MEDINFO 2004
M. Fieschi et al. (Eds)
Amsterdam: IOS Press

Cost-Effectiveness Analysis of Colorectal Cancer Screening Strategies in Singapore: A Dynamic Decision Analytic Approach

Swee Seong Wong[a], Adrian Peng Kheong Leong[b], Tze-Yun Leong[a]

[a] *School of Computing, National University of Singapore, Singapore*
[b] *Department of Surgery, National University Hospital, Singapore*

Abstract [1]

A dynamic decision analytic framework using local statistics and expert's opinions is put to study the cost-effectiveness of colorectal cancer screening strategies in Singapore. It is demonstrated that any of the screening strategies, if implemented, would increase the life expectancy of the population of 50 to 70 years old. The model also determined the normal life expectancy of this population to be 76.32 years. Overall, Guaiac Fecal Occult Blood Test (FOBT) is most cost effective at SGD162.11 per life year saved per person. Our approach allowed us to model problem parameters that change over time and study the utility measures like cost and life expectancy for specific age within the range of 50- 69 through to 70 years old.

Keywords:

Dynamic decision analysis, colorectal neoplasm, mass screening, cost-benefit analysis.

Introduction

Colorectal cancer ranks second among all cancers in Singapore, with age-standardized rates increasing two-fold in the periods 1993 to 1997 as compared to 1968 to 1972. The incidence of Colorectal Cancer in Singapore for both sexes begins to rise sharply at 50 years of age [1]. Early detection of cancerous growth can lead to higher chance of recovery with early treatment and thus save lives. Hypothetically, the benefits may include elevation of potential patient's suffering and saving in medical cost of colorectal cancer treatment.

The natural history of colorectal cancer makes it ideal for screening. It is widely accepted that cancers develop over many years as polyps. Symptomatic cancers are usually late stage, costly to treat and are associated with a poor prognosis. Pre-cancerous polyps, however, can be removed during screening procedures [2][3]. Population-screening programs enable early detection and removal of such pre-cancerous polyps and thus decrease the burden of cost to the health care system for treating colorectal cancer [4][5].

Objective

Singapore statistics and population characteristics are used to study the cost-effectiveness of a colorectal cancer screening program. The objective is to discriminate among several screening strategies in order to identify the one most cost effective. Five commonly used colorectal cancer screening strategies are being evaluated – Guaiac Fecal Occult Blood (FOBT), Immunochemical Fecal Occult Blood (FOBT(IMM)), Double Contrast Barium Enema (DCBE), Flexible Sigmoidoscopy (FSIG) and Colonoscopy (COL). Each screening strategy has its own accuracy in detecting cancerous growth and own cost and possible complication involved. Some strategies are easier to administer and hence will be expected to have higher response or compliance from the population. Trade-off is generally the concern in most problems whereby we look at the life years saved (benefit measure) verses cost (effort measure) in achieving the result (generally, higher cost yields better result). Different studies have drawn different conclusions.

In this work, we study the various strategies based on the Singapore local statistics. While the common assumption is such that it is indeed life saving to implement a screening policy than not, it is interesting to quantify the benefits gained in terms of life years saved with each strategy.

Approach

There are several existing studies on evaluating the most effective colorectal cancer screening methods. Most of them adopt the Markov approach to dynamic modeling while others use simulation techniques and cost-utility analysis [6]. Our approach is similar to dynamic modeling except that a semi-Markov model is used to more adeptly handle the different lengths of staging period in the various screening processes. For example, the FOBT is done on a yearly basis while DCBE is every 5 years. Also the model captures the time varying complexity of age dependent parameters. A single model is created to solve a policy discrimination problem, [7] with each screening strategy modeled as a separate policy for comparison. In order to study the effect on screening over the range of 50 to 70 years of age, the model starts with the population at age 50 and progresses over a time horizon of 50 years.

1. Based on work done at ReasonEdge Technologies Pte Ltd., Singapore

Materials and Methods

Screening Strategies

The 5 screening strategies studied are illustrated in Fig. 1. The screenings are for Singapore residents between the ages of 50-70. An individual starts off by going through the initial screening test (FOBT or FOBT (IMM) or FSIG or DCBE). The prevalence of cancer and polyps in a population as well as the sensitivity and specificity of the test influence the probability of the result being positive or negative. Colonoscopy is used directly as the initial test for one of the strategies. .

