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Title: Colorectal cancer screening: How health gains and cost-effectiveness vary by ethnic group, the impact on health inequalities, and the optimal age-range to screen

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Running title: Colorectal cancer screening: Variations by ethnic group.

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List of abbreviations

CEA Cost-effectiveness analysis
CRC Colorectal cancer
FOBTi Faecal occult blood immunochemical test
ICER Incremental cost-effectiveness ratio
MSLT Multi-state lifetable
QALY Quality-adjusted life-year

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Abstract

Background

Screening programmes consistently underserve indigenous populations despite a higher overall burden of cancer. In this study we explore the likely health gains and cost-effectiveness of a national colorectal cancer (CRC) screening programme for the indigenous Māori population of New Zealand (NZ).

Methods

A Markov model estimated: health benefits (QALYs), costs and cost-effectiveness of biennial immunochemical faecal occult blood testing (FOBTi) of 50-74 year olds, from 2011. Input parameters came from: literature reviews, the NZ Bowel Screening Programme Pilot, and NZ linked health datasets. Equity analyses substituted non-Māori values for Māori values of background (non-CRC) morbidity and mortality, CRC survival and incidence, screening coverage, and stage-specific survival. We measured the change in "quality-adjusted life expectancy" (QALE) as a result of the intervention.

Results

Based upon a threshold of GDP per capita (NZ$45,000), CRC screening in NZ using FOBTi is cost-effective: NZ$2930 (US$1970) per QALY gained (95% uncertainty interval: cost saving to $6850 ($US4610)). Modelled health gains per capita for Māori were less than for non-Māori: half for 50-54 year olds (0·031 QALYs per person for Māori vs 0·058 for non-Māori), and a fifth (0·003 c.f. 0·016) for 70-74 year olds and ethnic inequalities in QALE increased with CRC screening.

Conclusion

CRC screening in NZ using FOBTi is likely to be cost-effective, but risks increasing inequalities in health for Māori.

Impact

To avoid or mitigate the generation of further health inequalities, attention should be given to underserved population groups when planning and implementing screening programmes.

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Introduction

Indigenous and socially disadvantaged groups carry a disproportionate cancer burden in most countries, with these groups often having high incidence and poorer survival than non-indigenous and advantaged groups [1-3]. There is a consistent pattern of underserving these groups by health care systems. Organised cancer screening programmes offer potential to reduce inequalities in health through reductions in cancer incidence and mortality, however generally screening programmes are not designed with an equity focus and can exacerbate inequities due to poorer access to and through them for underserved populations [4]. Given this, it is important to assess the impact of any proposed cancer screening programmes in respect to their impact on underserved populations and inequalities in health, and to identify any modifiable factors that may help to maximise health gains (and inequality reductions) from proposed cancer screening programmes. In this study we aimed to examine the likely health gains and inequality impacts from the national rollout of a CRC screening programme on the indigenous Māori population of New Zealand using a modified cost-effectiveness approach.

Colorectal cancer (CRC) screening with faecal occult blood testing is effective at lowering CRC mortality [5], and has been found to be cost-effective for 50-74 year olds in a number of countries including Australia [6] England [7] and Ireland [8]. New Zealand is currently considering the national rollout of a CRC screening programme, however, little is known about how CRC screening impacts on indigenous health inequalities. Part of the difficulty in examining the impact of screening on indigenous populations results from the inconsistent collection of data on ethnicity/race [9]. We are aware of only one international study that has quantified likely ethnic or racial group differences in the health gains and cost-effectiveness of CRC screening. Theuer et al (2006) found that CRC screening was more cost-effective for Blacks than Whites, Latino and Asians, due to higher CRC incidence and worse survival [10].

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New Zealand is a good setting for exploring the impact of CRC screening on health inequalities given the routine collection of ethnicity data in health datasets, and linkage of many of these datasets. Indigenous peoples in Australia and New Zealand have a common pattern of *lower* CRC incidence [1] (although in New Zealand the gap in incidence is reducing over time), but *worse* survival once diagnosed [2, 11]. This pattern raises the question as to whether CRC screening will produce less health gain due to lower incidence), or equal or greater health gain due to improving survival by incidence stage shift. Also, given that Māori have worse survival than non-Māori in the New Zealand screening naïve context, and there is evidence of greater delays to treatment for Māori compared to non-Māori [11], there is a case that survival will improve (more) for Māori than non-Māori as a result of standardised improvements in treatment following the implementation of a well-organised screening programme. Complicating this pattern is the impact of lower screening coverage often achieved for indigenous populations [12]. In this study, we explore the above issues through a number of equity analyses, substituting non-Māori values for Māori values of background (non-CRC) morbidity and mortality, CRC survival and incidence, screening coverage, and stage-specific survival (equal treatment scenario). We also consider the optimal age range for screening, which has not previously been examined by ethnicity or indigeneity [13].

Cost-effectiveness analyses (CEAs) provide a useful framework for examining differences in the cost-effectiveness of interventions and inequalities in health gains between population groups; however some of the assumptions in CEA methods, such as using ethnic-specific life expectancy to calculate health gains (e.g. QALYs), may disadvantage indigenous populations and these need to be addressed [14]. Despite the importance of CEAs in decision-making, a recent (2015) systematic review found only 19 studies worldwide on the cost-effectiveness of health-related interventions with a focus on indigenous populations, with no studies on cancer screening [15].

