Possible impact of Incremental Cost-effectiveness Ratio (ICER) on decision making for cancer screening in Hong Kong: a Systematic Review

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Compliance with Ethical Standards

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Abstract

Objectives: To critically review the literature on cost-effectiveness of cancer screening interventions, and examine incremental cost-effectiveness ratios (ICER) that may influence government recommendation on cancer screening strategies, and funding for mass implementation in Hong Kong health care system.
Methods: We conducted a literature review of cost-effectiveness studies on Hong Kong population related to cancer screening published up to 2015, through hand search and database search of Pubmed, Web of Science, Embase, and OVID Medline. Binary data on government's decisions were obtained from Cancer Expert Working Group, Department of Health. Mixed-effect logistic regression analysis was used to examine the impact of ICER on decision. Using Youden's index, an optimal ICER threshold value for positive decision was examined by area under receiver operating characteristic curve (AUC).
Results: Eight studies reporting 30 cost-effectiveness pairwise comparisons of population-based cancer screening were identified. Most studies reported an incremental cost-effectiveness ratio (ICER) of a cancer screening strategy versus comparator with outcomes in terms of cost per life-years (55.6%), or cost per quality-adjusted life-years (55.6%). Among comparisons with a mean ICER of USD102,931 (range: 800-715,137), the increase in ICER value by 1,000 was associated with decreased odds (odds ratios: 0.990, 0.981-0.999; P=0.033) of positive recommendation. An optimal ICER value of USD61,600 per effectiveness unit yielded high sensitivity of 90% and specificity of 85%.
Conclusions: Linking published evidence to Government recommendations and practice on cancer screening, ICER influences the decision on the adoption of health technology in Hong Kong. Potential ICER threshold in Hong Kong may be higher than those of developed countries.

Key Points for Decision Makers

- An ICER threshold approach for policy decision making is common in developed countries but Research on the appropriate ICER threshold for positive decision in Hong Kong is lacking.
- Linking published evidence to Government recommendations and practice on cancer screening, ICER influences the decision on the adoption of health technology in Hong Kong.
- Potential ICER threshold for decision making of cancer screening in Hong Kong is USD$ 61,600 per effectiveness unit, beyond thresholds in other developed countries.

Manuscript

Introduction

Owing to the rapid development and increasing cost of health intervention, health economic evaluation is an essential approach to critically appraise the costs and benefits of new health interventions. Because of the limited healthcare resources, the integration of an emerging health intervention to healthcare system has to be well articulated with scientific justifications. From the perspective of health policy maker, the emerging health intervention not only has to be more effective than the conventional interventions but also good value for money.

By principle, health economic evaluation is a scientific process of review and assessment. Emerging health interventions in the Western countries are primarily assessed by a single advisory body, for example, National Institute for Health and Care Excellence (NICE)[1] in the United Kingdom (UK), Pharmaceutical Benefits Advisory Committee (PBAC) in Australia, Canadian Agency for Drugs and Technologies in Health (CADTH) in Canada, and Pharmaceutical Management Agency (PHARMAC) in New Zealand. Such advisory bodies in respective countries often monitor the effectiveness and cost-effectiveness of emerging interventions in healthcare, and therefore provide national guidance and recommendation on the decision of whether the health intervention is likely to be accepted or rejected for implementation in routine clinical practice. The incremental cost-effectiveness ratio (ICER) of a new intervention relative to the conventional intervention against the country-specific threshold value is a critical determinant for decision making, while other practical considerations including budgeting and ethical issues are also taken into account.