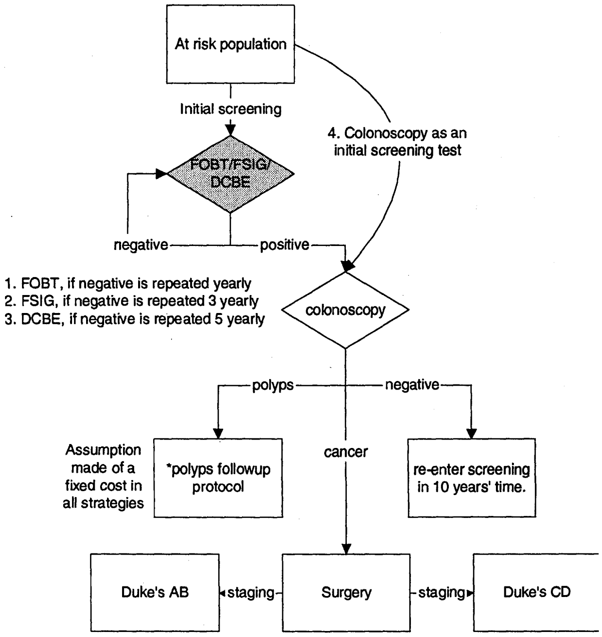

Figure 1 - The Screening Strategies

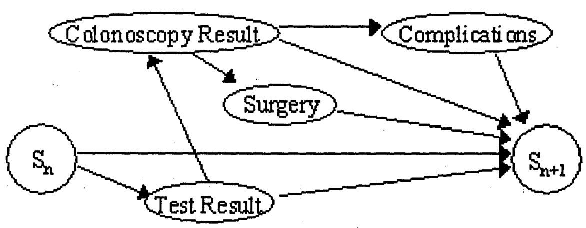

Figure 2 - Structure of the decision model for screening strategy FOBT

If the test result is positive (be it a false or true positive), colonoscopy test is performed. As a diagnostic procedure, colonoscopy is both highly sensitive and highly specific. It can, however, lead to complications, or even in a small percentage of cases, death. If cancer is found, surgery is performed. Staging is done at the time of surgery. The various stages of cancer (prevalence of Duke's A or B/Duke's C or D in the general population) as well as mortality rates of the procedure influence the cost to be incurred as well as the prognosis (life expectancy).

If the screening test is negative, the patient would undergo repeated tests within 1, 3, 5 or 10 years * depending on which screening strategy (FOBT both, FSIG, DCBE, or COL respectively) is chosen

Dynamic Decision Model

A semi-Markov decision model [7] is constructed using the ReasonEdge Modeler software[1]. A simplified diagram of the influence view from the Modeler illustrating the dependency relationship among various events is shown in Fig. 2. The circular nodes (S_n and S_{n+1}) denote the current and the next health states of a patient. The possible health states of a patient under the FOBT strategy are shown in Table 1. For example, a person may be in a state where the FOBT result is positive and colonoscopy negative with no complications (row 2 of the table). Death from complications or from other causes is also a possible health state. Fig. 4 shows a schematic state transition of a patient, unfolded to exemplify the different states in the model in which a patient will have to go through. Once a patient is diagnosed with polyps or colorectal cancer, he or she will drop out from the program and will not be in the screening cycle.

Table 1: Examples of possible Health States for Strategy FOBT

FOBT	COL	Complications	Cancer Type
Negative			
Positive	Negative	No	
Positive	Negative	Yes	
Positive	Positive	No	Duke's A or B
Positive	Positive	Yes	Duke's A or B
Positive	Positive	No	Duke's C or D
Positive	Positive	Yes	Duke's C or D
Positive	Positive	No	Polyps
Positive	Positive	Yes	Polyps
Dropout			
Dead			

Data Source and Assumptions

To populate the model, the values below are required. They are obtained from medical literature, local surgeons' expert opinions, or measured assumptions (see Appendix section).