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There are a range of current approaches to incorporate equity concerns into cost-effectiveness modelling methods in the literature [16, 17]. These approaches loosely fit into two groups: 1) those that aim to include the social value of health gains between groups using methods such as equity weighting and the social welfare function; and 2) those that attempt to incorporate equity of healthcare into the models by altering the configuration of the intervention(s) to achieve process and/or outcome equity. This paper is an example of the latter. The specific objectives of this study were: (i) to estimate the differences in health gain, and cost-effectiveness of a CRC screening programme of 50-74 year olds by ethnic group (Māori vs non-Māori); (ii) to explore the factors that drive differences in health gains between Māori and non-Māori, including background morbidity and mortality, CRC incidence screening coverage, and survival, (iii) to measure the impact of the intervention on absolute inequalities in quality-adjusted life expectancy (QALE) for Māori compared to non-Māori and; (iv) to determine whether the optimal (based on cost-effectiveness) screening age-range differs by sex and ethnic group.

Materials and Methods

We used a Markov model to estimate the health gains in quality-adjusted life years (QALYs), costs and cost-effectiveness of a national CRC screening programme with biennial FOBTi of 50-74yr olds (default age-group for initial analyses). The model consisted of a CRC submodel and a general part which integrated results from the submodel with general population characteristics. Two populations were modelled: a reference one without screening and an intervention one. The differences between the two determined benefits and costs.

Included in the model were all individuals aged 35 years and over in 2011, modelled through to death or age 110 years. We assumed this population to be screen-naïve. A multiple cohort approach was used, i.e. each five-year age-group in 2011 was modelled separately until death or age 110 years. A cycle length of one year was used in the modelling. The model was implemented in

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Microsoft Excel, using the Ersatz add-in for uncertainty analysis (Microsoft, www.Epigear.com). Ethical approval was received from the University of Otago Ethics Committee H13/049

As much as possible we captured socio-demographic heterogeneity by sex, age and ethnic group (Māori and non-Māori) for CRC incidence and mortality, transition parameters, survival, background mortality and morbidity and also in CRC screening participation. A health system perspective was used, with a 3% discount rate. Unrelated health system costs were included i.e., average expected costs to the health system by sex and age, including for years of life saved We are able to include these unrelated health care costs owing to the very detailed nature of New Zealand data [18]. This allows a much fuller approach to cost-effectiveness analysis and is in keeping with recent guidelines [19] (ie, including the inclusion of health care costs associated with extra lifespan as a result of the intervention). We note our BODE3 protocol is to include unrelated health care costs in all evaluations [20]. We assumed a cost-effectiveness threshold value based upon GPD per capita, that is, NZ$45,000 per QALY [21].

CRC submodel

The CRC submodel (Figure 1) generated adenoma incidence and, pre-clinical and clinical CRC incidence and prevalence, and CRC mortality rates by Dukes stage and disease prevalence for a non-screening population as compared to various screening options. The CRC submodel was developed following Whyte et al (2011) [22], with two differences. Unlike the Whyte model we did not include a direct link from normal epithelium to Dukes A (see Discussion). Second, Whyte et al modelled age-specific incidence of low risk adenomas for each age-group separately; to avoid implausible age-specific patterns we modelled the age pattern using a Weibull distribution. Other model parameters from Whyte et al (e.g. progression rates between adenoma and Dukes' stages, probability to present clinically) were used as priors and calibrated (and fitted) against New Zealand data on incidence (by age and stage, for 2011 [23]), and CRC mortality counts, using the solver tool in Excel. The fitted parameters were then used as priors in a Monte Carlo Markov Chain process to obtain a correlation

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matrix of all parameters for use in subsequent Monte Carlo analyses. The posterior parameter estimates are shown in Table S1. Estimates of eight year survival, by age and from New Zealand excess mortality rate modelling [24], were specified using a log normal function. Comparisons of model predicted versus observed mortality data are shown for the baseline in Figure S1.

Insert Figure 1 about here (at end of manuscript)

In the model, people detected with low risk adenomas resided in the state for one-year only (with attendant costs and disability weights), returning to the healthy population the following cycle after colonoscopy. Those identified as high-risk adenoma moved to annual surveillance colonoscopies, with a dropout rate from surveillance.

General model

The outputs from the CRC submodel (including QALYs related to CRC) acted as inputs to the general model which was used to calculate net QALYs gained by combining QALYs from the CRC intervention with those from all other diseases, net costs and the incremental cost-effectiveness ratio (ICER).

Inputs included proportions of the alive population (screened and unscreened) by sex, ethnic and age (single year) in each of the following states: low and high risk adenoma, false positive and true positive test results, preclinical and clinical Dukes stage CRC, and proportions dying each year of CRC (Table 1). We included three months of lead time in the model for those receiving the CRC screening intervention, by shifting the excess mortality curves for all stages of CRC to the right by 0.25 years. Our results were insensitive to the amount of lead time.

Insert Table 1 about here (at end of manuscript)

Our primary analyses included background (i.e. non-CRC) mortality rates and expected morbidity loss in the main life table. Morbidity loss was estimated by sex, ethnic group and age, using the total

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years of life lived with disability (YLDs) from a New Zealand Burden of Disease Study [25, 26], divided by the population count in the same group. Health gain could only occur in the envelope of 'good health' that reduced with increasing age, and was less for Māori. For example, a Māori woman aged 60-64 years has an expected YLD of 0·288, meaning a year of life gained in this population group has a maximum utility value of 0·712.

Intervention costs for screening were counted in each year. Excess costs (i.e. excess to that expected for an 'average' New Zealand citizen of the same sex and age [18]) and cost offsets varied for being in the first year of CRC diagnosis, remission or last six months of life if dying of CRC (Figure S2).

