The potential for tailored screening to reduce bowel cancer mortality for Aboriginal and Torres Strait Islander peoples in Australia: Modelling study

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ABSTRACT

Background: Australian Aboriginal and Torres Strait Islander peoples experience health and socioeconomic disparities, including lower life-expectancy, have a younger mean age of colorectal cancer (CRC) diagnosis, and lower CRC survival than non-Indigenous Australians. The National Bowel Cancer Screening Program (NBCSP) provides biennial CRC screening for Australians aged 50–74 years to reduce the burden of CRC. The 2019 participation rate was 42% nationwide and 23% in Aboriginal and Torres Strait Islander peoples. For Aboriginal and Torres Strait Islander peoples, this study aims to estimate the health outcomes and cost-effectiveness of the current NBCSP and extensions to include people < 50 years.

Methods: An existing microsimulation model, *Policy1-Bowel*, was adapted to the Aboriginal and Torres Strait Islander population and was used to evaluate three strategies assuming biennial iFOBT screening from 50-74, 45–74, or 40–74 years under two participation scenarios: 23% and 42% per screening round (psr.).

Results: At 23–42% participation psr., the current NBCSP was predicted to reduce lifetime CRC incidence and mortality by 14–24% and 23–39%, respectively, be cost-effective (incremental cost-effectiveness ratio <$13,000/life-year saved), and be associated with a benefits-and-burden balance of 51-53 number-needed-to-colonoscope (NNC) per CRC death prevented of . Lowering the screening start age to 40(45) would further reduce CRC incidence and CRC mortality by 7–11(4–5) percentage points, be cost-effective, and be associated with an incremental NNC- of > 95 (> 60).

Conclusion: For Aboriginal and Torres Strait Islander peoples, the current NBCSP is cost-effective but participation is limited. Lowering the screening start age will further reduce CRC incidence and mortality.

Policy summary: These findings highlight a need to increase NBCSP participation whilst exploring the feasibility and acceptability of lowering the NBCSP start age for Aboriginal and Torres Strait Islander peoples. These findings could inform new co-designed, community-led strategies to improve CRC outcomes for Aboriginal and Torres Strait Islander peoples.

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1. Background

Indigenous peoples worldwide experience disproportionally worse health outcomes, lower life expectancy, and higher social and economic disadvantages than their non-Indigenous counterparts [1]. Cancer is one of the leading causes for the disparities in health outcomes and life-expectancy for Indigenous peoples [2]. Cancer incidence, mortality and survival outcomes for Indigenous populations are disproportionly worse than non-Indigenous populations [2–4] Improved cancer prevention and early detection programmes including targeted culturally appropriate screening are needed to reduce health disparities for Indigenous peoples [4].

The Australian Indigenous population, Aboriginal and Torres Strait Islander peoples, represents ~3% of the total population and comprises hundreds of historically, culturally, and linguistically distinct groups. Significant gaps exist in health and socioeconomic status between Aboriginal and Torres Strait Islander peoples and non-Indigenous Australians, with Aboriginal and Torres Strait Islander peoples having poorer health outcomes, 8.6 and 7.8 years lower life-expectancy for men and women respectively, and other socioeconomic disadvantages [5–7].

Colorectal cancer (CRC) is the third most common cancer in Australia, for non-Indigenous Australians and Aboriginal and Torres Strait Islander peoples [8]. A national screening programme, the Australian National Bowel Cancer Screening Program (NBCSP), has been established to reduce the CRC burden. As part of the NBCSP a free biennial immunochemical faecal occult blood test (iFOBT) screening kit is posted to eligible individuals aged 50–74 years at their address as listed in Australia's universal health insurance scheme (Medicare) records. Individuals who complete a kit and are found to have a positive result are referred for a follow-up colonoscopy.

There are differences in the NBCSP participation and outcomes for Aboriginal and Torres Strait Islander peoples versus the general population. In 2017–2018, Aboriginal and Torres Strait Islander peoples were found to have a lower NBCSP participation (23% vs 42%), a higher iFOBT positive rate (10% vs 7%), and a lower compliance rate to follow-up colonoscopy (48% vs 66%) than the overall population [9]. Furthermore, Aboriginal and Torres Strait Islander peoples have a younger mean age of CRC diagnosis (61 vs 70 years, see Appendix Section 1), a higher proportion of CRC diagnosed before the NBCSP current commencement age of 50 (21% vs 9%; see Appendix Section 1), more likely to be diagnosed at advanced stage, and have a lower CRC survival rate than non-Indigenous Australians [10–12]. This suggests that Aboriginal and Torres Strait Islander peoples may benefit from increased participation in the NBCSP and/or starting CRC screening at an earlier age than the current commencement age of 50. For the general Australian population, predictive modelling has been used to evaluate the NBCSP and found that the existing programme targets the optimal screening age group and is cost effective [13–15]. Previous analysis for the general population has also found that starting screening at 45 years could be cost-effective, but it would increase colonoscopy demand and would be associated with a less favourable incremental benefits-to-harms trade-off than screening from 50 to 74 years; thus, improving participation is currently the optimal strategy for reducing the burden of CRC in the general population [16]. However, no study to date has evaluated the impact of NBCSP and interventions to improve NBCSP outcomes (such as increasing participation or alternative screening age ranges) for Aboriginal and Torres Strait Islander peoples. Hence, for Aboriginal and Torres Strait Islander peoples, this study aims to

(i) adapt an existing Australian CRC natural history and screening model (*Policy1-Bowel*);
(ii) evaluate the health outcomes and cost-effectiveness of the current NBCSP at 23% and 42% participation rates; and
(iii) evaluate the potential health benefits and cost-effectiveness of extending the NBCSP to include people in their forties.

