Original Article

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Economic Evaluation of Colorectal Cancer Screening: A Systematic Review

*K. Kittrongsiri[1] and U. Chaikledkaew[1]**

[1] Social and Administrative Pharmacy Excellence Research (SAPER) Unit, Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand

Abstract

Colorectal cancer (CRC) is a major public health problem worldwide. CRC screening in average-risk population aims to prevent new cases of CRC by detecting and removing pre-malignant lesions or to discover CRC at its early stage. Implementation of CRC screening program requires enormous of resources; therefore, it is important to carefully assess value for money of the program. Thus, the objective of this study aimed to systematically review the economic evaluation studies of different CRC screening methods in order to identify the optimal screening modality. A systematic review was carried out using PubMed Science Direct and Centre for Reviews and Dissemination (CRD) databases. Full economic evaluations assessing CRC screening in average-risk population from January 2003 to July 2013 were retrieved. Eighteen publications identifying optimal screening modalities were included in the review. Of 18 included studies, the studies were performed in ten different countries used four modeling approaches. Fifty six percent of included studies used cost-utility analysis, whereas the others used cost-effectiveness analysis. The method of gFOBT was the most assessed option, while FIT-biennial screening was the most reported optimal strategy. It was found that CRC screening was considered as a cost-effective or even cost-saving when compared with no screening. Although, the studies did not find the consensus conclusion on which screening method was the most effective or the modality of choice. Of implementing screening program in the country, the evaluation should be conducted to assess the benefits against the society acceptable costs because the transferability of results from one setting to another is limited.

Keyword: Corolectal cancer, Screening, Economic evaluation

INTRODUCTION

Colorectal cancer (CRC) is a major public health problem worldwide. It is the third most common cancer and the fourth leading cause of death due to cancer. It has been estimated that more than 1.2 million people get CRC resulting in about 0.6 million deaths annually. In Thailand, about 10,000 new CRC cases and 5,000 deaths annually are estimated. An age-standardised rate (ASR) among Europe region population was around 28.1 per 100,000, where in South-East Asia region the rate was only 7.4 per 100,000[1]. Although, the incidence of CRC among Thai population and neighbor countries are relatively low compared with the western countries, the disease is burden due to high treatment related cost[2]. The rising in incidence of CRC are expected due to the coming of ageing society. CRC screening is the main strategy to tackle the growing numbers of CRC. The screening aims to prevent new cases of CRC by detecting and removing pre-malignant lesions or to discover CRC at its early stage[3].

Many CRC screening modality are available and recommended. The four screening methods that are well established and recommended by national bodies are (i)

***Corresponding author:** Social and Administrative Pharmacy Excellence Research (SAPER) Unit, Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok 10400, Thailand, Tel: 66-2-644-8678 ext 5317, Fax: 66-2-644-8694, Email: usa.chi@mahidol.ac.th

guaiac-fecal occult blood test (gFOBT); (ii) fecal immunochemical occult blood test (FIT); (iii) flexible sigmiodoscopy (FSIG); and (iv) colonoscopy (COL)[3-5]. Each modality requires different range of resources and provides different range of health benefits. Of implementing the program, careful assessments are required to guide the efficient use of limited resources. The economic evaluation is the tool for assisting policy makers with evidences whether it is worth to implement the program, or which screening method should be selected. Until now, many economic evaluation studies have been conducted to assist policy makers in many countries. It is interesting to observe the results from the economic evaluation studies during the past ten years. Therefore, the study's objective was to systematically review the economic evaluation studies of different CRC screening methods in order to identify the optimal screening modalities.

MATERIALS AND METHODS

PubMed Science Direct and Centre for Reviews and Dissemination (CRD)— consisting 3 sub databases i.e.: The Database of Abstracts of Reviews of Effects (DARE), The NHS Economic Evaluation Database (EED), and The Health Technology Assessment (HTA) Database— databases were used. The searching was carried out using the MeSH terms as follows: "Colorectal Neoplasms", "Mass Screening", "Early Detection of Cancer", "Colonoscopy", "Occult Blood", "Costs and Cost Analysis", "Cost-Benefit Analysis", "Economics/economics", and "Quality of Life", combined with text words: economic evaluat*, cost effectiv*, cost utilit*, cost benefit, and cost evaluat*. The terms were combined to identify the relevant publications. In order to obtain all relevant articles, the manual search was performed by checking the reference lists of retrieved articles.