In Hong Kong, evaluations and recommendations on publically funded health interventions are not the responsibility of a single advisory body but different committees, depending upon the nature of the interventions. Drug Advisory Committee of Hospital Authority[2] has the role of recommending pharmaceutical interventions in Hospital Authority. Existing and new pharmaceutical interventions approved by Drug Advisory Committee are included in the Hospital Authority Drug Formulary[3] which has been initiated since 2005. Drugs in the formulary list are classified as general drugs with full government subsidy, special drugs with certain charges, and self-financing drugs. The health technology assessment process is subject to challenge for a lack of transparency to the general public and documentation of the scientific bases for decision making [4]. Different committees were set up to review scientific evidence and offer recommendations for the prevention of communicable and non-communicable diseases. In field of cancer screening interventions, the Cancer Expert Working Group (CEWG)[5], under the Cancer Coordinating Committee, provides recommendations on suitable cancer prevention and screening measures at the population level.

There is a growing body of health economic analyses that evaluated the health intervention utilized in the public sector of health services in Hong Kong and thereby compared with the ICER thresholds from other countries to inform decision making. However, ICER threshold adopted for comparison is rather diverse. Studies in UK adopted the threshold of GBP 20,000 - 30,000 cost per quality-adjusted life year (QALY) gained suggested by NICE[1] whereas studies in the United States (US) adopted the benchmark of USD 50,000 per life-year or per QALY gain suggested by a cost-effectiveness analysis of hospital renal dialysis study in 1992[6]. Countries are recommended to set their own ICER threshold to reflect how much they value for the gain in health of their populations, and to achieve appropriate drug pricing[7]. Although developed countries like the UK have adopted ICER thresholds, the ideal or widely accepted ICER threshold has yet to be established in Hong Kong or in mainland China by extension. One particular method[8] for threshold estimation is to infer the value of ICER threshold from the previous decisions, such that the relationship between the decision and ICER values of previous health interventions was applied to measure an overall threshold value over the past decision making processes. Alternative approach of setting the ICER threshold as three-fold of the national gross domestic product (GDP) per capita was recommended by the World Health Organization (WHO) [9]. However, no prior studies have been conducted for establishing such relationship. Research on the appropriate ICER threshold for recommendation and funding in Hong Kong is lacking.

The aims of this study were to explore whether ICER values of cancer screening interventions were associated with decisions on recommending and/or accepting the interventions in Hong Kong, and to estimate the ICER thresholds applied by health policy makers on cancer screening in Hong Kong.

Methods

Literature Search on Health Technology Assessment in Hong Kong

Search Engines and Strategies

A systematic literature search was conducted in databases of PubMed, Web of Science using the Web of Knowledge platform, Embase, and MEDLINE using the Ovid searching platform to identify studies that investigated the economic evaluation of health interventions to be considered in public clinical setting in Hong Kong. The Medical Subject Heading “Hong Kong”, “China”, and “Chinese” were combined with “cost-effectiveness”, “cost-effective”, “cost-benefit”, “cost-utility”, “cost-minimization”, “cost-minimisation”, “cost-saving”, “willingness-to-pay” and “economic evaluation” (Appendix 1). Studies were limited to English language, and the publication years to be between 1990 and 2015. The earliest year was chosen as 1990 because the concept of value for money in health emerged around early-1990s[10]. Additional hand search of google search engine was conducted to include the recent studies published in 2015 and past evidence from commissioned and non-commissioned reports to Food & Health Bureau, in case those reports were publicly available. If there were duplicated articles or reports, the most complete work done by authors was selected. After the initial check for duplicated articles, the abstracts of remaining articles were screened by authors (CW and BL) to exclude editorials, letters, commentaries, study protocols, case reports, pure literature reviews and meta-analyses, conference proceedings, past and current clinical guidelines, and recommendations.

Inclusion and Exclusion Criteria

After reviewing the full text of screened articles, the eligibility criteria of studies were (1) to involve the economic evaluations of cancer screening strategies against the status quo as the comparator, and (2) to evaluate the ICER of one screening strategy relative to the comparator. Articles without available full text or full report were excluded. Methodological quality of the included studies was assessed according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement[11], which was adopted as the evaluation of reporting standard of health economics analysis. Articles that lack transparency and reporting of three essential items (Target population and subgroups, comparators, and measurement of effectiveness) were further excluded from subsequent analyses.