2. Methods

A comprehensive microsimulation model, *Policy1-Bowel*, was used for this study. The model was developed using Microsoft Visual Studio C++. It was initially designed to simulate CRC natural history and screening for average risk Australians and has been comprehensively calibrated and validated [13–18]. The model was adapted for Aboriginal and Torres Strait Islander peoples. For each evaluation, a single age cohort consisting of 10 million virtual men and 10 million virtual women was simulated [8,19]. For each virtual individual, the simulation begins from age 20 and continues on an annual time-step until the individual dies or reaches 90 years of age, whichever occurs first. The life expectancy of Aboriginal and Torres Strait Islander peoples was modelled by incorporating the age-specific non-CRC-related mortality rates, which was derived by subtracting the CRC mortality rate in 2011–2015 from all-causes mortality rates in 2008–2012 for Aboriginal and Torres Strait Islander peoples [8,19].
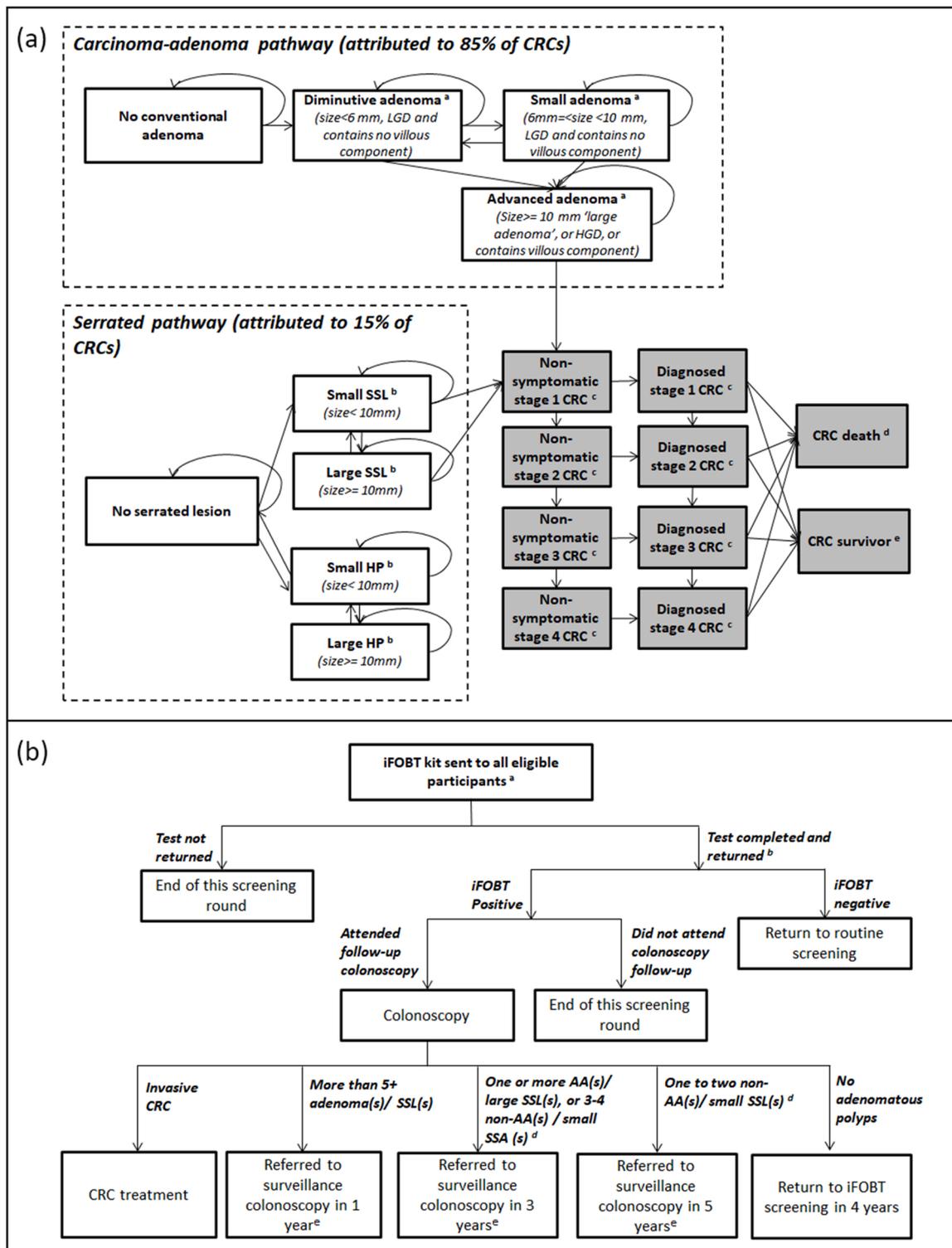
2.1. Modelled CRC natural history

Policy1-Bowel simulates the development of CRC via both the conventional adenoma-carcinoma pathway (i.e. the development of conventional adenoma into CRC) and serrated pathway (i.e. the development of hyperplastic polyps [HP] and sessile serrated lesions [SSL, also known as sessile serrated adenomas or polyps], assuming that only SSL can develop into CRC) (Fig. 1). The location, shape, size, degree of dysplasia, and architecture of adenoma, and location and size of HP and SSL are modelled. *Policy1-Bowel* simulates up to ten adenomas and ten serrated polyps simultaneously per individual. However, most virtual individuals will develop one or no adenoma and/or SSL in their lifetime. In the model, an adenoma that is large in size (>= 10 mm), with high-grade dysplasia, or with villous histology (referred as advanced adenoma) or a SSL (with any size) can further progress into stage 1 CRC without any symptoms; a non-symptomatic CRC can progress to an advanced stage over time or be diagnosed due to the onset of symptoms (referred as symptomatically-detected CRC). The model assumed ~85% of CRCs develop via the conventional adenoma-carcinoma pathway and the remaining 15% via the serrated pathway.