Input parameters

Model parameters were determined by a combination of literature review, data from the New Zealand Bowel Screening Programme Pilot [27], parameters used in previous models published in peer-reviewed literature, and analyses of New Zealand linked health datasets. For each parameter we determined an 'expected value' and distribution for use in probabilistic uncertainty analysis. (Table 1)

Model validation

The CRC mortality reductions estimated by our model under various screening scenarios were similar to those reported in randomized controlled trials (RCTs) and other CRC screening simulation models (e.g. CISNET and SimCRC [28]) (Table S2).

Analyses

We carried out a series of equity analyses: 1) we replaced Māori data with non-Māori values for baseline mortality and morbidity to address the issue that lower life expectancy of indigenous populations results in less opportunity for life years gained with screening; 2) we used non-Māori CRC incidence and incidence trends for Māori to explore their contribution to differences in ethnic-

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specific health gains and ICERs; 3) we assessed the impact of achieving equal screening coverage for Māori, and 4) we assessed the impact of improvements in treatment for Māori following the implementation of a screening programme, given evidence of greater delays to treatment for Māori compared to non-Māori leading to poorer survival [11]. For this last scenario, we replaced Māori excess mortality from CRC with the non-Māori rate, for Māori who are screened. This scenario ignores any improvements to non-Māori survival from treatment improvements, and likely overestimates the improvements for Māori by ignoring the influence of co-morbidities on treatment and survival. The equity analyses were modelled with expected values (rather than Monte Carlo analyses) to give stability in the estimates and to allow the measurement of the change in QALYs between scenarios.

We measured the impact of the CRC screening intervention on absolute inequalities in QALE by determining the absolute difference in QALE for Māori compared to non-Māori by age, sex and ethnic group, before and after the intervention. We subtracted the baseline difference (non-Māori minus Māori) in QALE from the intervention difference in QALE and converted to a number of healthy days (by multiplying by 365). To facilitate more specific comparisons of social group impacts, 50-54 and 70-74 year old age cohorts were run separately and for selection of the optimal age range to screen, the 40-44 year old age cohort was used. Tornado plots were constructed to examine the impact of uncertainty in each input parameter on uncertainty in the output ICER, by rerunning the model with the 2·5th and 97·5th percentile values of the input parameters (Figure S3).

Results

The modelled CRC screening intervention for 50-74 olds resulted in health benefits for all population groups. However, the size of the health gains and the cost-effectiveness of the intervention were greater for non-Māori compared to Māori and for men compared to women (Table 2). Non-Māori health gains were substantially greater than Māori: approximately two times greater for 50-54 year olds (0·058 QALYs per person for non-Māori, c.f. 0·031 for Māori), and five times greater for 70-74

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year olds (0·003 c.f. 0·016) (Table 2). Gains were greater for men than women aged 50-54 year olds (0·060 c.f. 0·049 QALYs gained) but similar for men and women aged 70-74 year olds (0·015 c.f. 0·014 respectively; Table 2).

Insert Table 2 about here (at end of manuscript)

The modelled CRC screening intervention was highly cost-effective for all sex and ethnic groups, given a willingness to pay threshold based on GDP per capita (e.g. NZ$45,000 per QALY) (Figure 2).

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Scenario analyses

Substituting non-Māori background mortality for Māori background mortality resulted in a 29% increase in Māori QALY gains compared to the default model (9,140 c.f. 7,060 QALYs; Table 3).

Insert Table 3 about here (at end of manuscript)

We used non-Māori CRC incidence and trends to explore the contribution of these factors to differences in health gains achieved for Māori compared to non-Māori. The scenario of using non-Māori incidence increased QALY gains, by 23% for Māori (8,730 c.f. 7,060 QALYs; Table 3). In contrast, changing the incidence trend from one that was flat (0% change per year for Māori in default model) to one of reducing background incidence (2·5% reduction per year for under 65 years and 1·5% for 65+ years) resulted in a 17% reduction in QALY gains for Māori (Table 3). The combination of using non-Māori incidence and applying reducing incidence trends, all but cancelled each other out, with a 2% net increase in measured QALY gains compared to the default analysis. Using values of non-Māori background morbidity had a smaller gain in QALYs for Māori, with a 3% increase relative to the default model. In all of the above scenarios there was little change to the

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costs (up to a 6% difference from the default costs), and therefore changes to the ICERs were primarily driven by changes in the health gains.

We additionally undertook analyses to explore the changes to QALY gains for Māori that might result from plausible changes to the intervention itself. Increasing Māori expected screening coverage to the level for non-Māori (i.e. from 45·4% to 58·3%) and using the same percentage population that never uptake screening (31·6%), increased Māori QALY gains by 29% compared to the default model. Improving stage-specific survival for Māori to the level of non-Māori only resulted in a 1% increase in Māori QALYs.

Change in absolute inequalities in QALE

The CRC intervention increases absolute inequalities in QALE for Māori compared to non-Māori. Absolute inequalities increase more for men than women, and the greatest gains are seen in the age groups that immediately begin screening in our model, age 50-74 years (Table 4). Non-Māori men aged 60-64 years gain an additional 25.6 (12.5, 40.3) healthy days compared to Māori of the same age while non-Māori women aged 30-34 years gain and additional 7.2 (-3.9, 17.8) healthy days (Table 4).