Only full economic evaluation studies compared different screening methods related to an average risk population, and published in English were included. Studies that are not original article e.g., editorial, review, or methodological article were excluded. The publications during January 1, 2003 – July 30, 2013 were retrieved. Studies met inclusion criteria were examined for the study's objective which was to investigate the optimal strategy. Although the studies did not clearly state their objectives, they were also included if the results were able to make conclusions. Based on the good reporting practice purposed by Drummond et al, the extraction data of all included studies were study settings, study perspective, interested interventions and comparators, time horizon, discount rate, and uncertainty analysis[6]. Other interested variables i.e.: type of model used in the analyses, type of economic evaluation and related outcomes and eligible age group for screening.

The reported optimal strategy in each study was determined. The optimal screening strategy was generally defined as the strategy that could provide maximum additional health benefits with acceptable incremental costs (or less costs) for the social's willingness to pay. Therefore, the cost-saving strategy, a strategy that provides additional heath gained with less costs, was also considered as optimal. The screening strategy in the analysis should provide complete information of primary screening method and the screening frequency. However, the information on eligible age of screening was not included because the age ranges used in the analysis were varied. Reported incremental cost-effective ratios (ICER) of the optimal strategies were beyond the scope of this review.

RESULTS AND DISCUSSION

Literature search was conducted in August, 2013. A total of 338 publications were primarily identified through search of two databases. After removal of 25 duplicated articles, 313 records were abstract reviewed and 52 potential relevant articles were found. All 52 articles were retrieved for full publication review. Additional five records were identified through manual search. All eligible publications were primarily assessed by the study objectives and reported outcomes.

(see Figure 1). Summary of data extraction from 18 included studies as shown in Table 1[7-22]. From eighteen included publications, the analyses were took place in ten different settings as follows: 4 (22%) in France[14,15,19,20], 4 (22%) in Canada[10,12,13,16], 2 (11%) in the US[11,24], 2 (11%) in UK[8,18], and one study (6%) in each setting i.e., Israel[7], Asia[9], the Netheland[17], Ireland[21], Iran[22], and Singapore[23]. Moreover, four different modeling approaches i.e.: Markov model[8-10,12-19,21-24], Micro simulation model[11], partially observed Markov model (POMM)[7] and simulation model[20] were observed. Markov model was used in 83% of the reviewed studies, whist other approaches were used with same proportion of 6%. The methods of cost-effectiveness analysis (CEA)[7,9,11,14,15,17,19,20] and cost-utility analysis (CUA)[8,10,12,13,16,18,21-24] were used in the evaluations in 44% and 56%, respectively.

Quality-adjusted life year (QALY) was the only outcome assessed in CUA studies[8,10,12,13,16,18,21-24]. In CEA studies, life-year gained[7,9,11,14,15,17,19] and CRC avoided[20] were used as outcomes in 39% and 5%, respectively. The perspective of the third party payer was used in 67% of included studies[7-8,10,14-16,18-22,24], while the societal perspective was used in only 22%[11-13,23], and about 11% failed to specify study perspective[9,17]. The lifetime horizon was used in 67%[8,10,11-13,16,18-19,21-24], the period of 30, 20, and 10 years were also used in 11%[7,15], 6%[14], and 11%[17,20], respectively, and not specified in 6%[9]. All studies applied discounting in the analyses. The discount rates used were different among study settings ranging from 3% to 5%[7-22]. Nine from sixteen studies (56%) used both deterministic and probability sensitivity analyses to handle uncertainty of results from the models[8,13-17,19,20,22]. Five studies (31%) used only deterministic approach in the analyses[7, 9, 11, 12, 21]. Two studies (13%) fail to specify about uncertainty analysis in their models[10,18].