Data Extraction

A standardized form was used when extracting the data reported in included studies. The primary data extracted from each article involved: first authorship, year of publication, design or type of economic evaluation, disease population (breast cancer, cervical cancer, colorectal cancer, liver cancer, gastric cancer, etc), frequency of screening, comparator of screening, targeted screening population, perspective, year cost, modelling characteristics, and cost-effectiveness outcomes. Modelling characteristics included type of models (Markov model, discrete-event simulation or no models), time horizons, discount rate, preference valuation for calculation of QALYs, and sensitivity analysis. Each health economic assessment of cancer screening strategy versus the comparator was defined as one comparative cost-effectiveness analysis. For each pairwise cost-effectiveness comparison, we obtained the ICER value at base-case scenario, as expressed in cost (USD) per life years gained, cost per QALYs gained, or cost per disability-adjusted life years (DALYs) averted of one screening strategy relative to the comparator. The ICER values expressed in Hong Kong dollar (HKD) were converted to USD as pegged in USD$1=HKD$7.8, and thus were not adjusted for year of valuation. Conclusion of included studies was grounded on the ICER value at base-case scenario, justifying the use of base-case ICER value. Studies that expressed ICER in other effectiveness units were excluded from subsequent retrospective analyses. In case when the ICER value was expressed in both the cost per life years gained and cost per QALYs gained in one comparison, cost per QALYs gained value was used as the ICER estimate in retrospective analyses.

Past Decisions from Government

Recommendations made by Cancer Expert Working Group (CEWG) on Cancer Prevention and Screening, Department of Health[5] were referred to the published clinical practice guidelines and recommendation report. As of the date of searching (January 2016) using the latest available data, decision of non-recommendation was assumed if the particular screening is not yet considered or recommended by the committee. Final decision to recommendation was recorded as binary outcomes of ‘Recommended’/‘Not recommended’. Decision of non-funding was assumed if the particular screening implemented to targeted population group is yet supported by Department of Health and government bureau. Two mass cancer screening programmes have been officially recommended by Department of Health. Since 2004, CEWG has recommended regular pap smear screening[5] and implemented Cervical Screening Programme. Furthermore, CEWG recommended individuals aged 50-75 years to consider the colorectal cancer screening by faecal occult blood test every 1-2 years, sigmoidoscopy every 5 years or colonoscopy every 10 years[5], and will thus implement the Colorectal Cancer Screening Pilot Programme in second half of 2016[12].

Statistical Analysis

In retrospective analysis, effects of ICER on decisions (recommendation and/or funding) were tested by mixed-effect logistic regression models with the adjustment of multiple comparative cost-effectiveness analyses reported in each study. Equation of logistic regression model was specified as below:

$$\ln (Y / 1 - Y) = \beta_0 + \beta_1(ICER) + \gamma(STUDY) + \varepsilon$$

where Y is dichotomous outcome variable, decision making; $ICER$ is the continuous independent variable, ICER value; β_0 and β_1 are fixed-effect regression coefficients of intercept and ICER value, respectively; $STUDY$ is the random-effect covariate; γ is the random intercept at the study level; and ε is the error term.

Goodness-of-fit of model was assessed using log likelihood value and Wald $\chi 2$ test. An odds ratio (OR) of ICER below 1 indicated that the decrease in ICER was associated with higher odds of a recommendation or acceptance for funding than a negative decision. The predicted probability of recommendation or acceptance for funding was calculated for each ICER value. Sensitivity analysis was performed on the cost-effectiveness comparisons reporting ICER values in terms of cost per QALYs gained or cost per DALY averted, which incorporated both the quantity and quality of life in the effectiveness unit.