1. Sensitivity and Specificity
2. Complication Rates
3. Cost of Procedures

1. ReasonEdge Technologies Inc. (http://www.reasonedge.com)

4. Incidences and 5-year survivals rates
5. Age specific mortality rates from all illnesses
6. Demographic distribution

Table 2: Cost and Life Expectancy

Units in SGD$ or years	FOBT	FOBT (IMM)	FSIG	DCBE	COL
Age 50-54					
Cost	501.82	1050.08	1139.31	786.34	1252.03
Life Expectancy	25.56	25.50	25.79	26.03	25.71
Cost per Life Year Saved	288.33	623.12	576.28	355.07	660.35
Age 55-59					
Cost	382.65	893.61	922.24	618.75	1218.09
Life Expectancy	21.44	21.42	21.74	21.95	21.94
Cost per Life Year Saved	145.70	342.75	315.53	197.19	390.24
Age 60-64					
Cost	252.31	688.82	675.83	442.56	724.56
Life Expectancy	17.67	17.69	18.02	18.19	17.92
Cost per Life Year Saved	65.42	177.69	160.81	101.17	176.51
Age 65-69					
Cost	103.08	340.49	365.40	259.26	718.17
Life Expectancy	14.27	14.31	14.56	14.73	14.92
Cost per Life Year Saved	18.89	62.03	63.60	43.86	117.72
Weighted Average Cost per Life Year saved.	162.11	368.06	340.36	211.57	402.24

In evaluating the costs for various strategies, only direct costs are accounted for. If polyps were discovered at colonoscopy, the patient will "dropout" of the screening strategy and will undergo a separate post-polypectomy pathway with a fixed cost associated with that protocol [8]. The cost of the treatment program for polyps is not considered here.

Results

Cost-Effectiveness Analysis

Results are reported by giving the average cost and life expectancy for the subgroups within the population from the age of 50-69 through to 70. FOBT is superior in terms of Cost per Year of Life Expectancy saved, as shown in Table 2. It costs SGD162.11 per life year saved per person to run such a screening program at 100% compliance. COL was the most expensive strategy.

The total cost of a screening program for the at-risk population is computed taking into consideration all the factors like the cost of the test, the cost of colonoscopy and its possible complications, and the cost of treating cancer, if detected.

Life expectancy for "no-screening" is computed by setting the value for compliance to zero. The model yields 76.32 years, which is the life expectancy of the population without any screening program. The difference in life expectancy would then be the "life-years saved". For example, taking the average age of 52.5 for the group 50-54, the life-years saved for FOBT screening is (25.56 + 52.5) – 76.32 = 1.74. The weighted average of cost per life year saved is weighted base on the population demography of Singapore for the different age groups.

The cost per life year saved, which may seem considerably lower than in other studies [9], is that patients with polyps detected would "drop out" of this program and are therefore not reflected in the cost figures. Another reason is because of the difference in how the life years saved is computed. In the model, the death from other causes for different age groups, are taken into account in simulating the colorectal cancer progression of the screening population until the age of 100. Fig. 3 shows the detailed cost per life year saved across the different age groups.

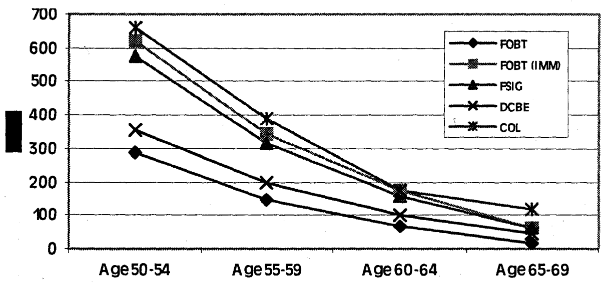

Figure 3 - Cost per Life Year Saved across the age groups

Discussion and Conclusion

Given that early detection of colorectal cancer at an earlier stage or detection of its precursors would reduce mortality [10], results from our analysis show that any of the 5 screening strategies would increase the life expectancy of a person in the at-risk population and is recommended. Overall, FOBT (guaiac) is the most cost-effective method of screening for Singapore residents aged 50-70 for colorectal cancer.