All available screening strategies, both established and innovative methods, been assessed in the analyses. The method of gFOBT was the most assessed strategy (89%), followed by FIT (72%), COL (67%) and FSIG (61%). All included studies found that all recommended screening modalities performed in the average risk populations were considered as a cost-effective or even cost-saving when compared with no screening. In terms of reported optimal choice, the results from 16 studies that reported only one optimal strategy were combined. Four screening methods of gFOBT, FIT, FSIG, and COL were found to be optimal. When different screening frequencies combined with the tests to produce screening strategies, total of eight different strategies were reported. Method of FIT-screening was reported as optimal choice in 9 studies (56%) with 3 different screening intervals ranging from every one year (4 studies, 25%)[12,13,19,23], two years (4 studies, 25%)[14,15,18,21], or once in a life-time (1 study, 6%)[17]. Three studies (19%) reported COL screening every 10 years as the optimal strategy[11,16,22]. Screening by gFOBT was suggested as the optimal choice in two studies (12%) and screening durations were every one year[9] and two years[20]. Screening with FSIG once in a lifetime was reported as optimal in one study (6%)[8] and the combination of FSIG every five years and gFOBT annually was also reported as optimal in one study (6%)[7]. Other two studies reported more than one option as the optimal choice[11,24]. The reported optimal strategies were similar with those been reported in 16 publications and ranges of age eligible for screening specified in 18 studies are also summarized in Table 1. Screening starting at age of 50 and end at age of 74 or 75 was the most used age range in the analysis (65%) in accordance with the present recommendations[10,12-17,19,20,22,23]. One study conducted by Zauber et al varied the range of age to assess the optimal eligible age range for stating recommendation[11]. From 18 studies, when compared range of screening modalities with no screening in the given society, five studies[8,12,17,18,24] identified range of cost-saving strategies as shown in Table 1.

