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Research Article

Cancer Epidemiology, Biomarkers & Prevention

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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Abstract

Background: Screening programs 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 screening program for the indigenous Māori population of New Zealand (NZ).

Methods: A Markov model estimated: health benefits (quality-adjusted life-year; QALY), costs, and cost-effectiveness of biennial immunochemical fecal occult blood testing (FOBTi) of 50- to 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 (noncolorectal cancer) morbidity and mortality, colorectal cancer 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), colorectal cancer screening in NZ using FOBTi is cost-effective: NZ$2,930 (US$1,970) per QALY gained [95% uncertainty interval: cost saving to $6,850 (US$4,610)]. Modeled health gains per capita for Māori were less than for non-Māori: half for 50- to 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- to 74-year-olds and ethnic inequalities in QALE increased with colorectal cancer screening.

Conclusions: Colorectal cancer 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 programs.
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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. Organized cancer screening programs offer potential to reduce inequalities in health through reductions in cancer incidence and mortality; however, generally screening programs 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 programs in respect to their impact on underserved populations and inequalities in health, and to identify any modifiable factors that may help to maximize health gains (and inequality reductions) from proposed cancer screening programs. In this study, we aimed to examine the likely health gains and inequality impacts from the national rollout of a colorectal cancer screening program on the indigenous Māori population of New Zealand using a modified cost-effective approach.

Colorectal cancer screening with fecal occult blood testing (FOBTi) is effective at lowering colorectal cancer mortality (5), and has been found to be cost-effective for 50- to 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 colorectal cancer screening program; however, little is known about how colorectal cancer screening affects 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 colorectal cancer screening. Theuer and colleagues found that colorectal cancer screening was more cost-effective for blacks than whites, Latinos, and Asians, due to higher colorectal cancer incidence and worse survival (10).

New Zealand is a good setting for exploring the impact of colorectal cancer screening on health inequalities given the

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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 colorectal cancer incidence (although in New Zealand the gap in incidence is reducing over time; ref. 1), but worse survival once diagnosed (2, 11). This pattern raises the question as to whether colorectal cancer 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 with non-Māori (11), there is a case that survival will improve (more) for Māori than non-Māori as a result of standardized improvements in treatment following the implementation of a well-organized screening program. 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 (noncolorectal cancer) morbidity and mortality, colorectal cancer 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 (CEA) 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., quality-adjusted life-year; QALY), 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).

There are a range of current approaches to incorporate equity concerns into cost-effectiveness modeling methods in the literature (16, 17). These approaches loosely fit into two groups: (i) 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 (ii) 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 article 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 colorectal cancer screening program of 50- to 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, colorectal cancer 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 with 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 QALYs, costs, and cost-effectiveness of a national CRC screening program with biennial FOBTi of 50- to 74-year-olds (default age group for initial analyses). The model consisted of a colorectal cancer submodel and a general part which integrated results from the submodel with general population characteristics. Two populations were modeled: 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 ages 35 years and over in 2011, modeled through to death or age 110 years. We assumed this population to be screen-naïve. A multiple cohort approach was used, that is, each five-year age-group in 2011 was modeled separately until death or age 110 years. A cycle length of 1 year was used in the modeling. The model was implemented in 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 colorectal cancer incidence and mortality, transition parameters, survival, background mortality and morbidity, and also in colorectal cancer screening participation. A health system perspective was used, with a 3% discount rate. Unrelated health system costs were included, that is, 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 (i.e., including the inclusion of health care costs associated with extra lifespan as a result of the intervention; ref. 19). 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).

Colorectal cancer submodel

The colorectal cancer submodel (Fig. 1) generated adenoma incidence, preclinical and clinical colorectal cancer incidence and prevalence, and colorectal cancer mortality rates by Dukes stage and disease prevalence for a non-screening population as compared with various screening options. The colorectal cancer submodel was developed following Whyte and colleagues (2011; ref. 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 and colleagues modeled age-specific incidence of low risk adenomas for each age group separately; to avoid implausible age-specific patterns we modeled the age pattern using a Weibull distribution. Other model parameters from Whyte and colleagues (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; ref. 23), and colorectal cancer 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 matrix of all parameters for use in subsequent Monte Carlo analyses. The posterior parameter estimates are shown in Supplementary Table S1. Estimates of 8-year survival, by age and from New Zealand excess mortality rate modeling (24), were specified using a log normal function. Comparisons of model predicted versus observed mortality data are shown for the baseline in Supplementary Fig. S1.