In our study, we have assumed time invariant in some of the parameters. For example, the prevalence of polyps and cancer are assumed to be invariant within the age group of 50-70. More analysis is needed to identify the key parameters or factors that have the significant impact on cost and life expectancy measures. Through comparing the assumptions made in different modeling approaches, we need to evaluate and refine on the life expectancy estimated. Currently we have also assumed independence in screening results between consecutive cycles. Depending on the time lag and specificity of the screening test, there might be a significant relation that we have not captured in our model.

Acknowledgment

This research is partially supported by Research Grant No. R-252-000-111-112/303 from the Agency for Science, Technology, and Research (A*Star) and the Ministry of Education in Singapore, and partially supported by ReasonEdge Technologies Pte. Ltd. in Singapore.

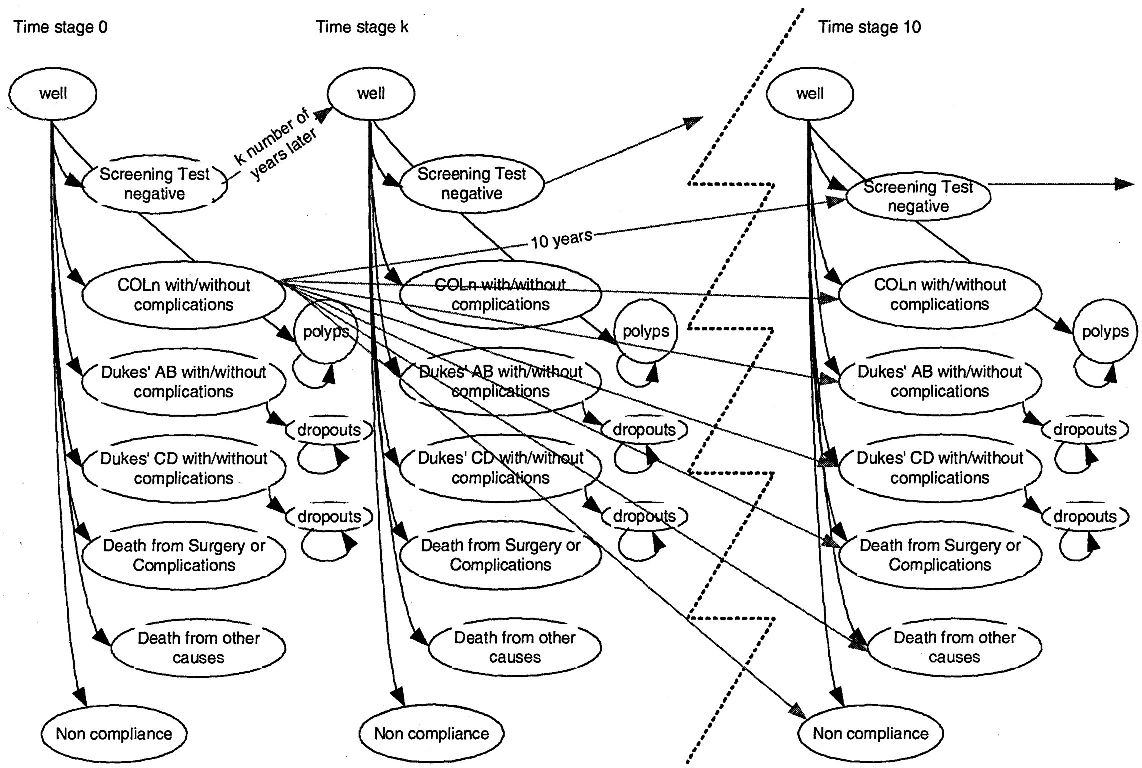

Figure 4 - Schematic state transitional diagram of the screening strategy

Table 3: Cost of Screening Procedures. The figures for cost of procedures were taken from the schedule of charges for a non-subsidized patient in Singapore restructured hospitals. The cost of colonoscopy itself is \$660. As 10% of colonoscopy is «incomplete», DCBE is needed to completely visualize the colon. Therefore, the cost of colonoscopy is on average \$660 + 0.1(\$80) = \$668. The exception is if DCBE is the initial screening test, a colonoscopy that followed a positive DCBE would cost \$660.