Performance of each threshold cut-off value for positive decision in term of sensitivities and specificities was calculated. Sensitivity and specificity were defined as the probability of positive decision given the condition that the ICER value was less than threshold cut-off value, and the probability of negative decision provided that the ICER value was greater than threshold cut-off value. Youden’s index is the sum of sensitivity and specificity minus one while the maximum value of Youden's index was used for identification of an optimal ICER threshold value for positive decision. The receiver operating characteristic (ROC) curve was obtained by plotting sensitivity against one minus specificity for each ICER cut-off value. Discrimination of ICER value was examined by area under ROC curve (AUC).

All statistical analyses were performed using STATA Version 13.0 (StataCorp LP. College Station, Tex). All significance tests were two-tailed and those with a p-value less than 0.05 will be considered statistically significant.

Results

Figure 1 lists the process of literature identification, abstract screening for eligibility, and selection of original studies during the literature and hand search presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram[13]. Systematic database search was completed in March 2015 and identified a total of 1,335 potentially relevant studies (PubMed: 446; Web of Science: 232; MEDLINE: 300; and Embase: 357) that met the searching criteria in four research databases. After the removal of duplicated (n=644) and non-original articles (n=237) by abstract screening, the full-text of 70 studies were assessed for eligibility. Among them, 64 were not related to cancer screening and one did not report the ICER value considered as poor methodological quality. After the addition of four eligible studies by hand searching, nine[14-22] cost-effectiveness studies related to cancer screening were finally included in this review. The earliest study[14] that assessed comparative cost-effectiveness of cancer screening was published in 2004.

Table 1 summarizes the characteristics of studies included in this review. This review identified 4 (44.4%) cost-effectiveness analyses and 5 (55.6%) cost-utility analyses which QALYs were used as the effectiveness unit of ICER value. Studies evaluated the cancer screening strategies designed for a wide range of disease population including colorectal cancer (33.3%), cervical cancer (22.2%), and breast cancer (22.2%). Source of clinical data were mostly adopted from purely published literature (66.7%) and cross-sectional data combined with literature data (22.2%). Most studies established a Markov modeling (88.9%), evaluated from perspective of healthcare provider (77.8%), and reported an ICER of a cancer screening strategy versus the comparator as outcomes in terms of cost per life-years (55.6%), or cost per QALYs (55.6%). One study that reported the cases detected as effectiveness unit of ICER value was not considered in retrospective analysis.

The retrospective analysis included eight studies have reported 30 cost-effectiveness pairwise comparisons of population-based cancer screening for colorectal (n=16, 53.3%), cervical (n=9, 30%), breast (n=4, 13.3%) and gastric cancers (n=1, 3.3%). General characteristics of the 30 pairwise comparisons and their respected decisions are shown in Table 2. Of the 30 pairwise comparisons analyzed, 20 (66.7%) received a positive recommendation for implementation by CEWG, and 15 (50%) were accepted by government for routine use at the time of analysis. Seven comparisons reported in 3 studies expressed ICER value in term of both cost per life year gained and cost per QALYs gained, in which the latter was used in the retrospective analysis. No strategies were deemed to be cost-saving, leading to a negative ICER value, relative to comparator.

Table 3 shows the effects of ICER value on past decision making of cancer screening strategies in retrospective analyses. Among comparisons with a mean ICER of USD 102,931 (median: 19,166; range: 800 - 715,137), the mean ICER value was four-time higher for non-recommended cancer screening strategies than for those that was recommended by CEWG (USD 222,837 vs 42,978). Similarly, for acceptance of strategies for funding on routine use, the mean ICER for non-acceptance was 2.5-fold higher than that for acceptance (USD 160,766 vs 45,096). Mixed-effect logistic regression models depicted that the increase in ICER value by USD 1,000 was associated with decreased odds (OR: 0.990, 0.981-0.999; P=0.033) of positive recommendation. The ICER at which the predicted probability of positive recommendation was 50% was between USD 134,685 - 195,209. Although there is no significant association between the ICER value and funding decision for routine use, the predicted probability of funding decision varied with the ICER value. The ICER at which the cancer screening had a 50% chance of funding was between USD 72,534 - 134,685. Figure 2 displayed the impact of ICER value on the predicted probabilities of positive decision that accepted for recommendation and funding. Sensitivity analysis using the cost-effectiveness comparisons reporting ICER value in terms of cost per QALY gained or cost per DALY averted demonstrated the estimated OR of less than one (OR: 0.995, 0.987-1.003; P=0.205), though not statistically significant.