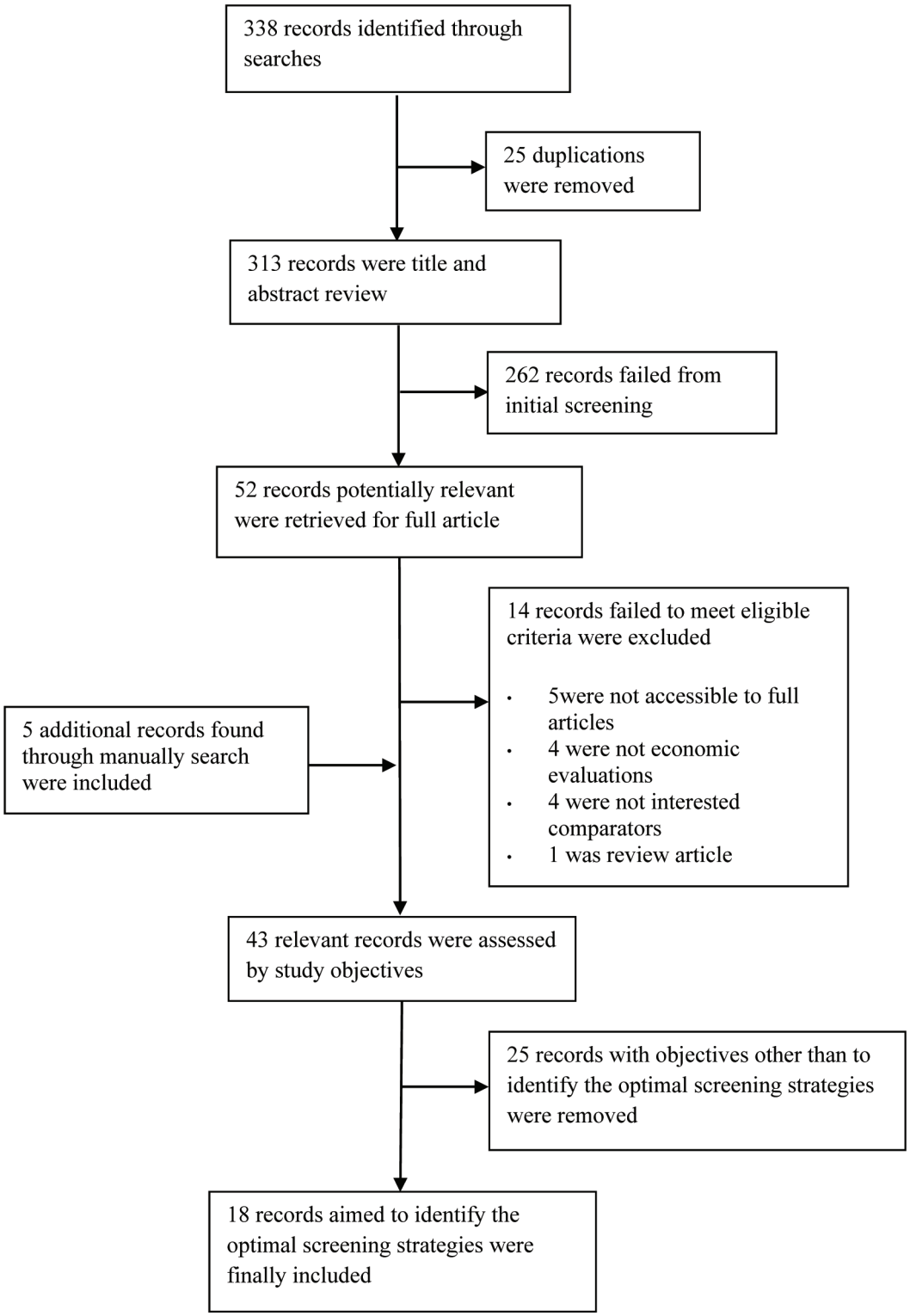

Figure 1. Flow chart of literature search results

Table 1. Summary of data extraction from 16 included studies[7-24].

Publication	Setting	Outcome	Perspective	Time horizon	Model type	Age of screening		Screening modalities assessed	Reported optimal strategy
						Start	End		
Leshno 2003[7]	Israel	LYG	Third party payer	30 years	Partially observed Markov model (POMM)	50	79	gFOBT-annual; COL-once, 10 yrs; sDNA-annual; FSIG-5 yrs + gFOBT-1yr	FSIG-5 yrs + gFOBT-1yr (50-79 yrs)
Tappenden 2007[8]	UK	QALY	Third party payer	Life-time	Markov	50	70	gFOBT-biennial; FSIG-once	FSIG-once (55 yrs)†
Tsoi 2008[9]	Asian	LYG	NA	NA	Markov	50	80	gFOBT-annual; COL-10 yrs	gFOBT-annual (50-80 yrs)
Ho 2008[10]	Canada	QALY	Third party payer	Life-time	Markov	50	75	gFOBT-annual, biennial; COL-10 yrs; COL-10 yrs	CTC-10 yrs (50-75 yrs)
Zauber 2008[11]	USA	LYG	Societal	Life-time	Micro simulation model: MISCAN & SimCRC	40, 50, 60	75, 85	gFOBT-1, 2, 3 yrs; FIT-1, 2, 3 yrs; FSIG-5, 10, 20 yrs; COL-5, 10, 20 yrs; FSIG-5 yrs + gFOBT-1yr	gFOBT/FIT-annual; FSIG-5 yrs + gFOBT-1yr; COL-10 yrs (50-75 yrs)
Heitman 2009[12]	Canada	QALY	Societal	Life-time	Markov	50	74	gFOBT-annual; FIT-annual; FSIG-5 yrs s COL-10 yrs; CTC-5 yrs DNA-annual	FIT- annual (55-75 yrs)
Heitman 2010[13]	Canada	QALY	Societal	Life-time	Markov	50	75	gFOBT-annual; FIT-annual; FSIG-5 yrs s COL-10 yrs; CTC-5 yrs DNA-annual	FIT- annual (55-75 yrs)†
Lejeune 2010[14]	France	LYG	Third party payer	20 years	Markov	50	75	gFOBT-biennial; FIT-biennial	FIT-biennial (55-75 yrs)
Heresbach 2010[15]	France	LYG	Third party payer	30 years	Markov	50	75	gFOBT-biennial; FIT-biennial; CTC-10 yrs	FIT-biennial (55-75 yrs)
Telford 2010[16]	Canada	QALY	Third party payer	Life-time	Markov	50	75	gFOBT-annual, biennial; FIT-annual; FSIG-5 yrs; COL-10 yrs;	COL-10 yrs (50-75 yrs)

Table 1. (cont.) Summary of data extraction from 16 included studies[7-24].