To inform model calibration, we reviewed published literature and national data sources that systematically collect data on the health status of Australians to identity the available data on CRC incidence and mortality rates and screening-related outcomes for Aboriginal and Torres Strait Islander peoples. The modelled pre-cancer natural history parameters were then calibrated to the published data identified in the review.

In the model, patients diagnosed with CRC are associated with an additional risk of dying (compared with individuals without CRC), which varies by cancer stage at diagnosis. The modelled 5-year stage-specific CRC survival rates for symptomatically-detected CRCs were informed by the observed rates among all CRC patients (including data from Aboriginal and Torres Strait Islander peoples and non-Indigenous Australians) diagnosed in public hospitals in Western Australia in 1993–2003, as Aboriginal and Torres Strait Islander specific rates were not available [20]. Where iFOBT screening is undertaken, a non-symptomatic CRC could also be diagnosed via iFOBT screening and colonoscopy assessment (referred to as *screen-detected CRC*). The modelled stage-specific survival for screen-detected CRC patients is assumed to be higher than for symptomatically-detected CRC patients, consistent with international findings [21–23]. The model assumes that patients who survive for five years after CRC diagnosis become CRC survivors. These survivors are assumed to have no additional risk of dying from the disease compared with individuals without CRC.

Detailed model assumptions for the CRC natural history and survival used for this study are provided Appendix Sections 2.1 and 2.2.

Fig. 1. The modelled (a) CRC natural history pathways and (b) screening delivery pathway (based on the NBCSP) and management of follow-up colonoscopy in *Policy1-Bowel* for Aboriginal and Torres Strait Islander peoples in Australia AA – advanced adenoma; CRC – colorectal cancer; HGD – high-grade dysplasia; HP – hyperplastic polyp; iFOBT – immunochemical faecal occult blood test; LGD-low-grade dysplasia; SSL – sessile serrated lesion.[a] The location, shape, size, degree of dysplasia, and architecture of conventional adenoma are modelled; the location and size of the SSL and HP are modelled. [b] CRC will first appear as Stage 1 cancer without any symptoms. Each year, a non-symptomatic cancer may be diagnosed because of the onset of symptoms or remain undiagnosed and possibly progress into a more advanced stage [c] CRC patients are associated with an additional risk of dying due to CRC, and the risk varies by cancer stage at diagnosis and time since CRC diagnosis[d] Patients who survived for five years after CRC diagnosis are assumed to have no additional risk of dying from CRC (i.e. become CRC survivor).

2.2. Modelled iFOBT screening strategies and participation scenarios

Consistent with the NBCSP current practice, *Policy1-Bowel* assumes that the NBCSP sends an iFOBT kit to eligible individuals once every two years and a proportion of the test kits will be completed and returned depending on the modelled screening participation rate (Fig. 1). Four strategies with different screening target age range assumptions for Aboriginal and Torres Strait Islander peoples were considered:

- A counterfactual strategy which assumed no screening (Strategy 1)
- Biennial NBCSP iFOBT screening at 50–74 years (Strategy 2, i.e. the current programme)
- Biennial NBCSP iFOBT screening with an extended age range of 45–74 years (Strategy 3), and
- Biennial NBCSP iFOBT screening with an extended age range of 40–74 years (Strategy 4)

For each strategy, two scenarios with different screening participation rates were modelled:

- Scenario 1 (a status quo scenario) assumed an average of 23% participation rate per screening round (referred to as psr. hereafter), derived from the observed NBCSP participation rate for Aboriginal and Torres Strait Islander peoples [9].
- Scenario 2 (a hypothetical scenario) assumed an average participation rate of 42% psr., similar to the observed nationwide NBCSP participation rate [9].

The modelled overall screening participation rate incorporates two different screening participation assumptions: one for individuals who have never taken part in the NBCSP (referred to as 'screening initiation rates') and another for those who have previously participated in the NBCSP at least once (referred to as 'rescreening probabilities'). The modelled screening initiation rates were informed by the observed participation rates for Aboriginal and Torres Strait Islander peoples (for Scenario 1) and all Australians (for Scenario 2). For both Scenario 1 and 2, the modelled rescreening probabilities were based on the data observed in 2013–2016 for all Australians who had participated in the previous screening rounds as data specific to Aboriginal and Torres Strait Islander peoples were not available [24,25]. See Appendix Section 2.3 for detailed screening participation assumptions.

For strategies that assumed people started screening in their 40 s (Strategy 3 and 4), we assumed people screening in their 40 s would have equivalent participation to those in their 50 s (observed NBCSP participation data only available for people aged 50–74 years). This is likely to overestimate participation for these individuals as the observed data shows that NBCSP participation rates increase by age [9].

2.3. Modelled colonoscopy follow-up and surveillance management

The model assumed ~53% of individuals who have a positive iFOBT result complete a follow-up colonoscopic assessment (referred to as a 'follow-up colonoscopy') for all strategies and scenarios considered in this study, based on reported colonoscopy assessment compliance rate for Aboriginal and Torres Strait Islander NBCSP participants in 2016 [25]. However, it should be noted that diagnostic assessment outcome reporting to the NBCSP register is not mandatory, and therefore the colonoscopy assessment compliance rate is likely to be underreported for both the general population and for Aboriginal and Torres Strait Islander peoples. Depending on the follow-up colonoscopy findings, individuals are referred back to the NBCSP for iFOBT screening after an interval of 4 years or to repeat colonoscopic assessments (referred as 'surveillance colonoscopies') after 1–5 years based on the 2011 guidelines recommendations [26]. Although updated Australian colonoscopy surveillance guidelines were published in 2019 [27], the timeframe for implementation of the updated guidelines into practice is unclear and

they have not been incorporated into this analysis.

