Colorectal cancer screening in Australia: An economic evaluation of a potential biennial screening program using faecal occult blood tests

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Abstract

Objective: To evaluate whether the introduction of a national, co-ordinated screening program using the faecal occult blood test represents 'value-for-money' from the perspective of the Australian Government as third-party funder.

Methods: The annual equivalent costs and consequences of a biennial screening program in 'steady-state' operation were estimated for the Australian population using 1996 as the reference year. Disability-adjusted life years (DALYs) and the years of life lost (YLLs) averted, and the health service costs were modelled, based on the epidemiology and the costs of colorectal cancer in Australia together with the mortality reduction achieved in randomised controlled trials. Uncertainty in the model was examined using Monte Carlo simulation methods.

Results: We estimate a minimum or 'base program' of screening those aged 55 to 69 years could avert 250 deaths per annum (95% uncertainty interval 99-400), at a gross cost of $A55 million (95% UI $A46 million to $A96 million) and a gross incremental cost-effectiveness ratio of $A17,000/DALY (95% UI $A13,000/DALY to $A52,000/DALY). Extending the program to include 70 to 74-year-olds is a more effective option (cheaper and higher health gain) than including the 50 to 54-year-olds.

Conclusions: The findings of this study support the case for a national program directed at the 55 to 69-year-old age group with extension to 70 to 74-year-olds if there are sufficient resources. The pilot tests recently announced in Australia provide an important opportunity to consider the age range for screening and the sources of uncertainty, identified in the modelled evaluation, to assist decisions on implementing a full national program.

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Colorectal cancer (CRC) is the fourth commonest cancer world wide.[1] Australia's incidence and mortality rates rank among the highest in the world.[2] In a population of 18 million in 1996 (see footnote), it was the second most prominent cancer with more than 11,000 new cases and almost 5,000 deaths.[2] These new cases and deaths were responsible for 67,000 disability-adjusted life years (DALYs) or 15% of the total burden of disease due to all cancers in 1996.[4] Total health system costs associated with CRC were approximately $205 million in 1993/94.[5]

A meta-analysis of four randomised controlled trials (RCTs) of biennial population screening using the faecal occult blood test (FOBT) has shown it to be efficacious in reducing the risk of mortality by 16%.[6] Acceptability was high with an average participation rate of 66%.[6] Mathematical simulation studies have demonstrated that the cost-effectiveness of such a program would be similar or even better than the current breast and cervical screening programs in the US, Denmark, the UK and Australia.[7-10] On the basis of these results, screening of asymptomatic individuals, starting at the age of 50 years, is recommended and national programs are under consideration in a number of countries.[11,12] Australia commenced pilot screening programs in three States: Queensland (November 2002) and Victoria and South Australia (early 2003).

As part of a larger priority setting study[13,14] commissioned by the Cancer Strategy Group, an advisory body of the Australian Government, an economic evaluation was undertaken to assess the economic credentials of introducing a national CRC screening program. Annual and biennial screening programs, targeting different age groups, were evaluated compared with the status quo. This paper describes the details of the evaluation of the biennial program because of the stronger evidence of efficacy (four RCTs as opposed to one RCT) and the better economic credentials.

1. In 2003, this population estimate is 20 million people. The reported incidence of CRC is 12,405 and deaths of 4,718 in 2000.[3]

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Methods

The evaluation

The annual equivalent benefits, costs and cost-effectiveness of a national CRC program were modelled and compared with the status quo using a cost-effectiveness analysis (see footnote 2). The evaluation assumed a hypothetical, nationally co-ordinated screening program, using a standard guaiac-based test for faecal occult blood test (FOBT) equivalent to those used in the RCTs, and delivered biennially to the Australian population of 1996 for those of 'average risk' (see footnote 3).[15] It also was assumed the program was in 'steady state' in order to represent the annual ongoing cost and consequences of the screening program delivered in 1996. This excludes the increase in detection of cancers and higher implementation costs early after the introduction of a program.

Based on a preliminary analysis, screening 55 to 69-year-olds was considered the minimum or 'base program' from an economic point of view. Extension of the program to younger and older age groups was also evaluated using marginal analysis. The comparator was the status quo of minimal opportunistic screening by FOBT (2%, expert opinion) and some de facto screening by colonoscopy (Victorian inpatient data). Table 1 provides a comparison of the main components of the status quo and the proposed program.

The perspective used was that of the Australian Government as third-party funder of such a program. A Working Party of the Cancer Strategies Group (CSG), comprising cancer experts, government policy makers and a consumer representative, was set up to advise and support the project. The CSG Working Party and DJB StJ provided the 'expert opinion' when there was no published evidence available and/or when the overseas evidence needed modification for the local context.