Insert Table 4 about here (at end of manuscript)

Optimal (based on cost-effectiveness) screening age-range

The optimal starting five-year age-group was considered from a cost-effectiveness perspective. For both ethnic groupings was 65-69 year olds (Table S3 and Table S4), then 65-74, 60-74, 60-79, and 55-79 (for 10, 15, 20 and 25 year age ranges respectively)

Discussion

Population cancer screening programmes offer the potential to both improve population health and address inequalities in health; however, national screening programmes consistently underserve

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indigenous populations and therefore risk increasing indigenous health and healthcare inequalities. From our study, national population CRC screening in New Zealand using biennial FOBTi is estimated to be cost-effective (similar to studies in other countries [6, 8, 29]), and would result in health gains for both Māori and non-Māori. However, due to the lower incidence of CRC, higher background mortality and likely lower screening coverage, this programme is likely to increase inequalities in QALE for Māori compared to non-Māori. This finding is consistent with findings from Australia's national CRC screening programme which has achieved lower coverage for the indigenous population of Australia (which also has a lower incidence of CRC) and has increased inequalities in cancer outcomes for indigenous Australians [12].

Achieving equal screening coverage for indigenous populations is possible, whilst rare [30]. Multiple parallel strategies would be required across the screening pathway to achieve equal bowel cancer screening coverage and healthcare access for Māori (including active Māori engagement in all aspects of the programme's development and implementation, active recruitment and follow-up of eligible Māori participants, and close monitoring of treatment access and quality) [31]. In our model we estimate that achieving equal coverage for Māori and non-Māori would increase the modelled health gains for Māori by 29% – not enough so that Māori gains were equivalent to those for non-Māori. CRC is one of only a few cancers for which Māori in New Zealand have lower incidence, and therefore, even with equal screening coverage the modelled health gains from CRC screening for Māori are less. It is theoretically possible to achieve equal health gains by increasing screening coverage for Māori to a level high enough to offset the lower CRC incidence and higher background mortality. However, these resources may be better used elsewhere to reduce indigenous health inequalities, perhaps on diseases or interventions that offer even greater potential for inequalities reductions e.g. tobacco control.

As a part of implementing a national screening programme, there is likely to be greater standardisation of care and monitoring of the screening pathway (including treatment). This

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improvement in CRC care will offer benefits to all CRC cases (screened and unscreened), but potentially even greater benefits for indigenous populations who experience less access to and quality of healthcare compared with non-indigenous populations. Providing 'equal treatment' is important in reducing inequalities in healthcare, but in our model achieves relatively minor health gains (only 2% increase in modelled health gains for Māori).

In this study we used a cost-utility approach to consider a range of equity scenarios. By standardising background levels of morbidity and mortality we acknowledge that existing inequalities in health are unfair but modifiable, and their inclusion in disease and economic models further works to further disadvantage these groups [14].

Strengths and limitations of this study

Our model was a macro-simulation model. Therefore, we did not incorporate the possible impacts of heterogeneity in adenoma growth rates that may impact on cost-effectiveness. Nevertheless, our model performed similarly to other simulation studies (Table S2).

Unlike Whyte et al (2011) [22] and Sharp et al (2012) [8], we did not include a transition probability directly from normal epithelium to CRC (i.e. Dukes A). Whyte suggests that this pathway is uncommon [22]. Such cancers will benefit less from screening (as there are no adenomas to be detected), meaning we may have modestly over-estimated the health gains from screening (i.e. our model is calibrated to incidence and mortality data, meaning we assume all cancers have an 'early detectable phase', whereas in reality they do not). To the best of our knowledge, any such bias is likely constant across sex, age and ethnic groups, meaning our social group comparisons are unlikely to be biased for this reason.

Within our model we use the costs published from the NZ pilot study [27], and applied them evenly across population groups. This spread the cost of any additional activities that were undertaken to increase screening for specific-groups across the entire population, compared to explicitly modelling

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an increase in costs for under-screened people (which would see the marginal cost-effectiveness for these groups worsen). It was beyond the scope of this paper, and data quality, to undertake such a marginal analysis of increased recruitment costs per screened person.

One possible limitation of our Markov modelling is allowing for lead time bias. We used a lead-time of three months for all stages of disease, consistent across age and ethnic-groups. Our sensitivity analyses, of varying lead times made inconsequential differences to QALYs gained and net costs. However, the adjustment for lead-time in macrosimulation models is relatively crude, and therefore, there may be some residual lead-time bias in our model, which would overestimate modelled CRC screening effectiveness.

There are numerous strengths to our modelling and data inputs. We used detailed New Zealand epidemiological and cost data to both specify parameters (e.g. the transition probabilities) and as input parameters themselves. Key inputs including of background morbidity and mortality, and CRC incidence and survival varied by sex, ethnic group and age, allowing us to examine social group differences in modelled health gains and ICERs.

Conclusions

While a national CRC screening programme in New Zealand is likely to be cost-effective and improve total population health, this will likely come with the unfortunate consequence of increasing inequalities in health. Based upon our model, the most effective way of limiting the inequalities likely to be generated by this programme is to give attention to improving screening coverage.