There are currently no data available to inform the compliance rate to surveillance colonoscopies for either Aboriginal and Torres Strait Islander peoples or the general Australian population. In this study, the compliance rate was assumed to be 80% for all strategies and scenarios, regardless of age and sex, as per the assumptions used in previous studies of the general Australian population [13–15,28]. Surveillance colonoscopies are assumed to stop at age 75.

2.4. Other model parameters and data sources

The test specificity and sensitivity of the modelled iFOBT test characteristics are provided in Table 1 (see Appendix Section 2.4 for detailed iFOBT test characteristics assumptions). The modelled test characteristics of iFOBT were obtained by calibrating to observed overall iFOBT positive rates and the proportion of follow-up colonoscopy assessments with negative findings for Aboriginal and Torres Strait Islander NBCSP participants in 2012–2017 with positive iFOBT result (see Appendix Sections 4.5 and 4.6 for the calibration outcomes) [29]. It should be noted that both calibration targets are reportedly higher for Aboriginal and Torres Strait Islander peoples than the general population, indicating a higher iFOBT false positive rate for Aboriginal and Torres Strait Islander peoples [29].

The modelled colonoscopy per-lesion detection rates were derived from the findings of systematic reviews of international data (Table 1) [33,34]. The model assumed the end of caecum was reached in all colonoscopy procedures. Individuals who had no polyps or cancer in the bowel were assumed to have a negative colonoscopy outcome (i.e. 100% test specificity). Polypectomy was assumed to be performed on all polyps detected by colonoscopy, except HP, with 100% completeness. The model assumed 0.12% of individuals undergoing colonoscopy (regardless of whether a polypectomy was performed to remove colorectal lesion) experienced a non-fatal colonoscopy-related serious adverse event (CSAE) based on the pooled estimate from a systematic review and meta-analysis of perforation and major-bleeding resulting from a colonoscopy [35].

A health services perspective was taken for the cost-effectiveness analysis. Costs considered were the direct costs associated with posting the iFOBT kits used in the NBCSP, laboratory analysis of completed iFOBT samples, general practitioner visit for follow-up of positive iFOBT results, colonoscopy procedures, and CRC treatment (Table 1). Overhead costs related to the NBCSP administration (other than the costs of sending test kits), cost associated with promotion of the NBCSP participation, and individuals' out-of-pocket costs were not included. All costs are presented in Australian dollars as at 2018 (AUD $1 = USD $0.7040, 31st December 2018).

2.5. Outcomes evaluated

2.5.1. Base case analysis

The modelled outputs for each strategy include the number of CRC cases, CRC deaths, colonoscopic assessments and potential CSAEs over the lifetime of 10,000 persons alive at 40 years, and costs and life-years per person over their lifetime. The discounted lifetime costs and life-years were calculated by accruing the predicted age-specific cost and life-years from age 20–90 years, discounting at a rate of 5% per annum from age 40 (i.e. the youngest screening commencement age across all strategies considered in this study). We used the same perspective and discount rate as in previous evaluations of the NBCSP [13–15,36].

In the cost-effectiveness analysis, incremental cost-effectiveness ratios (ICERs) were calculated for each dominating strategy (i.e. the strategy with the lowest cost when compared to strategies with similar or lower effectiveness) for each participation scenario separately. The ICER was calculated by dividing the incremental discounted costs by the incremental discounted life-years of the two strategies of interest. There is currently no official willingness-to-pay (WTP) threshold for health

Table 1

Summary of value and data sources of key model parameters used for baseline analysis.

Key model parameter	Modelled value	Reference	Aboriginal and Torres Strait Islander peoples' specific data or assumptions?
Screening participation (Scenario 1-23% participation rate psr.)			
1st invitation	11.7% (M), 12.9% (F)	See Appendix section 2.3.1	Yes
2nd invitation	7.6% (M), 8.4%(F)	See Appendix section 2.3.1	Partially
Subsequent invitation	4.9% (M), 5.5% (F)	See Appendix section 2.3.1	Partially
Re-screening probabilities	74–77%	See Appendix section 2.3.2	No
Screening participation (Scenario 2–42% participation rate psr.)			
1st invitation	26.4% (M), 30.6% (F)	See Appendix section 2.3.1	No
2nd invitation	17.6% (M), 19.9% (F)	See Appendix section 2.3.1	No
Subsequent invitation	11.2% (M), 12.9% (F)	See Appendix section 2.3.1	No
Re-screening probabilities	~74–77%	See Appendix section 2.3.2	No
Compliance to follow-up colonoscopy after positive iFOBT results	~53%	Based on the observed rate in 2016 [25]	Yes
Compliance to surveillance colonoscopy	80%	Assumption	No
Unit item cost			
iFOBT kit sent	A$10[a]	Assumption	No
iFOBT kit received	A$22[b]	Assumption	
GP consultation for abnormal screening result or referral letter	A$44.42	Average of MBS item 23, 36, 44, weighted by the number claims in July 2017-June 2018 [30]	
COL without complication[c]	A$1,800	Assumption	
COL with complication[c]	$17,351	DRG-AG item G48A, inflated to June 2018 value [31]	
Stage 1 CRC treatment	$46,531	Based on the findings of Ananda et al. 2016 value inflated to June 2018 [32]	
Stage 2 CRC treatment	$74,311		
Stage 3 CRC treatment	$110,009		
Stage 4 CRC treatment	$96,426		
Colonoscopy test detection rate (per lesion)			
Adenoma 1–5 mm	79.0%	Van Rijn et al. 2006 [38]	No
Adenoma 6–9 mm	85.0%		
Adenoma > 10 mm	92.0%		
SSL (any size)	78.0%		
CRC at any stage	95.0%	Pickhardt et al. 2011 [39]	
Completeness	100% to the end of caecum	Assumption	
Rate of non-fatal complication per procedure	1.2 per 1000 colonoscopies	Lin et al. 2016 [32]	
Rate of fatal complication per procedure	0	AIHW 2015 [15]	
iFOBT test characteristics (per person)[d]			