Based on the Youden's index, an ICER value of below USD 61,600 per effectiveness unit yielded a high sensitivity of 90% and specificity of 85% for positive recommendation. A lower ICER threshold value of below USD 8,044 was detected for positive decision of funding, with a sensitivity of 86.7% and a specificity of 73.3%. The ICER value yielded excellent discrimination for recommendation and funding, with an AUC of 0.890 (95% CI: 0.770 – 1.000) and 0.822 (95% CI: 0.656 – 0.988), respectively. Figure 3 demonstrates the ROC curve and the optimal ICER threshold value for positive decision.

Discussion

The health technology assessment is a standardized process to assess the value of a new health care intervention and the ICER value is an important element to be considered in this process. In Hong Kong, the funded health interventions must be recommended by advisory body but the health interventions recommended by advisory body are not necessarily funded by the government bureau for implementation. The health technology assessment for recommending cancer screening strategies is conducted by CEWG while the government bureau has the final decision to launch mass population-based screening program for individuals. This review identified 9 published studies consisting of 30 cost-effectiveness comparisons assessing the cost-effectiveness of cancer screening interventions relative to status quo in Hong Kong. The small number of cost-effectiveness comparisons identified in this review implied the limited health economic evidence on the cancer screening interventions in Hong Kong, calling for further cost-effectiveness analyses of other controversial cancer screening such as ovarian cancer screening, prostate cancer screening and endometrial cancer screening.

The retrospective analysis addressed two objectives 1) to examine whether the decision making of cancer screening strategies for recommendation or funding in routine clinical practice was based on the ICER value, and 2) to identify the ICER thresholds for previous decision on cancer screening in Hong Kong. In response to the first objective, findings reflected a significant relationship between the ICER values and the decisions to recommend cancer screening strategies by the CEWG, suggesting that the less ICER value of a cancer screening strategies had greater odds to be recommended by CEWG. Therefore, ICER value may play an important role of decision making during the health technology assessment of cancer screening strategies in Hong Kong. This result was in line with reimbursement decision making in developed countries[23-28], prompting that the ICER is one of the most influential factors affecting the recommendation of interventions submitted to local advisory bodies during the health technology assessment. Besides health economic evidence, factors related to clinical effectiveness, treatment alternatives, disease severity, and study design of clinical trials are also taken into consideration by the advisory bodies during the health technology assessment[29, 27].

To address the second objective, an implicit ICER threshold may exist in Hong Kong context. Our retrospective analyses implied that a threshold for ICER value around USD 61,600 per one effectiveness unit gained to get a positive recommendation of cancer screening strategies in Hong Kong. Interestingly, one gastric cancer screening strategy[18] was not yet recommended despite the fact that its ICER value (USD 17,886) was two-fold less than potential ICER threshold value. One plausible explanation of negative recommendation was in part due to other multiple practical considerations. The procedure to make of previous decisions considers a variety of practical issues including not only health economic evidence but also public acceptance, appropriateness of screening tools for mass population-based screening, and capacity of healthcare system in coping with screening and positive screening results. The potential ICER threshold in present analysis was slightly higher compared to the benchmark value in UK (around GBP 20,000 – 30,000 per QALY gained) and the US (USD 50,000 per life-year gained). In 2014, the per capita GDP in Hong Kong was around USD 40,187[30]. According to the WHO recommendation suggesting an ICER value of one to three-fold of the per capita GDP as cost-effective [9], the threshold of ICER value in present study was somewhat surrounded by the threshold recommended by WHO but the effectiveness unit of WHO threshold is DALY, not interchangeable with QALY and LY. Therefore we urge to increase attention to the establishment of ICER threshold value for decision making in other health interventions such as vaccine and pharmaceutical interventions. However, there is premature to seek for overall cost-effectiveness threshold for positive decision of healthcare interventions in Hong Kong health care system.

