the cost-effectiveness of screening. The lower the screening cost was, the better the cost-effectiveness of screening. Skally et al showed that cost and compliance were the main influences on cost-effectiveness for fDNA as a CRCS tool.\(^2\)\(^-\)\(^7\) Huang et al showed that ICER was more sensitive to changes in initial screening coverage when colonoscopy compliance was higher.\(^1\)\(^-\)\(^9\) When compliance to such new techniques such as CTC was increased more than the established strategies, they would be more cost-effective.\(^1\)\(^-\)\(^9\) Participation was an important factor for effectiveness and cost estimates.\(^2\)\(^-\)\(^7\)

To increase the cost-effectiveness of CRCS, it is necessary to increase the sensitivity of low-risk polyps, comply with colonoscopy and decrease the cost of screening. A related study showed that the expenditure of colonoscopy, which was paid by the examiner, significantly influenced the compliance of colonoscopy.\(^1\)\(^-\)\(^9\) The targeted reminder might be more cost-effective than the universal reminders when considering their effects on health disparity.\(^1\)\(^-\)\(^9\) Lara et al’s study suggested that qualified health centres could provide appropriate technical support, such as patient and provider reminder systems, provider assessment and feedback, and numerous support activities, which were proven to be cost-effective.\(^1\)\(^-\)\(^9\) Improved sensitivity might be an effective method for increasing cost-effectiveness.

There are some limitations to this study. Some parameters such as sensitivity and transition probability were from abroad or other early studies that may not be relevant to the Chinese population, particularly in Guangzhou. In a further study, it would be necessary to analyse the age-specific estimations of cost-effectiveness and obtain accurate parameters.

**CONCLUSION**

In conclusion, all screening strategies for CRC were cost-effective compared with no screening strategy. Double iFOBT was the best-buy option. The significant influencing factors were sensitivity of low-risk polyps, compliance with colonoscopy and the cost of primary screening. It was necessary to promote the screening of CRC, particularly colonoscopy, and decrease the cost of primary screening.

**Acknowledgements** We wish to acknowledge the staff of the Guangzhou and 12 district colorectal cancer screening programme offices and all the participants from the general community and hospital.
Figure 2  Tornado map comparing high-risk factor questionnaire (HRFQ) alone, single immunochemical faecal occult blood test (iFOBT), double iFOBT and HRFQ+double iFOBT colorectal cancer (CRC) screening strategies with no screening. cl, cost of stage I CRC; cII, cost of stage II CRC; cIII, cost of stage III CRC; cIV, cost of stage IV CRC; cade, cost of adenoma; ccolon, cost of colonoscopy; cpoly, cost of colonoscopic polypectomy; cscreening, primary screening cost; disc, discount rate; sensity, sensitivity; sensityade, sensitivity of low-risk polyps; sensityhade, sensitivity of high-risk polyps; ul, utility value of stage I CRC; ulII, utility value of stage II CRC; ulIII, utility value of stage III CRC; ulIV, utility value of stage IV CRC; ua, utility value of risk-low polyps; uhdade, utility value of high-risk polyps; uptake1, uptake of initial screening; uptake2, compliance with colonoscopy.

Contributors  QZ, H-IL, YL, H-ZL and G-ZL conceived the study and participated in its design and coordination. QZ and H-IL performed the statistical analyses and interpretation. QZ drafted the manuscript. All authors read and approved the final manuscript.

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Competing interests  None declared.

Patient and public involvement  Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication  Not required.

Ethics approval  Written informed consent to participate in the study was obtained from all participants. The ethics committee of the Guangzhou Center of Disease Control and Prevention approved this study proposal (GZCDC2016008).

Provenance and peer review  Not commissioned; externally peer reviewed.

Data availability statement  Data are available upon reasonable request. The datasets used or analysed during the current study are available from the corresponding author upon reasonable request.

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**Figure 3** ICER changes with rising cost of initial screening, compliance with colonoscopy and sensitivity of low-risk polyps: one-way sensitivity analysis. HRFQ, high-risk factor questionnaire; ICER, incremental cost-effectiveness ratio; iFOBT, immunochemical faecal occult blood test; QALY, quality-adjusted life year.

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**Figure 4** Cost-effectiveness scatterplot in terms of QALYs for all strategies. HRFQ, high-risk factor questionnaire; iFOBT, immunochemical faecal occult blood test; QALYs, quality-adjusted life years.
Figure 5  Cost-effectiveness acceptability curve in terms of QALYs for all strategies in probabilistic sensitivity analysis. HRFQ, high-risk factor questionnaire; iFOBT, immunochemical faecal occult blood test; QALYs, quality-adjusted life years.