Table 1 (*continued*)

Key model parameter	Modelled value	Reference	Aboriginal and Torres Strait Islander peoples' specific data or assumptions?
Specificity[e]	90.0%	Obtained via calibrating the modelled iFOBT positivity rate and COL outcome among positive iFOBT to data observed in the NBCSP for Aboriginal and Torres Strait Islander peoples in 2012–2017 [17]	Yes
Sensitivity for adenoma of any size	15.8%		
Sensitivity for adenoma > 5 mm	29.2%		
Sensitivity for adenoma > 10 mm	43.3%		
Sensitivity for CRC	64.4%		
Precancer and cancer natural history assumption	Baseline assumption	Obtained via calibrating to the age- and sex-specific CRC incidence rates and stage distribution of CRC cases at diagnosis for Aboriginal and Torres Strait Islander peoples. See Appendix Sections 2 and 4	Yes
5-year stage-specific survival rates for patients with symptomatically-detected CRC	Baseline assumption	Morris et al. 2007 [20]. See Appendix Section 2.2.	No

COL – colonoscopy; CTC – computed tomographic colonography; iFOBT – immunochemical faecal occult blood test; GP – general practitioner; N/A- not applicable; Sens – sensitivity; Spec – specificity; SSL – sessile serrated lesion.
  [a] Includes estimated cost of one-way postage ($2) and an iFOBT test kit ($8).
  [b] Includes estimated cost of one-way postage for the return of iFOBT test ($2) and cost of an iFOBT test being analysed in the lab ($20).
  [c] With/without polypectomy.
  [d] The present of SSL and HP was assumed to have no association with the positive outcome of iFOBT (i.e. having sessile serrated lesion would not increase the overall probability of the iFOBT outcome being positive) in the model. See Appendix for more detailed test characteristics assumptions.
  [e] For any adenoma.

economic evaluations of cancer screening in Australia. For this evaluation, we used a WTP threshold of $50,000/LYS for comparison with previous evaluations of the cost-effectiveness of the NBCSP in the general Australian population [13–15,36]. Strategies with an ICER greater than the WTP threshold are considered not cost-effective. It should be noted that it is not within the scope of this study to estimate the cost-effectiveness of improving NBCSP participation rate, as has been previously done. A cost-effectiveness analysis of improving NBCSP participation incorporating the additional cost of NBCSP promotion activities (e.g. mass media campaign, new screening delivering method etc) was not considered in this study [16].

Cancer screening is typically evaluated using a balance between the health benefits and burden of screening, diagnosis and treatment. In this study, the lifetime number of colonoscopies (including follow-up and surveillance colonoscopies) is used as a surrogate measure for the burden of screening. Potential harms of screening were measured by the number of CSAEs from colonoscopy. The benefits-and-burden balance (in line with the methods used in previous studies [13–15,38]) was measured using the incremental number-needed-to-colonoscopy (INNC) per CRC death prevented. An INNC was calculated by dividing the

number of colonoscopies by the number of CRC deaths prevented in the lifetime of 10,000 persons alive at 40 years for each dominating strategy (i.e. the strategy with the lowest number of colonoscopies when compared to strategies with similar or lower effectiveness), compared with the next most beneficial dominating strategy in the benefits-and-burden balance analysis.

2.5.2. Uncertainty analysis

Our literature review found that 56–68% of CRC were diagnosed at advanced (regional and distant) stages for Aboriginal and Torres Strait Islander peoples (see Appendix Section 4.2 for more details) [12,39,40]. For the base case analysis, *Policy1-Bowel* was calibrated to predict that 62% of symptomatically-detected CRCs were diagnosed at advanced stages in the absence of screening. Uncertainty analyses were performed to assess the impact of assuming a lower (56%) or higher (68%) proportion of advanced CRCs at diagnosed for all screening strategies under Scenario 1 (23% participation psr.).

2.5.3. Sensitivity analyses

A number of the aforementioned key model parameters were informed by data observed for the general population or based on assumptions, due to lack of data specific to Aboriginal and Torres Strait Islander people. Therefore, one-way sensitivity analyses were performed to assess the impact of alternative assumptions for these key model parameters, which includes the CRC incidence rates, stage-specific survival rate for symptomatically-detected CRC, screening initiation rates, re-screening probabilities, compliance to follow-up colonoscopy and surveillance colonoscopy, and test characteristics of iFOBT and colonoscopy (Appendix Section 6). The number of CRC deaths and ICER were estimated for all screening strategies in Scenario 1 (23% screening participation psr.).

2.5.4. Supplementary normative analyses for model validation

A supplementary normative analysis was performed to evaluate all screening strategies in a hypothetical scenario assuming perfect (i.e. 100%) NBCSP participation, follow-up colonoscopy attendance, and surveillance colonoscopy attendance. Findings of this analysis illustrate the maximal effects of screening in fully compliant individuals. They are not a direct reflection of the effectiveness of screening for 'real world' participation. To assess the validity of the *Policy1-Bowel* predicted reduction in CRC incidence and mortality for biennial iFOBT screening at 50–75 and 45–75 years (assuming perfect compliance to screening and follow-up recommendations), the results were compared with findings from a Cancer Intervention and Surveillance Modelling Network (CISNET) comparative modelling study [41], which was used to support the latest US Preventive Service Task Force colorectal cancer screening recommendations for the general population.