Our synthesized evidence revealed the lack in standardization of reporting of ICER values, year costs of resource unit or annual discount rate, as conformed to CHEERS checklist. For instance, the presentation of ICER value was typically expressed in either cost per life-year gained or cost per QALY gained. Only 9 out of 30 (30%) pairwise comparisons expressed the ICER value in cost per QALY gained (Table 2), suggesting the need for evidence for preference or utility valuation in cancer health status to enable the QALY calculation. Furthermore, there was a paucity of cost-effectiveness studies alongside a cohort study, or from the societal perspective accounting for indirect cost incurred by patients and their caregivers. Only one study (11.1%) extrapolated the clinical data from cohort study to cost-effectiveness analysis but none of the effectiveness data were sourced from randomized controlled trials. In two studies adopting societal perspective, indirect cost was incorporated by estimating patient time including screening time and travel time. In order to present rationale and evidence to health policy makers and public society, future cost-effectiveness analyses are urged to adopt both the healthcare provider and societal perspectives.

Limitations

Discrepancies in effectiveness unit presented in included studies limited the interpretation of potential ICER threshold value identified in this review which adopted the life-year, QALYs or DALYs as effectiveness units. The potential ICER threshold value is interpreted with caution when the ICER value was estimated by other effectiveness units. Secondly, the potential ICER threshold value based on studies between 2004 and 2015 may not reflect the actual value in the future. Temporal trend on the ICER threshold was observed according to UK NICE's decision making, suggesting the inflation of ICER threshold over time[27]. Thirdly, the health intervention may be recommended and funded with restrictions for use in European health care system. For example, the Scottish health technology assessment can accept the technology for either restricted use or routine use, and reject for use in NHS Scotland. However, there is no published data on whether the recommended or funded health intervention is under restricted use in Hong Kong. Dependent variables were only coded as binary fashion, collapsing 'funded with restriction' into 'funded' decision category. Fourthly, relevant factors influencing decision making and cost-effectiveness analysis were not controlled in retrospective analysis. Given the small number of cost-effectiveness comparisons and studies identified in this review, there was lacking in capacity to control for other relevant factors in retrospective analysis. Finally, the potential ICER threshold value was not generalizable to Chinese in other populations other than Hong Kong, and applied to any type of cancer screening in general.

Conclusion

The ICER value may be one of the most important determinants of recommending mass cancer screening interventions by advisory body, but was not associated with implementation of population-based screening program in Hong Kong. Based on a critique of the evidence from cancer screening strategies, we found that ICER value may influence past decisions of health technology assessment in Hong Kong. Potential ICER threshold for what is considered a cost-effective intervention to be recommended in Hong Kong was established by this retrospective analysis, in which USD 61,600 per effectiveness unit was slighter beyond benchmark value in developed countries such as UK and US but surrounded by WHO recommended threshold based on one to three times annual GDP per capita.

Author Contributions

CKHW designed the study, acquired data, analyze and interpret the data, draft the manuscript. BHHL acquired data, interpret the data and revised the manuscript. VYWG interpret the data, interpret the data and draft the manuscript. CLKL designed the study, interpret the data and revised the manuscript. All authors approved the manuscript.