Health benefits

The health benefit was estimated in DALYs, which combines mortality, measured as years of life lost (YLLs) and morbidity, measured as years lived with disability (YLDs). The estimated change in DALYs in the presence of the hypothetical screening program is equal to the sum of the estimated change in the YLLs and the YLDs associated with CRC. The methodology used in Burden of Disease (BOD) studies[4,16,17] was adapted for this study.[13,14] Consistent with the previous BOD studies, all future health benefits and costs were discounted at 3% (see footnote 4) to indicate a time preference for delaying costs and having health benefits now rather than in the future.

2. The generic term of cost-effectiveness analysis is used to include the cost-utility analysis ($/DALY) and cost-effectiveness ($/YLL), as adopted by the Washington Panel.[30]

3. 'Average risk' in this case corresponds to asymptomatic individuals above the age of 50 years with no family history of colorectal cancer and no other special risk factors; it also includes at a slightly higher risk of up to double the average, individuals with one first-degree relative diagnosed with CRC above the age of 55 years.

Table 1: Comparison of status quo and proposed national program.

Program components	Status quo	National program
Infrastructure	Opportunistic program, no formal structure of recruitment, co-ordination and registry.	National recruitment campaign, co-ordination and registry.
Screening by FOBT – includes the kit, transport, processing, GP visit.	Small local programs offered on an ad hoc basis to the general public by volunteer organisations. Minimal participation rate around 2%.	Targeted general practice delivered program similar to the Australian cervical cancer screening program. Biennial program. Participation rate in RCT was 66%, which equates to 33% per annum.
Screening by colonoscopy.	Assume 15% of current colonoscopies are de facto screening colonoscopies.	Assume the de facto screening colonoscopies reduce due to introduction of a national program.
Diagnostic work-up – includes a colonoscopy and an initial and follow-up specialist visit.	Diagnostic work-up of individuals with positive FOBT. Small number of screen-induced diagnostic work-up.	Diagnostic work-up of individuals with positive FOBT. Assume all positive FOBT are followed up, rate dependent on the positivity of the FOBT detection method.
Treatment (stage specific).	Based on current stage distribution.	Shift to earlier stage at diagnosis. Shift in stage distribution predicted by modelling based on mortality reduction achieved in RCTs.
Palliation.	For non-survivors predicted by stage-specific five-year survival rates.	For non-survivors predicted by stage-specific five-year survival rates.
Follow-up surveillance – by repeat diagnostic work-up in 3-5 years.	Small number of screen-induced surveillance follow-up.	Assume 25% of those with a positive FOBT will have a polyp >10mm and will be followed up according to guidelines.
Complications of colonoscopy.	Perforation and mortality.	Perforation and mortality. These will increase with an increase in colonoscopies.