3. Results

3.1. Model calibration

Our review identified published data for Aboriginal and Torres Strait Islander peoples to inform model calibration, including: age- and sex-specific rates of CRC incidence, CRC mortality, positive iFOBT positive, and proportion of colonoscopy assessments with negative findings among people with positive iFOBT result, and stage distribution of CRC cases at diagnosis. The *Policy1-Bowel* model was calibrated to all published data identified except CRC mortality rates. National CRC deaths estimates are known to be undercounted by 23% due to a coding issue and a data correction for Aboriginal and Torres Strait Islander peoples was not yet publicly available when the study was conducted [8,42]. The calibrated *Policy1-Bowel* model predicted a higher CRC mortality rate than the latest reported data for Aboriginal and Torres Strait Islander peoples [8]. The model predicted sex-specific mean age of CRC diagnosis were consistent with the findings of a separate analysis of CRC

incidence data for Aboriginal and Torres Strait Islander peoples in 1996–2014. See Appendix Section 4 for detailed model calibration results.

3.2. CRC incidence and mortality

In the absence of screening (Strategy 1), 445 CRC cases and 191 CRC deaths were predicted to occur per lifetime of 10,000 Aboriginal and Torres Strait Islander peoples (Table 2). Compared with no screening, the NBCSP current practice (Strategy 2) was predicted to prevent 61 CRC cases and 45 CRC deaths (equivalent to 14% and 23% reduction respectively) at the observed 23% participation rate psr., and to prevent 108 CRC cases and 76 CRC deaths (equivalent to 24% and 39% reduction respectively) at a 42% participation rate psr.

At the observed 23% participation rate psr., lowering the screening start age from 50 to 45 years (Strategy 3) could prevent an additional 15 CRC cases and 8 CRC deaths, and lowering the screening start age from 50 to 40 years (Strategy 4) could prevent an additional 29 CRC cases and 16 CRC deaths per lifetime of 10,000 Aboriginal and Torres Strait Islander peoples. At 42% participation psr., an additional 18 CRC cases and 8 CRC deaths are estimated to be prevented (Strategy 3), and an additional 36 CRC cases and 19 CRC deaths prevented (Strategy 4) per lifetime of 10,000 Aboriginal and Torres Strait Islander peoples.

3.3. Colonoscopy burden and colonoscopy-related serious adverse events

The current NBCSP (Strategy 2) was predicted to result in 2,260 colonoscopies and 2.7 CSAEs at 23% NBCSP participation psr., and 3,990 colonoscopies and 4.7 CSAEs at 42% NBCSP participation psr. per lifetime of 10,000 Aboriginal and Torres Strait Islander peoples (Table 2). At a 23% participation rate psr., extending the screening start age from 50 to 45 years (Strategy 3) would result in an additional 540 colonoscopies and 0.5 CSAEs; extending the screening start age from 50 to 40 years (Strategy 4) would result in an additional 1,330 colonoscopies and 1.5 CSAEs per lifetime of 10,000 Aboriginal and Torres Strait Islander peoples. At 42% participation psr., the equivalent estimates are additional 790 colonoscopies and 0.9 CSAEs (Strategy 3), and additional 1,880 colonoscopies and 2.2 CSAEs (Strategy 4).

3.4. Benefits-and-burden balance

The benefits-and-burden balance of the current programme (Strategy 2) was predicted to result in a 51–53 incremental number-needed-to-colonoscope (INNC) per CRC death prevented compared with no screening across both participation scenarios (Table 2). Lowering the screening start age to 40 (INNC: 97–103 per CRC death prevented across the two participations scenarios) or 45 years (INNC: 62–95) was predicted to be associated with a higher INNC per CRC death prevented (i.e. a less favourable benefits-and-burden balance) than the current programme (Table 2).

3.5. Cost-effectiveness

Given the indicative WTP threshold of $50,000/LYS in Australia [43], the current programme (Strategy 2) was predicted to be cost-effective (ICER of $10,802/LYS-$11,927/LYS, compared with no screening) for Aboriginal and Torres Strait Islander peoples in both screening participation scenarios (Table 3). Lowering the screening start age from 50 to 45 (Strategy 3; ICER: $25,636/LYS-$28,145/LYS) or to 40 years (Strategy 4; ICER: $30,384/LYS-$38,396/LYS) were both predicted to be cost-effective in both screening participation scenarios.

3.6. Uncertainty and sensitivity analyses

In the uncertainty analysis, varying the proportion of advanced CRCs at diagnosed were found to have a negligible impact on the predicted

Table 2
Model-predicted lifetime number of incident CRC, CRC deaths, colonoscopies and colonoscopy-related serious adverse events per 10,000 people alive at 40 years for all screening strategies for Aboriginal and Torres Strait Islander peoples in Australia.

Screening age range (years)	CRC incidence			CRC mortality			Number of colonoscopies[a]	Number of CSAEs	INNC per CRC death prevented
	N	% reduction vs. no screening	Additional cases prevented vs. current practice	N	% reduction vs. no screening	Additional cases prevented vs. current practice			
No screening	445	N/A	N/A	191	N/A	N/A	N/A	N/A	N/A
Scenario 1 (23% screening participation psr.)									
50–74[b]	384	14%	N/A	146	23%	N/A	2,260	2.7	51
45–74	369	17%	15	138	28%	9	2,800	3.3	62
40–74	355	20%	28	130	32%	16	3,590	4.2	103
Scenario 2 (42% screening participation psr.)									
50–74[b]	337	24%	N/A	115	39%	N/A	3,990	4.7	53
45–74	319	28%	18	107	44%	8	4780	5.6	95
40–74	301	32%	35	96	50%	20	5,870	6.9	97

CRC – colorectal cancer; CSAE – colonoscopy-related serious adverse events; INNC – incremental number needed to colonoscope; N/A – not applicable.
[a] Numbers were rounded to three significant figures.
[b] Current NBCSP's target screening age range.