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Table 1 Input parameters for modelling CRC screening in the New Zealand setting

Variable		Base Case	Range	Distribution	Source
Performance of screening test					
FOBTi sensitivity for adenomas[#]		21%	19-22%	Beta (595, 2236)	[8]
FOBTi sensitivity for CRC[#]		71%	48-100%	Beta (353, 143)	[8, 32, 33]
FOBTi specificity for adenomas/CRC[#]		95%	84-99%	Beta (1733, 91.2)	[8, 32, 34]
Uptake and adherence with screening/diagnostic tests					
Proportion of population screened per round*	Non-Māori	58.3%	40-70%	Beta (56, 40)	[27]
	Māori	45.4%	30-60%	Beta (45, 54)	[27]
Proportion of population that never uptake FOBTi*	Non-Māori	31.6%	20-50%	Beta (27, 58)	[27]
	Māori	38.9%	25-55%	Beta (37, 57)	[27]
Proportion of FOBTi tests that need to be repeated		7%	0-14%	Beta (11, 150)	[27]
Colonoscopy adherence		96%	90-100%	Beta (95, 4)	NZ Ministry of Health Pilot Data [27] value 86.1%, but scaled up for use of private colonoscopy.
Performance of diagnostic tests					
Colonoscopy sensitivity for low-risk adenomas		100%			Assumed
Colonoscopy sensitivity CRC		100%			Assumed
Surveillance of high risk adenomas					
High risk surveillance group dropout rate (i.e. annual)		14%	10-19%	Beta (19, 114)	[8]
Harms of screening					
Colonoscopy probability of perforation		0.12%	0.1-0.14%	Beta (0.09, 74)	[27]
Probability of death following perforation		5.19%	0.0-9.07%	Beta (26, 466)	[8]
Probability of (major) bleeding following colonoscopy		0.27%	0.07-0.41%	Beta (7, 2714)	[27]
Disease/state morbidity					
Disability weight (DW) first 9 months CRC diagnosis and treatment		0.288	0.194-0.404	Beta (20.3, 50.2)	Based on GBD DWs and Australian disaggregation by clinical phase [35, 36]
DW for one month assumed terminal CRC state		0.548	0.383-0.703	Beta (19.8, 16.3)	[35, 36]
DW for three months assumed pre-terminal CRC		0.539	0.379-0.691	Beta (20.6, 17.6)	[35, 36]

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Variable		Base Case	Range	Distribution	Source
DW per annum post diagnosis and treatment (i.e. remission)		0.167	0.107-0.252	Beta (16.8, 83.9)	[35, 36]
DW for screening test (scenario analysis only)		0.000115	0.000048-0.00022	Beta (1.7, 280)	Set to ½ of value for colonoscopy
DW for colonoscopy		0.000237	0.000096-0.00044	Beta (6.7, 555)	GBD 2010 [26], using "abdo/pelvic problem, mild"
DW for bleed from colonoscopy		0.00237	0.00160-0.00338	Beta (23.5, 167.2)	GBD 2010 [26], using "abdo/pelvic problem, moderate"
DW for perforation from colonoscopy		0.0376	0.0252-0.0520	Beta (20.1, 41.6)	GBD 2010 [26], using "abdo/pelvic problem, severe"
Incidence, mortality and survival rates					
CRC annual incidence trend (%)	Non-Māori under 65	-0.025	(-0.03; -0.02)	Normal Mean: -0.025 SD 0.00255	[23]
	Non-Māori 65+	-0.015	(-0.02; -0.01)	Normal Mean: -0.015 SD 0.00255	[23]
	Māori	0	(-0.01; 0.01)	Normal Mean: 0 SD 0.0051	[23]
CRC Annual Mortality Trend (%)		-0.13%	-0.18 to -0.08	Normal Mean: -0.0013 SD 0,00026	[23]
Colorectal cancer excess mortality and survival			Varied by sex, age, ethnicity and stage.	Nil	From analyses of linked cancer-mortality data [24], extended to by stage and operationalized as log-normal survival probabilities in model.
Background (i.e. non-CRC) mortality with 1.75%/2.25% annual decrease for non-Māori/Māori			Varied by sex, ethnicity and age	Nil	From projected life tables by sex, age and ethnicity [37]
Background or expected morbidity			Varied by sex, ethnicity and age	Nil	Prevalent YLDs from New Zealand BDS [35]
Direct costs (all in NZ$)					
Cost per person invited who does not supply sample		$44.07		Gamma (100, 0.44)	[27]

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Variable		Base Case	Range	Distribution	Source
Cost per person invited and FOBT results obtained		$96.35		Gamma (100, 0.96)	[25]
Cost per repeat/spoilt FOBT		$15		Gamma (100, 0.15)	[25]
Cost per colonoscopy (true or false positive combined)		$654		Gamma (100, 6.55)	[25]
Cost per bleeding complication following colonoscopy		$5262		Gamma (6.6, 795)	Purchasing power parity (PPP) adjusted average of 3 international studies [8, 22, 38]
Cost per perforation complication following colonoscopy		$17,481		Gamma (11, 1588)	PPP adjusted average of 3 international studies [8, 22, 38]
Health system costs					
Base cost by sex and age of any citizen, with excess costs‡ by phase of CRC pathway (1st year of diagnosis, last 6 months of life if dying of CRC, and remission)		Figure S2.		Log-normal, 10% SD (correlated 1.0 across all sex, age and ethnic groups)	See [25] for methods and data.

DW = disability weight.

#Sensitivity and specificity of FOBT test were negatively correlated -0.5 (i.e. as increasing sensitivity of a test is usually accompanied by decreasing in specificity).

*Māori/non-Māori coverage parameters were positively correlated 0.5 (i.e. equivalent to saying that if the coverage was randomly drawn as high for non-Māori, then one would expect it to be more likely to be high for Māori too).