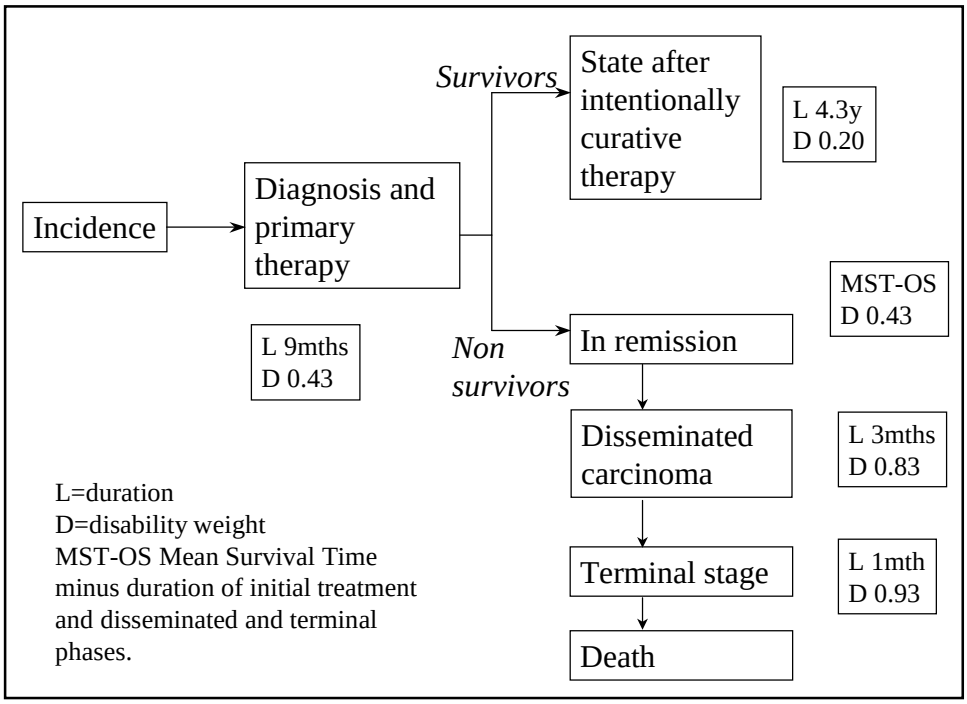


Figure 1: Colorectal cancer disease model showing different phases for survivors and non-survivors.

The YLD estimations

Figure 1 shows the single disease-based model used to estimate the YLDs associated with each phase of CRC for survivors and non-survivors in the Australian Burden of Disease and Injury study.[4] For our study, a separate model was used for each of the CRC Duke's stages A to D. Incident cases were allocated to one of the four stage-models according to the current and predicted distribution of the stages. The proportions of survivors and non-survivors were based on five-year, stage-specific survival rates.[18] The YLDs were calculated as the product of incidence and average duration of the health state weighted for severity expressed in disability weights (DW)[19] as a proportion between 0 (full health) and 1 (worst possible health state).

The YLL estimations

The original BOD studies used observed incidence and mortality from which to calculate YLLs. In our study the number of deaths, and hence YLLs, were modelled from predicted mortality based on the five-year survival rate. For each death averted (or increase in survivors from the model), the YLLs recovered was estimated from the difference between the discounted life expectancy for that age-group and the discounted mean survival time for CRC patients in each age group. The Australian 1996 Cohort Life Expectancy was used as a standard against which YLLs were calculated. [4]

Epidemiological parameters used in the model

National data were used for cancer incidence, mortality, age of onset, mean survival time for each age group, and duration associated with each phase of the model for survivors and non-survivors.[2,4] Data from the South Australian Cancer Registry provided the stage distribution and five-year survival rates.[18] The distribution of patients in stages A to D, at time of diagnosis (0.14 : 0.33 : 0.31 : 0.21) was close to the combined distributions in the control groups from the RCTs. On advice from the CSG Working Party the five-year survival rates from each stage, which were an average over 15 years of data, were increased by 5% to reflect current improved survival rates (92%: 75%: 44%: 5%).

Based on a meta-analysis of three of the randomised controlled trials,[20-22] in the presence of a screening program, it was assumed that the CRC incidence would be unchanged but the mortality rate would fall by 14%. A CRC stage shift from status quo to 0.26 : 0.28 : 0.32 : 0.15 (coincidentally similar to the stage distribution achieved in the Swedish study)[21] achieved this mortality reduction in our model. The fourth randomised controlled trial, the Minnesota study,[23] was excluded because the high positivity rate of their FOBT – almost 10% – resulted in 28% of the subjects having one or more colonoscopies.

Health service utilisation, costs and assumptions

The main health service utilisation assumptions used in the model and the sensitivity analysis are summarised in Table 2. Estimates of the total health care utilisation and the gross and net costs were modelled in Excel for the proposed screening program and compared with the status quo comparator.

Table 3 shows the screening pathway comparing the health services, their costs and the resource utilisation for the status quo situation and in the presence of the proposed program directed at those aged 55 to 69-years-old. Gross costs (screening program costs only) included the infrastructure, FOBT screens, diagnostic work-up and the cost of complications arising from the diagnostic procedures resulting from the screening program. Net costs

4. Consistent with PBAC and NHMRC, a discount rate of 5% was also modelled with no difference on final results.

Table 2: Assumptions used in the primary analysis and in the sensitivity analysis.