Table 3
Model-predicted undiscounted and discounted cost, life-years, and incremental cost-effectiveness ratio per person aged 20 years associated with all screening strategies in Aboriginal and Torres Strait Islander peoples.

Screening age range (years)	Undiscounted		Discounted		
	Cost	LYs	Cost	LYs	ICER ($/LYS)
Scenario 1 (23% screening participation psr.)					
No screening	$3,894	52.71	$1,060	35.114	N/A
50–74[a]	$3,798	52.75	$1,135	35.120	$11,927
45–74	$3,798	52.76	$1,183	35.122	$28,145
40–74	$3,845	52.77	$1,258	35.124	$30,384
Scenario 2 (42% screening participation psr.)					
No screening	$3,894	52.71	$1,060	35.114	N/A
50–74[a]	$3,670[b]	52.78	$1,174[b]	35.124	$10,802
45–74	$3,698[b]	52.79	$1,250[b]	35.127	$25,636
40–74	$3,785[b]	52.81	$1,374[b]	35.130	$38,396

ICER – incremental cost-effectiveness ratio; LY – life-year; LYS – life-years saved; N/A – not applicable
[a] Current NBCSP target screening age range.
[b] Costs associated with interventions required to increase screening participation are not included in the analysis.

reduction in lifetime CRC incident cases, CRC deaths and ICER. Detailed outcomes in the uncertainty analysis are provided in Appendix Section 5.

In the one-way sensitivity analysis, the predicted reduction in lifetime CRC deaths was found to be sensitive to the alternative assumptions assessed for: screening initiation rate for the subsequent screening invitation rounds, follow-up colonoscopy compliance, and rescreening probabilities (Fig. 2). The current NBCSP practice and biennial iFOBT screening at 45–74 years were found to remain cost-effective in all sensitivity analyses. Extending the screening start age to 40 years was found to be cost-effective in most of the sensitivity analyses, except when alternative screening initiation rates were assumed. Detailed ICER estimates for the screening strategies are provided in Appendix Section 6.

3.7. Supplementary normative analysis for model validation

Detailed supplementary normative analysis outcomes are provided in Appendix Section 7. The predicted lifetime CRC incidence reductions for biennial iFOBT screening at 50–74 and 45–74 years in this analysis were consistent with the CISNET models predictions [41]. The predicted lifetime CRC mortality reductions were found to be higher than the predictions of the three CISNET models. It is likely because *Policy1-Bowel,* which calibrated to data observed for Aboriginal and Torres Strait

Islander peoples (known to have a different CRC mortality risk profile than the general population), assumed a higher proportion of CRC diagnosed at advanced stage and lower CRC survival than the CISNET models, which modelled the US average-risk general population. Given the aforementioned differences in the cancer stage distribution and survival assumptions, *Policy1-Bowel* predicted a higher mortality benefits from screening due to more advanced cancers were prevented (via precancerous lesion detected and removed after having a positive screening result) or detected at an earlier stage.

4. Discussion

This is the first study to evaluate the NBCSP for Aboriginal and Torres Strait Islander peoples and provide detailed estimates of its health benefits and cost-effectiveness. The observed 23% NBCSP participation psr. was predicted to reduce lifetime CRC incidence and mortality rates by 14% and 23% respectively, was associated with a benefits-and-burden balance of 51 NNC per CRC death prevented and was cost-effective. Increasing NBCSP participation and/or extending the NBCSP to include people under 50 years could further improve CRC outcomes for Aboriginal and Torres Strait Islander peoples. Firstly, increasing participation to the 42% psr. Australia-wide average could save more lives and maintain a similar benefits-and-burden balance of 53 NNC per CRC death prevented. Secondly, extending the NBCSP to include Aboriginal and Torres Strait Islander peoples in their forties could prevent more CRC cases and deaths and potentially be cost-effective, but with a less favourable benefits-and-burden balance (62–103 NNC per CRC death prevented) than maintaining the 50–74 age range. This finding can be compared to previous findings in the general population that starting screening at 40 years would not be cost-effective, but that starting screening over 45 years could potentially be cost-effective [13]. There are two major drivers of differences in the findings for the different populations – firstly, the higher the rates of participation in the existing NBCSP (starting at age 50 years), the more incremental the benefits of starting earlier, and secondly, the higher the underlying burden of disease and reduced life expectancy, the greater the benefits of starting earlier. Both of these factors contribute to the cost-effectiveness and the benefits-to-harms balance being more favourable towards starting screening for Aboriginal and Torres Strait Islander peoples in their forties, compared to the general population.