‡ Excess to 'average' New Zealander

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Table 2 Costs, QALYs and ICERs (95% uncertainty intervals) for biennial screening of varying age ranges, by sex by ethnic group, among the 2011 population# modelled out to death

	Total	Men	Women	Māori	Non-Māori
Population-level, all 30+ year olds in 2011 for biennial screening for ages 50-74, commencing in screen naïve population in 2011					
Cost of intervention (NZ$; millions)	$1520 ($1310 to $1778)	$755 ($639 to $895)	$766 ($652 to $897)	$148 ($127 to $174)	$1370 ($1175 to $1608)
Net cost (NZ$; millions)	$293 ($-48 to $700)	$52 ($-153 to $251)	$241 ($87 to $401)	$66 ($35 to $96)	$226 ($-91 to $559)
QALYs gained	101,800 (78,800 to126,000)	53,600 (39,100 to 70,200)	48,200 (37,700 to 58,700)	6578 (4760 to 8730)	95,200 (73,100 to 118,000)
ICER*	$2930 ($cs to $6850)	$1020 ($cs to $5060)	$5070 ($cs to $8950)	$10,500 ($4500 to $17,900)	$2420 ($cs to $6230)
Per 50-54 years old person (screen naïve) in 2011 under biennial screening for ages 50-74					
Net cost (NZ$)	$204 ($16 to $391)	$102 ($-115 to $316)	$300 ($137 to $469)	$346 ($208 to $480)	$186 ($-12 to $380)
QALYs gained	0.055 (0.042 to 0.068)	0.060 (0.044 to 0.078)	0.049 (0.039 to 0.061)	0.031 (0.024 to 0.041)	0.058 (0.044 to 0.072)
ICER*	$3770 ($279 to $7700)	$1770 ($cs to $5910)	$6100 ($2604 to $9940)	$11,100 ($5920 to $17,300)	$3270 ($cs to $7150)
Per 70-74 years old person (screen naïve) in 2011 under biennial screening for ages 70-74					
Net cost (NZ$)	$-31 ($-76 to -$5)	$-46 ($-101 to $0)	$-22 ($-59 to -$14)	$18 ($5 to -$32)	$-41 ($-86 to -$3)
QALYs gained	0.015 (0.011 to 0.018)	0.015 (0.011 to 0.020)	0.014 (0.011 to 0.018)	0.003 (0.002 to 0.005)	0.016 \(0.012 to 0.020)
ICER*	$cost saving ($cs to $390)	$cost saving ($cs to $43)	$cost saving ($cs to $1010)	$4910 ($1360 to $9160)	$cost saving ($cs to $177)

Discount rate 3%.

Cost-saving (cs)

#Population counts for age-groups 30+, 50-54yrs and 70-74yrs: non-Māori men: 1,102,110; 129,850; 65,070; non-Māori women: 1,199,960; 135,320; 70,530; Māori men: 126,900; 15,700; 4,500; Māori women: 144,900; 17,700; 5,100.

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Table 3 Equity and scenario analyses (expected value analysis; costs and QALYs gained for offering CRC screening to 50-74 year olds)

	Population group	**Intervention cost (NZ$ millions)**	**Net cost (NZ$ millions)**	**QALYs gained (% change from default)**	**ICER**
Default model (expected value only analysis)	Total	$1,510	$262	104,000	$2,530
	Non-Māori	$1,360	$201	96,600	$2,090
	Māori	$148	$61	7,060	$8,650
Equity analyses					
1. Māori background mortality and trend replaced with non-Māori values	Māori	$149	$52	9,140 (29%)	$5,670
2. Māori background morbidity replaced with non-Māori values	Māori	$158	$61	7,320 (3%)	$8,350
3. (1 and 2)	Māori	$158	$52	9,490 (34%)	$5,460
4. Māori CRC incidence trends replaced with non-Māori values	Māori	$146	$73	5,920 (-17%)	$12,300
5. Māori CRC incidence replaced with non-Māori values	Māori	$150	$43	8,730 (23%)	$4,900
6. (4 and 5)	Māori	$147	$59	7,200 (2%)	$8,150
Other scenario analyses					
Discount rate 0%	Total	$2,420	-$168	260,000	Cost-saving
	Non-Māori	$2,173	-$221	241,000	Cost-saving
	Māori	$247	$53	19,000	$2,790
Discount rate 6% (double baseline)	Total	$1,030	$374	46,500	$8,060
	Non-Māori	$932	$319	43,500	$7,350
	Māori	$98	$54	2,950	$18,580
Excluding both background morbidity and disease DWs (i.e. life years saved)	Total	$2,420	-$168	320,000	Cost-saving
	Non-Māori	$2,170	-$221	296,000	Cost-saving
	Māori	$247	$53	24,390	$2,180
Including small morbidity for screening test (i.e. DW of 0.000115 per annum applied to everyone screened, at each screen)	Total	$1,510	$262	103,100	$2,550
	Non-Māori	$1,360	$201	96,100	$2,100
	Māori	$148	$61	7,010	$8,720

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Table 4 Change in absolute inequalities in undiscounted QALE for Māori compared to non-Māori resulting from national CRC screening with FOBTi for 50-74 year olds.