Publication	Setting	Outcome	Perspective	Time horizon	Model type	Age of screening Start	Age of screening End	Screening modalities assessed	Reported optimal strategy
Van Rossum 201117	Netheland	LYG	NA	10 years	Markov	50	75	CTC- 5 yrs; DCBE- 5 yrs; sDNA- 3 yrs; FSIG-5 yrs + gFOBT-1yr gFOBT-once; FIT-once	FIT-once†
Whyte 201118	UK	QALY	Third party payer	Life-time	Markov	55	74	gFOBT-biennial; FIT-biennial; FSIG-once	FIT-biennial (60-74 yrs)†
Hassan 201119	France	LYG	Third party payer	Life-time	Markov	50	75	gFOBT-annual, biennial; FIT-annual, biennial; FSIG-5 yrs; COL-10 yrs; Capsule Endoscopy-5 years	FIT-annual (50-75 yrs)
Lucidarme 201220	France	CRC avoided	Third party payer	10 years	Simulation model	50	74	gFOBT-biennial; COL-10 yrs; CTC-10 yrs	gFOBT-biennial (50-74 yrs)
Sharp 201221	Ireland	QALY	Third party payer	Life-time	Markov	55	74	gFOBT-biennial; FIT-biennial; FSIG-once	FIT-biennial (55-74 yrs)
Barouni 201222	Iran	QALY	Third party payer	Life-time	Markov	50	75	gFOBT-annual, biennial; FIT-annual; FSIG-5 yrs; COL-10 yrs; CTC- 5 yrs; DCBE- 5 yrs; sDNA- 3 yrs; FSIG-5 yrs + gFOBT-1yr	COL-10 yrs (50-75 yrs)
Dan 201223	Singapore	QALY	Societal	Life-time	Markov	50	75	FIT-annual; FSIG-once, 5 yrs; COL-once, 10 yrs; CTC; DCBE; sDNA- 5 yrs	FIT-annual (50-75 yrs)
Sharaf 201324	USA	QALY	Third party payer	Life-time	Markov	50	80	FIT-biennial; FSIG-once COL-10 yrs; FSIG-5 yrs + gFOBT-1yr	FIT-biennial; FSIG-once; FSIG-5 yrs + gFOBT-1yr (50-79 yrs)†

†The strategies were report as cost-saving strategies.

There were few limitations in this review, these are (i) the review did not point out the differences of assumptions used in the models due to the complexity of data, (ii) the review did not provide information on ICER of the reported optimal strategies because of different approaches e.g., perspectives, cost calculations, year of reported ICER, assumptions, discounting rates, used in the analyses and such data may be inappropriate for comparisons.

CONCLUSION

According to the review, different approaches e.g., perspectives, cost calculations, assumptions used in the model, discount rate, society's willingness to pay, were observed. These limit the generalizability and transferability of results. Thus, the use of results from economic evaluations produced in other settings should be interpreted with caution. Although, all included studies found that all recommended screening modalities performed in the average risk populations were considered as a cost-effective or even cost-saving when compared with no screening. The studies did not find the consensus conclusion on which screening method was the most effective or the modality of choice. It can be concluded that the appropriate screening methods are gFOBT, FIT, FSIG and COL which are currently recommended by the national bodies. Whist, none of the innovative method e.g., CTC, capsule endoscopy, or stool-DNA was reported as optimal choice due to higher costs and comparable effectiveness. Based on the results in this review, FIT-biennially screening seems to be the most promising strategy owing to its effective, affordable and cost-effective. However, the question of which age groups should be eligible to screen cannot be directly concluded since it depends on the local epidemiology data. In order to provide the screening in recommended age range of 50-75 years which covered 26 age cohorts, tremendous resources are required. In counties with limited resources, such programs might not be feasible. This review can be used as the guidance for further analysis specifically designed to the setting and combined with local data where the screening program will be implemented. Besides the cost-effective data, the feasibility data are required in order to produce complete set of data readily for firm decision making.

REFERENCES

1. Ferlay J, Shin HR, Bray F, *et al*. GLOBOCAN 2008 v2.0, Cancer incidence and mortality worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: http://globocan.iarc.fr, accessed on 12/09/2013.
2. Chindaprasirt J, Sookprasert A, Wirasorn K, *et al*. Cost of colorectal cancer care in hospitalized patients of Thailand. *J Med Assoc Thai* 2012; 95Suppl 7: S196-200.
3. Levin B, Lieberman DA, McFarland B, *et al*. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA *Cancer J Clin* 2008; 58(3):130-60.
4. US Preventive Services Task Force (USPSTF). Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2008; 149(9):627-37.
5. European Commission.Cancer screening in the European Union Report on the implementation of the Council Recommendation on cancer screening. Luxembourg; 2008.
6. Drummond M, Sculpher M, Torrance G, *et al*. Method for the economic evaluation of health care programmes. 3rd ed. Oxford: Oxford University Press, 2005.
7. Leshno M, Halpern Z, Arber N. Cost-effectiveness of colorectal cancer screening in the average risk population. *Health Care Manag Sci* 2003; 6(3): 165-74.