Variable	Primary analysis	Sensitivity analysis	Rationale for distribution
Current rate of opportunistic FOBT screening	2%	Triangular distribution from 0.015 peaking at 0.03 and ending at 0.07	2%,[23] expert opinion 5%[39]
Participation rate[a] with proposed biennial screening program	66% i.e. 33% per annum	Triangular distribution from 40%, peaking at 66% and ending at 82%	66%[6] 50%[39] 40% to 82% CSG working party
FOBT positivity rate/ colonoscopy rate[b]	2%	Triangular distribution from 0.015 peaking at 0.03 and ending at 0.07	2% [20,22] 5%[39]
Deaths from colonoscopies	2/10,000	Uniform distribution from 1 and 3 per 10,000	0.2%[15]
De facto screening colonoscopies	15%	Uniform distribution between 0% and 15%	Calculated from inpatient data
Follow-up surveillance of polyps[c]	25%	Triangular distribution from 7%, peaking at 20% and ending at 30%	25%;[40] expert opinion
Program / $1996	$7.9 million	Uniform distribution of reported costs +/-10%	Consistent with other cost variation
Costs of colonoscopy	$1,000	Uniform distribution of reported costs +/-20%	Costs were fairly consistent from Australian reports but vary widely if public or private sector.
Other costs	As stated in assumptions in Table 3	Uniform distribution of reported costs +/-10%	Costs were fairly consistent from Australian reports but vary if public or private sector.
Mortality (biennial) reduction	14%	Normal distribution (mean 13, SD 3.6)	Modification of modelled change in mortality with CI from literature[6]
Disability weight uncertainty	Refer Figure 1	Uniform distribution from 0.5 to twice the disability weight for Dx, remission or 'cured' phases of CRC	Expert opinion

Notes:
(a) Assumed to be constant across all age groups.
(b) Assumed all positive FOBT are followed up with a colonoscopy.
(c) Approximately 25% of individuals with positive FOBT have a polyp (adenoma) greater than 10mm[20,22] that should be followed up.

Table 3: The health service cost and resource utilisation for base program (55-69-year-olds).

Screening pathway	Service	Unit	Unit cost $1996[a]	Status quo (no. of units)	Proposed biennial screening program (no. of units)
1. Infrastructure	Recruitment, co-ordination and registry	Program	7.9 million[b]	0	1
2. Screens	FOBT kit, transport, processing, GP visit	Screen	41[41,42]	45,000	740,000
3. De facto screening colonosopies	Colonoscopy[c]	Colonoscopy	1,000[43]	11,000	
4. Diagnostic work-up	Colonoscopy[c] Initial visit + follow up	Pos FOBT Pos FOBT	1,000[43] 176[38,41]	900 900	15,000 15,000
5. Complications	Perforation	0.0017 per colonoscopy[15]	15,000[38]	19	25
6. Treatment	Dukes A (surgery) Dukes B (surgery) Dukes C (surgery + adjuvant chemotherapy) Dukes D (palliative chemotherapy + surgery)	Stage specific Stage specific Stage specific Stage specific	14,000[38] 14,000[38] 22,000[38] 19,000[38]	570 1,300 1,200 800	1,000 1,100 1,200 600
7. Palliation	Advanced	Mortality	25,000[9]	1,900	1,600
8. Follow-up surveillance	Diagnostic work-up see above but in 3-5 years' time	25% positive FOBT	880[d 38,41]	3,000	4,000

Notes:
(a) All costs are presented in real prices for the 1996 reference year with future costs discounted to present value at 3% per annum.[44]
(b) Commonwealth screening program (personal communication, 2000).
(c) Colonoscopy includes immediate complications such as haemorrhage, and full hospital costs (not just medical fee for procedure).
(d) Costs incurred on average in four years' time therefore discounted back to 1996.

included projected treatment savings, savings from reduced de facto screening by colonoscopy, and the additional expense anticipated from increased follow-up activity.

Infrastructure costs were allocated to the base program on the assumption that costs would not change greatly with the inclusion of other age groups into the screening program. Costs falling on participants were not included.

Sensitivity analysis

A multiway probabilistic sensitivity analysis was performed using @RISK software.[24] The input uncertainty distributions were based on a combination of the reported confidence intervals for that variable, the range of reported values in the literature and expert opinion on the range of likely values under Australian conditions (see Table 2). The output distributions reported are the 2.5 (lower limit) and 97.5 (upper limit) percentiles of the 2000 Monte Carlo simulations because of their skewed distribution. This skewed distribution occurred as four of the input variables had a skewed distribution (see Table 2). In addition, the @RISK software identifies major influential factors and the input uncertainty distributions that have the greatest impact on the results by regression and correlation of inputs and outputs for each of the iterations of the simulation.

Results

The costs, benefits and cost-effectiveness of the base program, together with the incremental costs of screening additional age groups, are summarised in Table 4. The results are expressed as cost (Australian dollars) per YLL avoided, as well as cost per DALY avoided, to enable comparison with published cost-effectiveness and cost-utility studies.

Benefits, costs and incremental cost-effectiveness ratios (ICER=ΔC/ΔE)

A base program (screening 55 to 69-year-olds) would have prevented 250 deaths and avoided 3,200 DALYs due to CRC in 1996. Extension to the older age groups (70 to 74 years, or 70 years and over) would have avoided significantly more DALYs than addition of younger age groups (50 to 54 years or 45 to 54 years).