Age group and sex		Baseline QALE			QALE with CRC screening			Additional healthy days under CRC screening for non-Māori
		Māori	Non-Māori	Difference	Māori	Non-Māori	Difference	
Men	30-34	35.99	43.1	7.11	36.07(36.05,36.1)	43.22(43.19,43.27)	7.15(7.11,7.19)	14.8(0.6,30.4)
	35-39	31.89	38.66	6.77	31.97(31.95,32)	38.79(38.75,38.83)	6.82(6.78,6.86)	15.9(1.5,31.7)
	40-44	27.85	34.26	6.41	27.94(27.91,27.97)	34.39(34.35,34.44)	6.46(6.42,6.5)	17.7(2.9,33.7)
	45-49	23.93	29.92	5.99	24.01(23.99,24.04)	30.06(30.02,30.11)	6.05(6.01,6.09)	20.6(5.7,37.3)
	50-54	20.18	25.68	5.5	20.26(20.24,20.29)	25.83(25.78,25.88)	5.57(5.52,5.61)	23.8(8.6,41.1)
	55-59	16.68	21.6	4.92	16.75(16.73,16.78)	21.74(21.7,21.79)	4.99(4.95,5.03)	25.3(11.2,41)
	60-64	13.5	17.74	4.24	13.56(13.55,13.59)	17.88(17.84,17.92)	4.31(4.28,4.35)	25.6(12.5,40.3)
	65-69	10.64	14.18	3.54	10.68(10.67,10.69)	14.27(14.24,14.3)	3.59(3.57,3.62)	19.1(9.8,29.2)
	70-74	8.09	10.94	2.85	8.11(8.11,8.12)	10.99(10.98,11.01)	2.88(2.86,2.89)	11.1(5.6,16.9)
Women	30-34	37.59	44.22	6.63	37.68(37.65,37.71)	44.32(44.3,44.35)	6.65(6.62,6.68)	7.2(-3.9,17.8)
	35-39	33.53	39.91	6.38	33.61(33.59,33.64)	40.01(39.99,40.04)	6.4(6.37,6.43)	7.8(-3.3,18.6)
	40-44	29.5	35.67	6.17	29.59(29.56,29.62)	35.78(35.75,35.81)	6.19(6.16,6.22)	9.1(-2.1,19.9)
	45-49	25.59	31.5	5.92	25.67(25.65,25.7)	31.62(31.59,31.65)	5.95(5.92,5.98)	11.1(-0.2,22.2)
	50-54	21.83	27.39	5.56	21.91(21.89,21.94)	27.51(27.48,27.54)	5.6(5.57,5.63)	14(3,25.3)
	55-59	18.22	23.29	5.08	18.29(18.27,18.31)	23.41(23.39,23.44)	5.12(5.09,5.15)	17.4(7.1,27.6)
	60-64	14.88	19.35	4.47	14.94(14.93,14.96)	19.47(19.44,19.5)	4.52(4.5,4.55)	19.7(10.3,29.5)
	65-69	11.93	15.64	3.71	11.97(11.96,11.98)	15.72(15.7,15.74)	3.76(3.74,3.78)	16.3(9.4,23.5)
	70-74	9.31	12.23	2.92	9.34(9.33,9.34)	12.28(12.27,12.29)	2.94(2.93,2.95)	9.5(5.5,13.8)

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Figure legends

Figure 1 Natural history model*

Figure 2 Cost-effectiveness acceptability curves by sex and ethnic grouping for CRC screening in New Zealand

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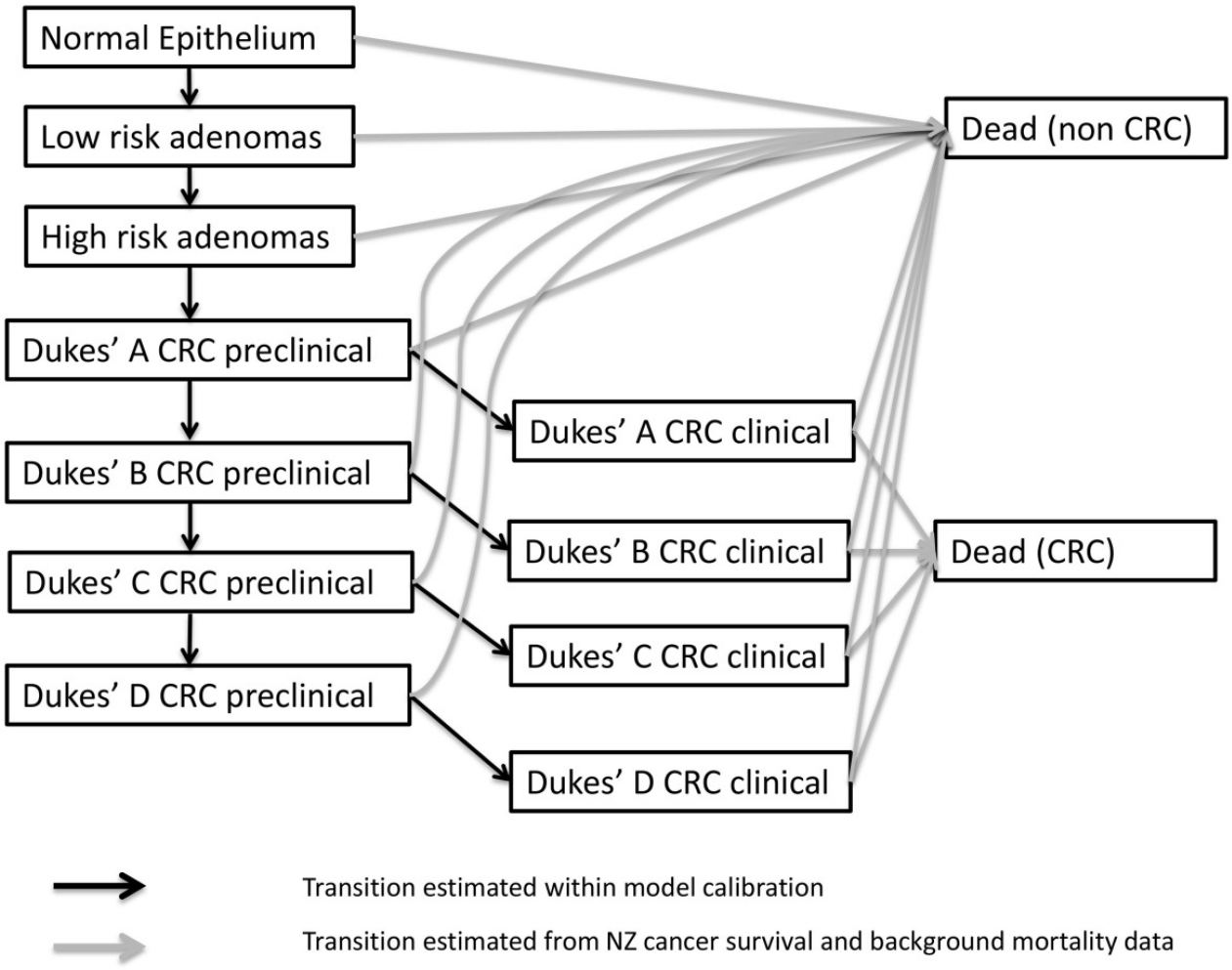
Figure 1