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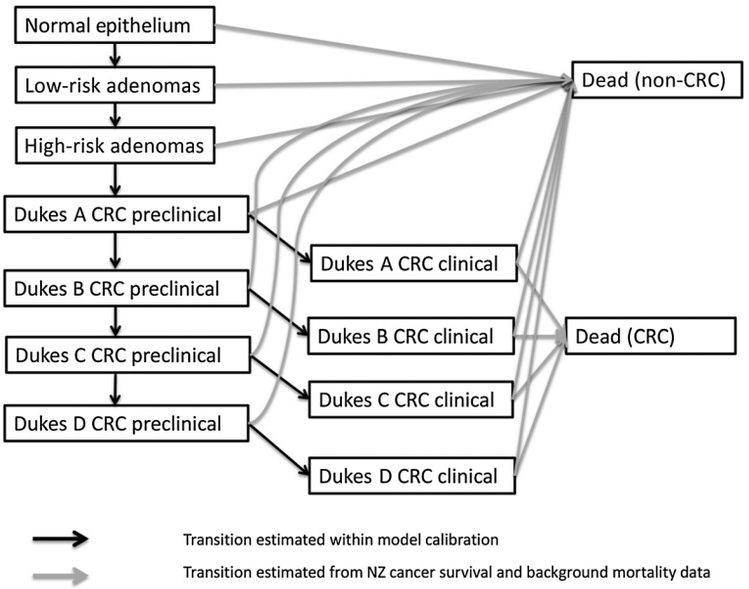

Figure 1.
Natural history model.

Adapted from: Whyte et al 2011 (22)

In the model, people detected with low-risk adenomas resided in the state for 1 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 colorectal cancer submodel (including QALYs related to colorectal cancer) acted as inputs to the general model which was used to calculate net QALYs gained by combining QALYs from the colorectal cancer 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 group, 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 colorectal cancer, and proportions dying each year of colorectal cancer (Table 1). We included 3 months of lead time in the model for those receiving the colorectal cancer screening intervention, by shifting the excess mortality curves for all stages of colorectal cancer to the right by 0.25 year. Our results were insensitive to the amount of lead time.

Our primary analyses included background (i.e., noncolorectal cancer) mortality rates and expected morbidity loss in the main life table. Morbidity loss was estimated by sex, ethnic group, and age, using the total years of life lived with disability (YLD) 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 ages 60 to 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 colorectal cancer diagnosis, remission or last 6 months of life if dying of colorectal cancer (Supplementary Fig. 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 colorectal cancer mortality reductions estimated by our model under various screening scenarios were similar to those reported in randomized controlled trials (RCT) and other colorectal cancer screening simulation models (e.g., CISNET and SimCRC; Supplementary Table S2; ref. 28).

Analyses

We carried out a series of equity analyses: (i) we replaced Māori data with non-Māori values for baseline mortality and morbidity to address the issue that lower life expectancy of indigenous population results in less opportunity for life years gained with screening; (ii) we used non-Māori colorectal cancer incidence and incidence trends for Māori to explore their contribution to differences in ethnic-specific health gains and ICERs; (iii) we assessed the impact of achieving equal screening coverage for Māori; and (iv) we assessed the impact of improvements in treatment for Māori following the implementation of a screening program, given evidence of greater delays to treatment for Māori compared with non-Māori leading to poorer survival (11). For this last scenario, we replaced Māori excess mortality from colorectal cancer 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

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Table 1. Input parameters for modeling colorectal cancer screening in the New Zealand setting