The gross annual cost of the base program in 1996 would have been $55 million, including infrastructure costs of $7.9 million. Inclusion of anticipated treatment savings from less advanced disease ($7.6 million), plus savings from a reduction in de facto screening colonoscopies ($13 million), offset by additional costs of follow-up surveillance ($4.3 million) produces a net annual cost of $39 million. Addition of the older age groups would cost significantly less than addition of the younger age groups.

The ICER of the base program would be $17,000/DALY (gross) or $12,000/DALY (net) and is even better for the older age groups. Extending the program to include 50 to 54-year-olds would increase benefits, but at a substantial cost of $29,000/DALY gross ($24,000/DALY net), which amounts to almost double the cost per DALY of the baseline program.

Sensitivity analysis

For the base program the point estimate for the number of deaths avoided is 250, with lower and upper limits of 99 and 400. The

Table 4: Incremental cost analysis – point estimates (PE) and lower and upper limits (LL,UL) of the uncertainty intervals of health benefits, costs and cost-effectiveness ratios for biennial screening for colorectal cancer in Australia, 1996.

Age group (years)	Extension to include 45-49			Extension to include 50-54			Base program 55-69[a]			Extension to include 70-74			Extension to include 75+		
	PE	**LL**	**UL**	**PE**	**LL**	**UL**	**PE**	**LL**	**UL**	**PE**	**LL**	**UL**	**PE**	**LL**	**UL**
Health benefit															
Deaths	**26**	8.0	39	**42**	16	65	**250**	99	400	**120**	50	200	**200**	81	320
YLLs	**490**	150	750	**730**	270	1100	**3,200**	1,300	5,000	**1,100**	440	1,700	**1,400**	560	2,200
DALYs	**490**	150	750	**730**	270	1100	**3,200**	1,200	5,000	**1,100**	430	1,700	**1,300**	510	2,200
Costs ($m)															
Gross costs	**27**	22	51	**22**	18	40	**55**	46	96	**13**	10	24	**19**	16	36
Net costs	**25**	21	54	**18**	15	41	**39**	33	92	**5.7**	4.5	21	**8.8**	6.8	31
ICER															
Gross costs /DALY	**56,000**	42,000	216,000	**29,000**	22,000	97,000	**17,000**	13,000	52,000	**12,000**	9,000	36,000	**15,000**	11,000	46,000
Gross costs /YLL	**56,000**	42,000	216,000	**29,000**	22,000	97,000	**17,000**	13,000	52,000	**12,000**	8,900	35,000	**14,000**	10,000	42,000
Net costs /DALY	**50,000**	40,000	223,000	**24,000**	20,000	96,000	**12,000**	10,000	47,000	**5,300**	4,500	29,000	**6,600**	5,500	35,000
Net costs /YLL	**50,000**	40,000	226,000	**24,000**	20,000	97,000	**12,000**	10,000	47,000	**5,300**	4,500	28,000	**6,400**	5,400	33,000

Notes:
(a) The base program includes infrastructure costs of $7.9 million.
Figures have been rounded to two significant digits.[30]
The results for the 'extension' programs are incremental results to the base program and do not show results for the combined (base + extension) program.

gross costs may be as low as $46 million or as high as $96 million. The corresponding ICER range from a low of $13,000/DALY to a high of $52,000/DALY (see Table 4).

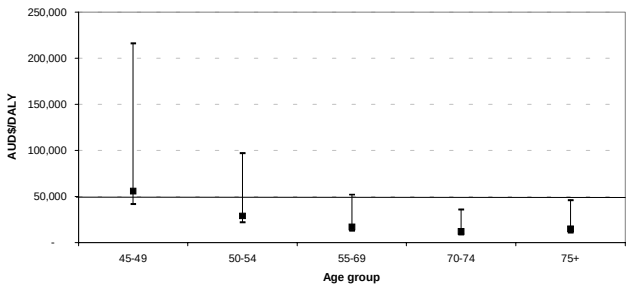
If $50,000/DALY were acceptable to the policy makers as a threshold value for the ICER, then biennial screening of the 55 to 69 age group, with extension to the 70 to 74 age group and ultimately the 75 and over age group, should be cost-effective (see Figure 2). The probability that the 50 to 54 age group would meet this threshold are significantly lower, with the 45 to 49 age group weaker still.