Adapted from: Whyte et al 2011 [22]

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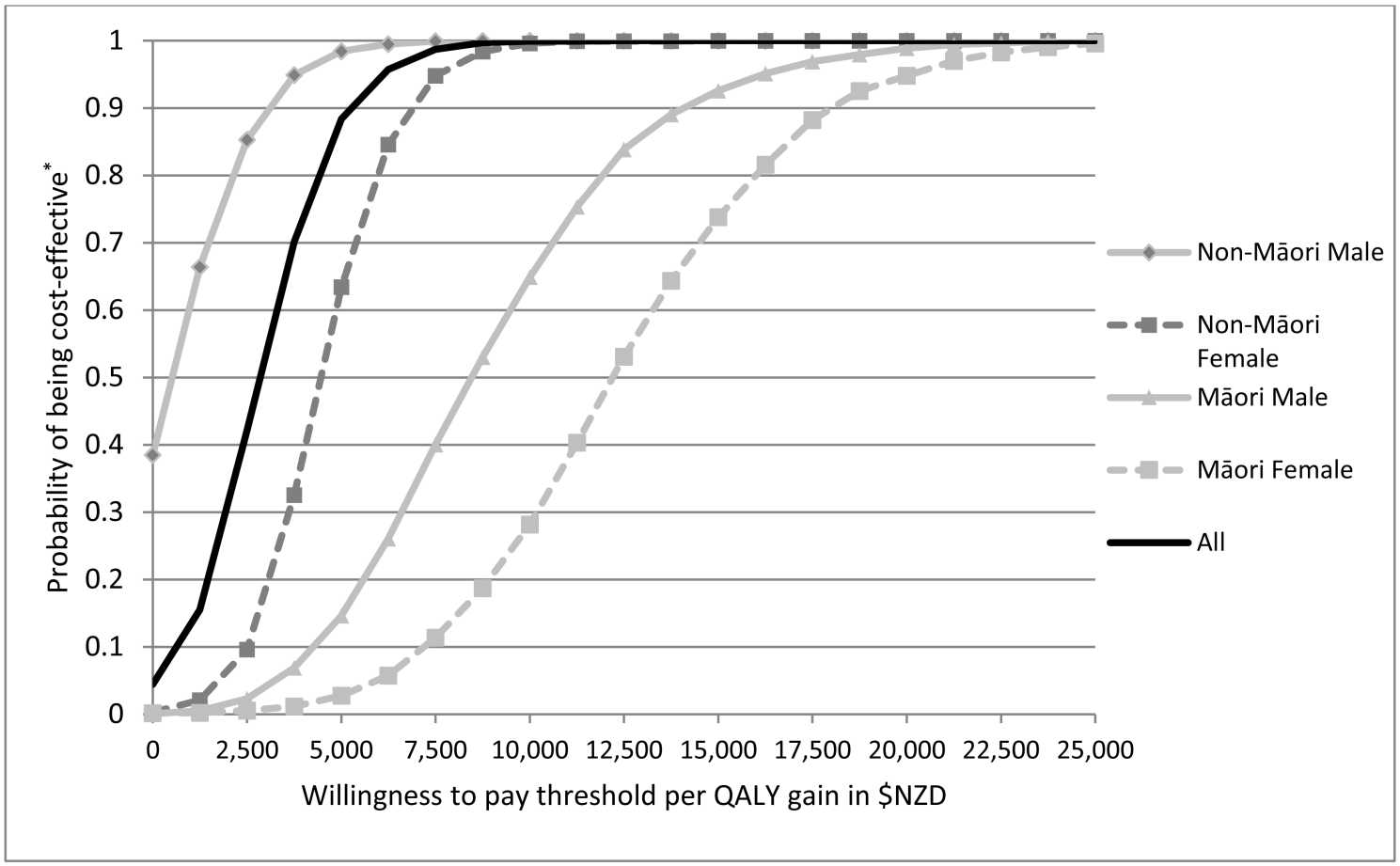
Figure 2



*Proportion of ICERs from the Monte Carlo simulation that are under the willingness to pay threshold.

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Cancer Epidemiology, Biomarkers & Prevention

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Colorectal cancer screening: How health gains and cost-effectiveness vary by ethnic group, the impact on health inequalities, and the optimal age-range to screen.

Melissa McLeod, Giorgi Kvizhinadze, Matt Boyd, et al.

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