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Figure Legends

Figure 1. PRISMA Flow Diagram of the literature search and selection process
Figure 2. Impact of ICER value on the predicted probabilities of positive decision accepted for recommendation and funding
Figure 3. Performance characteristics for each ICER cut-off value using receiver operating characteristic and the optimal ICER threshold value for positive decision

Table 1. Description and modeling characteristics of nine included studies

	n	(%)		n	(%)
Year of publication			Reporting of ICER		
2000-2005	1	(11.1)	LY & QALY	3	(33.3)
2006-2010	3	(33.3)	LY only	2	(22.2)
2011-2015	5	(55.6)	QALY only	2	(22.2)
Funding source			Others	2	(22.2)
Government	7	(77.8)	Model type		
No funding	2	(22.2)	Markov	8	(88.9)
Industry	0	(0.0)	No modelling	1	(11.1)
Types of economic evaluation			Time horizon		
Cost-effectiveness	4	(44.4)	Lifetime	2	(22.2)
Cost-utility	5	(55.6)	50- or 60-year	3	(33.3)
Disease population			20- or 30-year	2	(22.2)
Colorectal cancer	3	(33.3)	5- or 15-year	2	(22.2)
Cervical cancer	2	(22.2)	Year cost		
Breast cancer	2	(22.2)	2001-2010	5	(55.6)
Colorectal, cervical & breast cancers	1	(11.1)	Not reported	4	(44.4)
gastric cancer	1	(11.1)	Annual discount rate		
Target population			3.0%	7	(77.8)
Female only	5	(55.6)	3.5%	1	(11.1)
Age 50 or above	2	(22.2)	Not reported	1	(11.1)
Others	2	(22.2)	Preference or utility valuation		
Study Perspective			Yes by assumption	3	(33.3)
Healthcare provider	7	(77.8)	Yes by direct valuation	1	(11.1)
Societal	2	(22.2)	Yes by indirect valuation	1	(11.1)
Both	0	(0.0)	No QALY calculation	4	(44.4)
Source of clinical data			Sensitivity analysis		
Cohort data	1	(11.1)	Deterministic	3	(33.3)
Cross-sectional data & literature	2	(22.2)	Probabilistic	5	(55.6)
Literature only	6	(66.7)	No	1	(11.1)

Note: ICER=Incremental cost-effectiveness ratios; LY=life-year; QALY=quality-adjusted life-year

Table 2. Thirty cost-effectiveness pairwise comparisons of population-based cancer screening and their respected past decisions

						Decision making			
First author	**Year of publication**	**Type of Cancer**	**Intervention**	**Comparative arm (status quo)**	**ICER (USD)**	**Recommendation**[5]	**Year**	**Funding**[5]	**Year**
Kim[14]	2004	cervical cancer	Cytology screening every 5 years	no screening	800	✓	2004	✓	2004
Kim[14]	2004	cervical cancer	Cytology screening every 4 years	no screening	1,042	✓	2004	✓	2004
Kim[14]	2004	cervical cancer	Cytology screening every 3 years	no screening	1,444	✓	2004	✓	2004
Kim[14]	2004	cervical cancer	Cytology screening every 2 years	no screening	2,262	✓	2004	✓	2004
Wong[15]	2015	colorectal cancer	I-FOBT every 2 years	no screening	2,976	✓	2013	✓	2016
Wong[15]	2015	colorectal cancer	I-FOBT every 1 year	no screening	3,155	✓	2013	✓	2016
Wong[15]	2015	colorectal cancer	Colonoscopy every 10 years	no screening	3,622	✓	2013	X	
Kim[14]	2004	cervical cancer	Cytology screening every 1 year	no screening	4,739	✓	2004	✓	2004
Wong[15]	2015	colorectal cancer	G-FOBT every 2 years	no screening	5,240	✓	2013	✓	2016
Wong[15]	2015	colorectal cancer	G-FOBT every 1 year	no screening	5,871	✓	2013	✓	2016
Tsoi[16]	2008	colorectal cancer	FOBT every 1 year	no screening	6,222	✓	2013	✓	2016
Tsoi[16]	2008	colorectal cancer	Colonoscopy every 10 years	no screening	7,211	✓	2013	X	
Woo[17]	2007	cervical cancer	Pap smear screening every 5 years	no screening	7,416	✓	2004	✓	2004
Tsoi[16]	2008	colorectal cancer	Sigmoidscopy every 5 years	no screening	8,044	✓	2013	X	
Wong[18]	2014	gastric cancer	Helicobacter pylori screening and treatment for screening positive	no screening	*17,886	X		X	
Woo[17]	2007	cervical cancer	Pap smear screening every 4 years	no screening	20,447	✓	2004	✓	2004
Woo[17]	2007	cervical cancer	Pap smear screening every 3 years	no screening	43,340	✓	2004	✓	2004