Variable		Base case	Range	Distribution	Source
Performance of screening test					
FOBTi sensitivity for adenomas[a]		21%	19%–22%	β (595, 2,236)	(8)
FOBTi sensitivity for CRC[a]		71%	48%–100%	β (353, 143)	(8, 32, 33)
FOBTi specificity for adenomas/CRC[a]		95%	84%–99%	β (1,733, 91.2)	(8, 32, 34)
Uptake and adherence with screening/diagnostic tests					
Proportion of population screened per round[b]	Non-Māori	58.3%	40%–70%	β (56, 40)	(27)
	Māori	45.4%	30%–60%	β (45, 54)	(27)
Proportion of population that never uptake FOBTi[b]	Non-Māori	31.6%	20%–50%	β (27, 58)	(27)
	Māori	38.9%	25%–55%	β (37, 57)	(27)
Proportion of FOBTi tests that need to be repeated		7%	0%–14%	β (11, 150)	(27)
Colonoscopy adherence		96%	90%–100%	β (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 colorectal cancer		100%			Assumed
Surveillance of high-risk adenomas					
High-risk surveillance group dropout rate (i.e., annual)		14%	10%–19%	β (19, 114)	(8)
Harms of screening					
Colonoscopy probability of perforation		0.12%	0.1%–0.14%	β (0.09, 74)	(27)
Probability of death following perforation		5.19%	0.0%–9.07%	β (26, 466)	(8)
Probability of (major) bleeding following colonoscopy		0.27%	0.07%–0.41%	β (7, 2,714)	(27)
Disease/state morbidity					
Disability weight (DW) first 9 months colorectal cancer diagnosis and treatment		0.288	0.194–0.404	β (20.3, 50.2)	Based on GBD DWs and Australian disaggregation by clinical phase (35, 36)
DW for one month assumed terminal colorectal cancer state		0.548	0.383–0.703	β (19.8, 16.3)	(35, 36)
DW for three months assumed pre-terminal colorectal cancer		0.539	0.379–0.691	B (20.6, 17.6)	(35, 36)
DW per annum post diagnosis and treatment (i.e., remission)		0.167	0.107–0.252	β (16.8, 83.9)	(35, 36)
DW for screening test (scenario analysis only)		0.000115	0.000048–0.00022	β (1.7, 280)	Set to $\frac{1}{2}$ of value for colonoscopy
DW for colonoscopy		0.000237	0.000096–0.00044	β (6.7, 555)	GBD 2010 (26), using "abdo/pelvic problem, mild"
DW for bleed from colonoscopy		0.00237	0.00160–0.00338	β (23.5, 167.2)	GBD 2010 (26), using "abdo/pelvic problem, moderate"
DW for perforation from colonoscopy		0.0376	0.0252–0.0520	β (20.1, 41.6)	GBD 2010 (26), using "abdo/pelvic problem, severe"
Incidence, mortality, and survival rates					
Colorectal cancer annual incidence trend (%)	Non-Māori under 65	−0.025	(−0.03 to −0.02)	Normal Mean: −0.025 SD 0.00255	(23)
	Non-Māori 65+	−0.015	(−0.02 to −0.01)	Normal Mean: −0.015 SD 0.00255	(23)
	Māori	0	(−0.01 to 0.01)	Normal Mean: 0 SD 0.0051	(23)
		−0.13%	−0.18 to −0.08		(23)

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Table 1. Input parameters for modeling colorectal cancer screening in the New Zealand setting (Cont'd)

Variable	Base case	Range	Distribution	Source
Colorectal cancer Annual Mortality Trend (%)			Normal Mean: −0.0013 SD 0.00026	
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-colorectal cancer) 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		γ (100, 0.44)	(27)
Cost per person invited and FOBT results obtained	$96.35		γ (100, 0.96)	(25)
Cost per repeat/spoilt FOBT	$15		γ (100, 0.15)	(25)
Cost per colonoscopy (true or false positive combined)	$654		γ (100, 6.55)	(25)
Cost per bleeding complication following colonoscopy	$5,262		γ (6.6, 795)	Purchasing power parity (PPP) adjusted average of 3 international studies (8, 22, 38)
Cost per perforation complication following colonoscopy	$17,481		γ (11, 1,588)	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[c] by phase of colorectal cancer pathway (first year of diagnosis, last 6 months of life if dying of colorectal cancer, and remission)	Supplementary Fig. S2.		Log-normal, 10% SD (correlated 1.0 across all sex, age and ethnic groups)	See (25) for methods and data

Abbreviation: DW, disability weight.
[a]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).
[b]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).
[c]Excess to "average" New Zealander.

improvements for Māori by ignoring the influence of co-morbidities on treatment and survival. The equity analyses were modeled 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 colorectal cancer 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- to 54-year-old and 70- to 74-year-old age cohorts were run separately and for selection of the optimal age range to screen, the 40- to 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 (Supplementary Fig. S3).