The major influences on the uncertainty of the health benefits were the size of the mortality reduction and the screening participation rate. The FOBT positivity and the participation rates have greatest bearing on the cost estimates. The major influences on the uncertainty of the ICER are the size of the mortality reduction and the FOBT positivity rate. Other influences are the participation rate and the expected reduction in the number of de facto screening colonoscopies due to the presence of a screening program.

Comparison with other economic studies

Previous economic evaluations of screening using FOBT are outlined in Table 5. Their ICERs range from $3,000/LYS to $56,000/LYS in $A1996 and most are reporting net costs. Our result of $17,000/YLL (gross) (see footnote 5) or $12,000/YLL (net) is at the lower end of the spectrum. This is not surprising. First, we have modelled the program in steady-state operation,

Figure 2: Point estimates and 95% uncertainty intervals of the cost-effectiveness ratio.



The point estimate, indicated by the square block, provides an estimate of the ICER under ideal conditions whereas the 95% uncertainty intervals, based on Monte Carlo simulation, provide an indication of the range of expected values in the Australian context.

Table 5: Previous economic evaluations on colorectal cancer (CRC) screening using FOBT.

Paper	Cost per LYS[a] ($1996)[b]	Comments
England 1989[27]	$8,000	Mathematical models
Eddy 1990[37]	$15,000	Markov Model, 50-year-old cohort, annual FOBT, 100% compliance
Tsuji 1991[45]	$29,000	Compared with 'no screen', some direct costs to patients
Byers 1992[46]	$14,000	Markov model (Eddy), expert opinion, uncontrolled screening studies
Shimbo 1994[32]	$30,000 (B), $14,000 (I)	Compared immunological (I) with biochemical (B), 40-year-old cohort, 100% compliance
Wagner (OTA 1990) 1991[25]	$56,000	Markov model, comparator 'no screen'
Brown 1993[47]	$44,000	Eddy's Markov model, Mandel impact figures, comparator controls from trial
Salkeld 1996[9]	$26,000	Mandel, comparator 'no screen', annual FOBT, Minnesota study population, 50 to 80 years
Wagner 1996[26]	$19,000, $14,000	Eddy's Markov model, comparator 'no screen', annual FOBT
Gyrd-Hansen 1998[8]	$2,700-$6,600	Day and Walter model, Kronborg data, comparator 'no screen', costs and incremental costs, biennial and annual, many age groups
Bolin 1999[38]	$36,000 annual $33,000 biennial	Markov model (based on the OTA), 50-year-old cohort, 100% compliance
Frazier 2000[7]	$32,000	Markov model, no screen comparator, 50-year-old cohort US population, annual FOBT
Helm 2000[28]	$26,000, $3,400, $3,200	Deterministic model, Mandel, Kronberg and Hardcastle data, US population 45-75 years, 60% compliance
Khandker 2000[29]	$21,000	State transition model, 50-year-old cohort, annual FOBT, 100% compliance
Sonnenberg 2000[48]	$11,000 (1) $26,000 (2)	Markov model, 50-year-old cohort, comparator 'no screen', annual FOBT, (1) 100% compliance, (2) 66% compliance
Vijan 2001[49]	$9,000	Markov model, 50-year-old cohort, comparator 'no screen', annual FOBT, 75% compliance
	Cost per QALY	
Whynes 1998[10]	Males: $5,000-$11,000 Females: $2,800-$10,000	Model, Hardcastle data, NHS comparator breast cancer, incremental 5 simulations 1) trial; 2) K population; 3) + lifetime costs; 4) change compliance at screen 4; 5) high initial compliance

Notes:
(a) Cost per life year saved is equivalent to cost per year of life lost 'saved' – all figures are rounded to two significant digits.
(b) Conversions to Australian dollars were done using purchasing power parities.[50]

excluding the more costly start-up and implementation period. Second, many have modelled the cost and consequences for a cohort of 50-year-olds using mathematical simulation methods. Our analysis has demonstrated that including the 50-to-54-year-olds will increase the average cost/YLL. Third, early studies have used data from the Minnesota study, which has a high positivity rate resulting in higher cost and cost per benefit ratio. Fourth, we report here a biennial screening program. Application of our model to an annual screening population resulted in a higher health benefit (400 deaths averted and a reduction of 5,000 DALYs), at higher costs of $100 million gross, resulting in a higher ICER of $20,000/DALY. Finally, they have also included different costs and cost offsets in addition to the costs of the basic screening program. Our analysis shows the ICER differs for gross and net costs particularly in the older age groups.