						Decision making			
First author	**Year of publication**	**Type of Cancer**	**Intervention**	**Comparative arm (status quo)**	**ICER (USD)**	**Recommendation**[5]	**Year**	**Funding**[5]	**Year**
Woo[17]	2007	colorectal cancer	Colonoscopy every 10 years	no screening	55,369	✓	2013	X	
Wong[19]	2007	breast cancer	Mammography screening every 2 years	no screening	61,600	X		X	
Wong[20]	2012	breast cancer	Mammography screening every 2 years	no screening	72,534	X		X	
Woo[17]	2007	colorectal cancer	Sigmoidscopy every 5 years	no screening	108,879	✓	2013	X	
Woo[17]	2007	breast cancer	Mammography screening every 2 years	no screening	109,155	X		X	
Woo[17]	2007	colorectal cancer	Colonoscopy every 7 years	no screening	113,616	X		X	
Woo[17]	2007	colorectal cancer	FOBT every 1 year plus sigmoidscopy every 5 years	no screening	134,685	X		X	
Woo[17]	2007	colorectal cancer	Colonoscopy every 5 year5	no screening	195,209	X		X	
Woo[17]	2007	colorectal cancer	Sigmoidscopy every 3 years	no screening	276,414	X		X	
Woo[17]	2007	colorectal cancer	FOBT screening every 1 year	no screening	279,990	✓	2013	✓	2016
Woo[17]	2007	colorectal cancer	FOBT screening every 2 years	no screening	291,499	✓	2013	✓	2016
Wu[21]	2011	cervical cancer	Pap smear screening every 1 year plus HPV DNA screening every 1 year	Pap smear screening every 1 year	532,132	X		X	
Woo[17]	2007	breast cancer	Mammography screening every 1 year	no screening	715,138	X		X	

Note: ICER= incremental cost-effectiveness ratios; FOBT= fecal occult blood test; G-FOBT= guaiac FOBT; I-FOBT= immunochemical FOBT; HPV= human papillomavirus;

* ICER value obtained from ‘'Screen and rescreen once' scenario for men

Table 3. Effects of ICER value on past decision making of cancer screening strategies by retrospective analysis

	Recommendation						
	Odds ratio				Goodness-of-fit		
	Probability	Estimate	95% CI	P-value	Log likelihood	Wald $\chi 2$	P-value
ICER value (in 1,000k)	66.7%	0.990	.981 - .999	0.033	-14.696	4.56	0.0328
ICER value					-11.827	9.02	0.0027
≤USD50,000	94.1%		reference				
>USD50,000	30.8%	0.028	.003 - .288	0.003			
	Acceptance						
	Odds ratio				Goodness-of-fit		
	Probability	Estimate	95% CI	P-value	Log likelihood	Wald $\chi 2$	P-value
ICER value (in 1,000k)	50.0%	0.993	.986 - 1.001	0.106	-18.547	2.61	0.106
ICER value					-14.796	3.59	0.581
≤USD50,000	76.5%		reference				
>USD50,000	15.4%	0.032	.001 - 1.125	0.058			

Note: ICER=Incremental cost-effectiveness ratios