Results

The modeled colorectal cancer screening intervention for 50- to 74-year-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 with Māori and for men compared with women (Table 2). Non-Māori health gains were substantially greater than Māori: approximately two times greater for 50- to 54-year-olds (0.058 QALYs per person for non-Māori, c.f. 0.031 for Māori), and five times greater for 70- to 74-year-olds (0.003 c.f.

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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[a] modeled 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)	$1,520 ($1,310 to $1,778)	$755 ($639 to $895)	$766 ($652 to $897)	$148 ($127 to $174)	$1,370 ($1,175 to $1,608)
Net cost (NZ$; 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 to 126,000)	53,600 (39,100 to 70,200)	48,200 (37,700 to 58,700)	6,578 (4,760 to 8,730)	95,200 (73,100 to 118,000)
ICER	$2,930 ($cs to $6,850)	$1,020 ($cs to $5,060)	$5,070 ($cs to $8,950)	$10,500 ($4,500 to $17,900)	$2,420 ($cs to $6,230)
Per 50–54-year-old person (screen naïve) in 2011 under biennial screening for ages 50–74					
Net cost (NZ$)	$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	$3,770 ($279 to $7,700)	$1,770 ($cs to $5,910)	$6,100 ($2,604 to $9,940)	$11,100 ($5,920 to $17,300)	$3,270 ($cs to $7,150)
Per 70–74-year-old person (screen naïve) in 2011 under biennial screening for ages 70–74					
Net cost (NZ$)	−$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 $1,010)	$4,910 ($1,360 to $9,160)	$cost saving ($cs to $177)

NOTE: Discount rate 3%.

Cost-saving (cs).

[a]Population counts for age groups 30+, 50–54 years and 70–74 years: 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.

0.016; Table 2). Gains were greater for men than women aged 50- to 54-year-olds (0.060 c.f. 0.049 QALYs gained) but similar for men and women aged 70- to 74-year-olds (0.015 c.f. 0.014 respectively; Table 2).

The modeled colorectal cancer 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) (Fig. 2).

Scenario analyses

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

We used non-Māori colorectal cancer incidence and trends to explore the contribution of these factors to differences in health gains achieved for Māori compared with 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 with 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 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% up to 58.3%) and using the same percentage population that never uptake screening (31.6%), increased Māori QALY gains by 29% compared with the default model. Improving stage-specific survival for Māori to the level of non-Māori only resulted in a 1% increase in Māori QALYs (results not shown).

Change in absolute inequalities in QALE

The colorectal cancer intervention increases absolute inequalities in QALE for Māori compared with 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, ages 50 to 74 years (Table 4). Non-Māori men ages 60 to 64 years gain an additional 25.6 (12.5–40.3) healthy days compared with Māori of the same age while non-Māori women aged 30 to 34 years gain and additional 7.2 (−3.9 to 17.8) healthy days (Table 4).

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- to 69-year-olds (Supplementary Tables S3 and S4), then 65 to 74, 60 to 74, 60 to 79, and 55 to 79 (for 10-, 15-, 20-, and 25-year age ranges, respectively).

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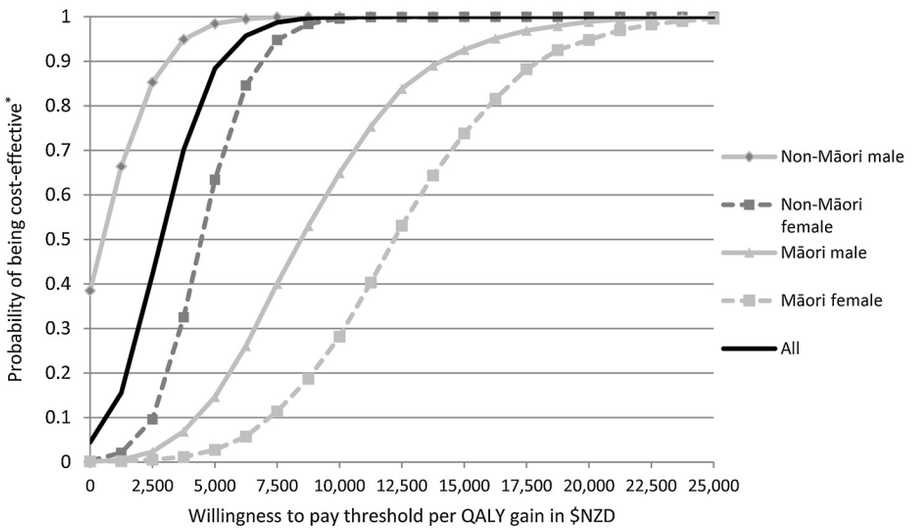