Our range of ICERs from the sensitivity analysis, for biennial screening, of $13,000/YLL to $52,000/YLL (gross) and $10,000/YLL to $47,000/YLL (net) includes most of the reported ICERs. Only one study had a higher ICER ($56,000/LYS),[25] which has since been revised to $14,000/LYS and $19,000/LYS.[26] Whereas four studies had more favourable ICERs ranging from $2,700/LYS to $9,000/LYS.[8,27-29] The only study to report a utility measure reported an ICER of $2,800/QALY to $11,500/QALY.[10]

Discussion

Our study is noteworthy in its use of the DALYs as an outcome measure. The use of DALYs in evaluation studies, as opposed to burden of disease descriptions, is in its infancy. The DALY, by combining mortality and morbidity in a single measure, has the potential to enable comparisons across a range of interventions. Indeed, comparisons were made between divergent interventions applied across the cancer continuum from prevention to psychosocial care as part of the larger priority-setting exercise with good response from those involved in cancer control.[13,14] There has only been one previous study to our knowledge that has used a similar measure, the QALY, in an evaluation of FOBT screening for CRC.[10] Both DALYs and YLLs are reported here to allow direct comparison with other economic studies that have used life-years saved, which are reported to be a standard and more reliably measured health benefit.[30] Part of that concern is the reliability of the disability weight and the estimation of the YLDs. For this intervention, the contribution of the YLDs to the numerical value of the DALYs is so small that the DALY value is almost equivalent to the YLL value.

In the presence of scarce resources, a sensible decision-making process entails starting with a minimum or base program and then giving consideration to expansion to include various design combinations using marginal analysis techniques. In this case additional age groups have been evaluated. In our population, the optimum cost-effectiveness was reached at 55 years and older (see Figure 2), suggesting that this might be a better starting point than the recommended 50 years. Review of the data in other cost-effectiveness reports supports our findings. We chose to target 55 to 69-year-olds as the 'base program' because, from an economic point of view, this represented the minimum program the Australian Government could introduce. Review of the final results (see Table 4) and discussion with the CSG Working Group identified targeting 55 to 74-year-olds as the optimum program, based on current information. Inclusion of those 75 and over would depend on further certainty about the compliance rates in that age group. This cost-effectiveness profile may vary between countries, however, depending on population profiles, the epidemiology of CRC, availability of health care resources and variations in clinical practice, incentives to health care professionals and institutions, health care system design, and acceptable threshold values.[31]

5. Note we are using the YLL component of the DALY only in this comparison, as the studies being assessed did not include a morbidity measure in their evaluations.

Table 6: Cost-effectiveness of primary prevention programs using same economic protocol.[13,14]

Interventions	Annual cost (savings)	DALYs saved (lost) per year	Cost per DALY[a]		
Increments	**$ millions**		**Point**	**Lower**	**Upper**
National Tobacco Campaign					
Gross costs (no offsets)	9.0	11,000	840	540	1,200
Net costs (or net saving)	(39)		Dominant	Dominant	Dominant
National SunSmart Program					
Gross costs (no offsets)	2.5	10,000	250	240	500
Net costs (or net saving)	(37)		Dominant	Dominant	Dominant
National Fruit and Vegetables Campaign					
Gross costs (no offsets)	2.5	3,600	680	510	16,000
Net costs (or net saving)	(12)		Dominant	Dominant	Dominant

Note:
(a) The net cost per DALY estimates provided include the point estimate (i.e. the result from the primary economic analysis) together with the upper and lower bound estimates from the sensitivity analysis.

While the highest level of evidence, in terms of internal validity, has been used to model the point estimates, the sensitivity analysis is more informative. The single point estimate provides an indication of the efficacy of the program under ideal conditions, such as an RCT. As such it provides an optimistic value for the costs and consequences of the program, with costs and ICER close to the lower limit and benefits close to the upper limit of the uncertainty analysis. Therefore, reporting only the point estimate may underestimate costs and the ICER. Furthermore, a single point estimate suggests a certainty about the final values that does not exist for many reasons, including the uncertainty around the original study results, the effectiveness in less than ideal conditions and their generalisability to the Australian context. Knowledge of the range of potential benefits, costs and cost-effectiveness from the sensitivity analysis (see Table 4) provides for more informed decision-making both within a single program and across programs. If the funding for a program is limited, it may be worthwhile to implement a conservative option that assumes the extreme values of maximum cost, minimum benefits and lowest anticipated ICER. It is often more feasible to extend the reach of a program, if it proves to be more effective than anticipated, than to reduce an existing program.