Possible Screening Procedures	Cost of procedure SGD$	Histology SGD$	Total costs SG
FOBT	10	NA	10
FOBT (Imm)	30	NA	30
DCBE	80	NA	80
FSIG	130	80	240
COL (diagnostic)	660 (668)	80	740

References

[1] *Singapore Cancer Registry 2000; Report No 5.* pages 78-81.

[2] Winawer SJ, O'Brien MJ, Waye JD, Kronborg O, Bond J, Fruhmorgen P, Sobin LH, Burt R, Zauber A, Morson B. Risk and surveillance of individuals with colorectal polyps. Who Collaborating Center for the Prevention of Colorectal Cancer. *Bull World Health Organization* 1990;68(6):789-795.

[3] Markowitz AJ, Winawer SJ. Screening and surveillance for colorectal cancer. *Semin Oncol.* 1999 Oct;26(5):485-498.

[4] Podolsky D K. Going the Distance - The Case for True Colorectal-Cancer Screening. Editorial in *NEJM.* July 20, 2000. Vol. 343, No. 3.

[5] Colorectal cancer screening. Technical review 1. Rockville, Md.: Agency for Health Care Policy and Research, 1998. (AHCPR publication no. 98-0033.)

[6] Pignone M, Saha S, Hoerger T, Mandelblatt J. Cost-effectiveness analyses of colorectal cancer screening: A System-

atic review for the U.S. preventive services task force. *Ann Intern Med.* 2002;137:96-106.

[7] Leong TY. Multiple perspective dynamic decision making. *Artificial Intelligence.* 105 (1998) 209-261.

[8] Winawer SJ, Stewart ET, Zauber AG, et al. A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. *NEJM.* 2000;342:1766-1772

[9] Wagner JL, Herman RC , Wallace S. Cost-effectiveness of colorectal screening in the elderly. *Ann Intern Med.* 1991; 115 (10): 807-817.

[10]Ngoi SS, Wong JE, Goh PM Screening for colorectal cancer in Singapore. *Singapore Med.* 1990 Oct;31(5):439-442.

[11]Surveillance, Epidemiology and End Results (SEER) is available on the net at http://www.seer.cancer.gov/

[12]Lun KC. Mortality Analyses of the 1990 Singapore population: I. General Life Tables. *Annal Acad Med Singapore.* 1995 May; 24(3): 382-392.

Address for correspondence

Swee Seong Wong (wongss@comp.nus.edu.sg)
School of Computing. 3 Science Drive 2,
Singapore 117543. Singapore.

Appendix

*Table 4: Cost of Realated Treatments. * Computation for cost of treating complications of colonoscopy is the weighted ratio of the costs for treating an iatrogenic bleed plus that for an iatrogenic perforation*

Other Procedures related to complications and treatment	Cost SGD$
Colonoscopy with polypectomy (therapeutic colonoscopy)	800
Resection of Duke's A or B	20,000
Resection of Duke's C & D, with follow up adjuvant therapy	35,000
Cost of treating complications of colonoscopy	8,706*

Table 5: Complication Rates

Screening	Bleeding	Perforation	Death
FSIG	0.0001	0	.0
COL	0.001	0.0007	0.00005

*Table 6 – Incidences and 5 year Survival Rates. *US Cancer registries (SEER) quote local, regional and distant CRC lesion's 5-year survival rates at around 91%, 66%, 8% respectively [11]. However, local colorectal surgeons estimate the 5-year survival rates for Duke's A & B to be 0.8 and Duke's C & D to be 0.2.*

Type	Incidence	5 year survival
Polyps	0.2340000	0.99
Dukes A & B	0.0001385	0.8*
Dukes C & D	0.0001835	0.2*
Total Dukes A-D	0.0003220	NA

Table 7 – Sensitivity and Specificity

Screening	Sensitivity	Specificity
FOBT for polyps	0.1	0.9
FOBT for cancer	0.6	0.9
Immunochemical FOBT for polyps	0.4	0.95
Immunochemical FOBT for cancer	0.9	0.95
DCBE for polyps	0.3	0.9
DCBE for cancer	0.7	0.9
FSIG for polyps or cancer	0.6	0.98
COL for polyps or cancer	0.9	1

Demographic Distribution

The age distribution across the age group 50-54, 55-60, 60-64, 65-69 is 39%, 22%, 22% and 17% respectively [12].