*Proportion of ICERs from the Monte Carlo simulation that are under the willingness to pay threshold.

Figure 2.
Cost-effectiveness acceptability curves* by sex and ethnic grouping for colorectal cancer screening in New Zealand.

Discussion

Population cancer screening programs offer the potential to both improve population health and address inequalities in health; however, national screening programs consistently underserve indigenous populations and, therefore, risk increasing indigenous health and healthcare inequalities. From our study, national population colorectal cancer screening in New Zealand using biennial FOBTi is estimated to be cost-effective (similar to studies in other countries; refs. 6, 8, 29), and would result in health gains for both Māori and non-Māori. However, due to the lower incidence of colorectal cancer, higher background mortality and likely lower screening coverage, this program is likely to increase inequalities in QALE for Māori compared with non-Māori. This finding is consistent with findings from Australia's national colorectal cancer screening program which has achieved lower coverage for the indigenous population of Australia (which

Table 3. Equity and scenario analyses (expected value analysis; costs and QALYs gained for offering colorectal cancer 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 colorectal cancer incidence trends replaced with non-Māori values	Māori	$146	$73	5,920 (−17%)	$12,300
5. Māori colorectal cancer 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
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 colorectal cancer screening with FOBTi for 50–74-year-olds.

Age group and sex	Baseline QALE			QALE with colorectal cancer screening			Additional healthy days under colorectal cancer 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)

also has a lower incidence of colorectal cancer) and has increased inequalities in cancer outcomes for indigenous Australians (12).

Achieving equal screening coverage for indigenous populations is possible, while 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 program'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 modeled health gains for Māori by 29%—not enough so that Māori gains were equivalent to those for non-Māori. Colorectal cancer is one of the only a few cancers for which Māori in New Zealand have lower incidence, and, therefore, even with equal screening coverage the modeled health gains from colorectal cancer 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 colorectal cancer 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, for example, tobacco control.

As a part of implementing a national screening program, there is likely to be greater standardization of care and monitoring of the screening pathway (including treatment). This improvement in colorectal cancer care will offer benefits to all colorectal cancer 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 1% increase in modeled health gains for Māori).

In this study, we used a cost-utility approach to consider a range of equity scenarios. By standardizing 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 affect cost-effectiveness. Nevertheless, our model performed similarly to other simulation studies (Supplementary Table S2).

Unlike Whyte and colleagues (2011; ref. 22) and Sharp and colleagues (2012; ref. 8), we did not include a transition probability directly from normal epithelium to colorectal cancer (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 with explicitly modeling an increase in costs for underscreened people (which would see the marginal cost-effectiveness for these groups worsen). It was beyond the scope of this article, and data quality, to undertake such a marginal analysis of increased recruitment costs per screened person.

One possible limitation of our Markov modeling 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 modeled colorectal cancer screening effectiveness.

There are numerous strengths to our modeling and data inputs. We used detailed New Zealand epidemiologic 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 colorectal cancer incidence and survival varied by sex, ethnic group, and age, allowing us to examine social group differences in modeled health gains and ICERs.

Conclusions

Although a national colorectal cancer screening program 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 program is to give attention to improving screening coverage.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: M. McLeod, D. Sarfati, N. Wilson, T. Blakely
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Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): G. Kvizhinadze, M. Boyd, J. Barendregt, T. Blakely
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): M. McLeod, G. Kvizhinadze, M. Boyd, J. Barendregt, T. Blakely
Writing, review, and/or revision of the manuscript: M. McLeod, G. Kvizhinadze, M. Boyd, J. Barendregt, D. Sarfati, N. Wilson, T. Blakely
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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

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