The sensitivity analysis has further implications for policy because it provides an indication of the main drivers for the costs and consequences of the program, and some of these will hopefully be explored in the current pilot studies. The positivity of the FOBT influences both cost and cost-effectiveness. The newer generation of immunochemical tests that are specific for human haemoglobin may reduce costs even further. A Japanese study that compared the two methods showed that the immunochemical test was three times as cost-effective as the guaiac tests.[32]

The implementation of an evidence-based policy is often dependent on other factors in addition to the cost-effectiveness of the program.[33] As part of this study, the CSG Working Party utilised the Program Budgeting and Marginal Analysis (PBMA) approach to identify broader dimensions of benefit that might affect resource choices, in addition to the reported ICERs. The additional factors considered were 'public health significance', 'equity', 'acceptability to stakeholders' and 'feasibility of options for change' to Australia's cancer control strategy.[13,14] CRC is an important public health issue worldwide. Special action may be required to encourage participation for disadvantaged groups such as the Indigenous population, low socio-economic groups, those from non-English speaking backgrounds, and rural residents. Recent reports from the United States, for example, show CRC screening rates tend to be lower in African Americans and Hispanics, in groups with lower education, and in those lacking insurance cover or a usual source of care.[34,35]

Acceptability to the main stakeholders will affect the participation rates, which is one of the major influential factors, and this may be an issue not only for different age groups but also for many disadvantaged groups. The acceptability of a CRC screening program to consumers, for example, needs to be established. Medical practitioners will need to be convinced of the efficacy and quality assurance aspects of the program if they are to encourage participation. In Australia, there are sufficient well-qualified colonoscopists,[14,36] but their uneven distribution across the nation may affect the feasibility of the program. The value of commencing the program at a different age to breast cancer screening (currently 50 years) may have to be weighed against commencing screening at too early an age. The risk is that this may lead to non-compliance in later years when the likelihood of disease is higher.[32] Consideration of these influential factors would contribute to a more successful and equitable program.

As this study was part of a larger priority-setting exercise, we can compare screening for CRC cancer with other cancer control options. It is more costly and less cost effective than the primary prevention options shown in Table 6 that were evaluated that may be cost neutral or may even save money.[13,14] On the other hand, the program is expected to have a similar cost-effectiveness to the current cervical cancer screening and breast cancer screening programs.[7,8,10]

Our study differs from previously published cost-effectiveness studies in several respects. The main difference is the comparison of the age group at which to start screening. The risk of developing CRC rises substantially from about the age of 50 and this may be why a starting age of 50 years is often recommended. Many of the economic analyses used mathematical simulation methods to model a cohort of 50-year-olds, but unfortunately did not provide information on screening at different age groups. Gyrd-Hansen[8] modelled six different screening programs. Extrapolation of their data demonstrates minimal health benefit and high costs for inclusion of the 50 to 54-year-olds, similar to our findings. Eddy[37] showed this effect when comparing screening starting at 40 years with 50 years. The anticipated health gain is very small but the costs are almost double. Previous Australian studies used a model based on an artificial cohort of 50-year-olds[38] or the population in the Minnesota study.[23] Our use of a cross-sectional model has enabled the comparison on an aggregate level of different subgroups, such as age in this case.

The comprehensiveness of the cost analysis, with separate reporting of both 'gross costs' and 'net costs' estimates, should also be noted. This knowledge is important for the decision-making process. The gross costs include the infrastructure costs of the program and they provide the perspective of the CRC Screening Program itself. The net costs, on the other hand, incorporate the long-term costs and potential savings to the health system overall. Recovery of these costs/savings is not a forgone conclusion and may depend on several practical and theoretical considerations that include workforce restructuring, management policies, political acceptability, professional interests and public reaction. We did not consider the costs of future medical care unrelated to colorectal cancer, which will occur because of the decrease in premature mortality. Inclusion of these costs remains controversial.[30,31]

Conclusion

The findings of this study have a number of policy implica-

tions for countries recommending or considering implementing screening programs for CRC. If less than $50,000 per DALY is used as the yardstick for acceptable cost-effectiveness, then a biennial population-screening program using FOBT provides value-for-money, particularly if screening starts at the age of 55 rather than the most commonly advocated age of 50. In this age of screening, it is important that policy makers be mindful of the influential factors driving costs and consequences and include appropriate incentives to control or modify these factors. This could include disincentives if there is potential for provider-induced demand.

Pilot programs provide better information on important facets of the program in the local setting. If pilot programs are part of a staged approach to implementation, careful consideration should be given to the age range for screening. Investigation of age and the other influential factors in the pilot program is recommended to confirm the findings of this modelling exercise before implementing a full national program.

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