8. Tappenden P, Chilcott J, Eggington S, *et al*. Option appraisal of population-based colorectal cancer screening programmes in England. *Gut* 2007; 56 (5):677-84.
9. Tsoi KK, Ng SS, Leung MC, *et al*. Cost-effectiveness analysis on screening for colorectal neoplasm and management of colorectal cancer in Asia. *Aliment Pharmacol Ther* 2008; 28(3):353-63.
10. Ho C, Heitman S, Membe SK, *et al*. Computed tomographic colonography for colorectal cancer screening in an average risk population: systematic review and economic evaluation. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2008.
11. Zauber AG, Lansdorp-Vogelaar I, Knudsen AB, *et al*. Evaluating test strategies for colorectal cancer screening: a decision analysis for the US Preventive Services Task Force. *Ann Intern Med* 2008; 149:659-69 .
12. Heitman S, Au F, Hilsden R, Manns B. Fecal Immunochemical Testing in Colorectal Cancer Screening of Average Risk Individuals: Economic Evaluation. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2009.
13. Heitman SJ, Hilsden RJ, Au F, Dowden S, Manns BJ. Colorectal Cancer Screening for Average-Risk North Americans: An Economic Evaluation. *PLoS Med* 2010; 7(11): e1000370.
14. Lejeune C, Dancourt V, Arveux P, *et al*. Cost-effectiveness of screening for colorectal cancer in France using a guaiac test versus an immunochemical test. *Int J Technol Assess Health Care* 2010; 26(1):40-7.
15. Heresbach D, Chauvin P, Grolier J, *et al*. Cost-effectiveness of colorectal cancer screening with computed tomography colonography or fecal blood tests. *Eur J Gastroenterol Hepatol* 2010; 22(11): 1372-9.
16. Telford JJ, Levy AR, Sambrook JC, *et al*. The cost-effectiveness of screening for colorectal cancer. *CMAJ* 2010; 182(12):1307-13.
17. van Rossum LG, van Rijn AF, Verbeek AL, *et al*. Colorectal cancer screening comparing no screening, immunochemical and guaiac fecal occult blood tests: a cost-effectiveness analysis. *Int J Cancer* 2011; 128(8):1908-17.
18. Whyte S, Chilcott J, Halloran S. Reappraisal of the options for colorectal cancer screening in England. *Colorectal Dis*. 2012; 14(9):e547-61.
19. Hassan C, Benamouzig R, Spada C, *et al*. Cost effectiveness and projected national impact of colorectal cancer screening in France. *Endoscopy* 2011; 43(9):780-93.
20. Lucidarme O, Cadi M, Berger G, *et al*. Cost-effectiveness modeling of colorectal cancer: computed tomography colonographyvs colonoscopy or fecal occult blood tests. *Eur J Radiol* 2012; 81(7): 1413-9.
21. Sharp L, Tilson L, Whyte S, *et al*. Cost-effectiveness of population-based screening for colorectal cancer: a comparison of guaiac-based faecal occult blood testing, faecal immunochemical testing and flexible sigmoidoscopy. *Br J Cancer* 2012; 106(5):805-16.
22. Barouni M, Larizadeh MH, Sabermahani A, *et al*. Markov's modeling for screening strategies for colorectal cancer. *Asian Pac J Cancer Prev* 2012; 13(10):5125-9.
23. Dan YY, Chuah BY, Koh DC, *et al*. Screening based on risk for colorectal cancer is the most cost-effective approach. *Clin Gastroenterol Hepatol* 2012; 10(3):266-71 e1-6.
24. Sharaf RN, Ladabaum U. Comparative effectiveness and cost-effectiveness of screening colonoscopy vs. sigmoidoscopy and alternative strategies. *Am J Gastroenterol* 2013; 108(1):120-32.