4.1. Increasing NBCSP participation and compliance to follow-up colonoscopy

The NBCSP participation for Aboriginal and Torres Strait Islander peoples is 23% in 2016 [9] and we found that improving participation
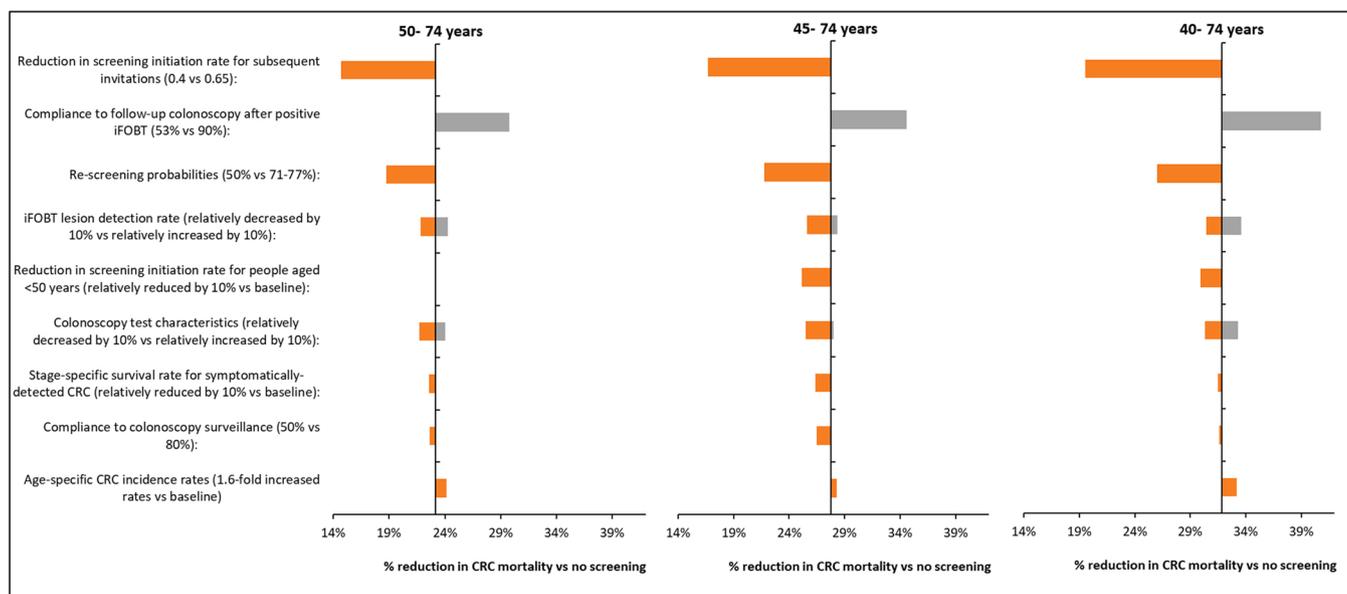
Fig. 2. Model estimated % reduction in lifetime number of CRC deaths per 10,000 persons alive at 40 years for all strategies at Scenario 1 (23% screening participation rate psr.) in one-way sensitivity analyses. The y-axes crossed the x-axes at 23%, 28%, and 32% for strategies assuming screening at 50–74, 45–74 and 40–74 years respectively, showing the % reduction in CRC mortality predicted for each strategy in the baseline analysis.

would reduce the CRC burden for Aboriginal and Torres Strait Islander peoples. Exploring the barriers and facilitators to CRC screening for Aboriginal and Torres Strait Islander peoples has been the subject of previous studies [44–49]. Key barriers identified included a lack of understanding and low awareness of CRC and the NBCSP, and mistrust of government and state services through negative personal and historical experiences [44–49]. Other barriers were associated with screening delivery methods used as part of the current NBCSP, which relies on the postal system to delivery NBCSP kits to individuals' home address as listed in Medicare records [44–49]. The address held by Medicare may not be up-to-date/accurate for populations who do not have a fixed address, living in remote areas, or homeless, which are situations that are more commonly experienced by Aboriginal and Torres Strait Islander peoples compared with non-Indigenous Australians.

In 2016, the Aboriginal and Torres Strait Islander peoples were reported to have lower rates in completing a follow-up diagnostic colonoscopy assessment after having a positive iFOBT result (53% vs 68%) and experienced longer waiting time between positive screen and assessment (76 vs 54 days) compared with nationwide average [25]. As shown in the previous study that improving diagnostic colonoscopy assessment rate in people with positive iFOBT results would improve the effectiveness of screening and reduce CRC mortality [18]. Identifying enablers and barriers of diagnostic colonoscopy access should be given a high priority when planning for CRC prevention for Aboriginal and Torres Strait Islander peoples.

The diagnostic colonoscopy assessment data in the national register is incomplete and should be improved. As the reporting of diagnostic colonoscopy assessment is not mandatory to the national register in Australia, the proportion of people who completed a follow-up diagnostic assessment after a positive iFOBT result is known to be under-reported [25,50]. Furthermore, of the reported colonoscopy assessments in 2016, about 27% were reported to have polyps detected and sent to histopathology analysis but results were not received by the register [25]. Given the model-predicted reduction in CRC mortality is sensitive to the diagnostic colonoscopy compliance rate assumed in the model (shown in the sensitivity analysis), this study is likely to have underestimated the effectiveness of NBCSP by assuming the under-reported 53% compliance rate [25] to diagnostic colonoscopy assessments for Aboriginal and Torres Strait Islander peoples. Improving

the completeness of the diagnostic colonoscopy assessment data will benefit the ongoing research and activities that focus on monitoring and improving the NBCSP performance.

4.2. Lowering screening start age

The national screening participation rate for people in their forties is not currently available as they are currently ineligible. For strategies that assumed screening starts from 40 or 45 years, people in their 40 s were assumed to have equivalent participation rates to those in their 50 s. Under this assumption, the study predicted that lowering the screening start age from 50 to 40 or 45 years could prevent up to 16–20 additional CRC deaths in the lifetime of 10,000 Aboriginal and Torres Strait Islander peoples and would be associated with ICER of $25,636/LYS- $38,396/LYS. However, the observed data (for people aged 50–74 years) show that NBCSP participation rates increase by age [9]. As shown in the sensitivity analysis, if the screening initiation rate was decreased by 10% for people aged under 50 years, lowering screening start age from 50 to 40 or 45 years would remain cost-effective (ICER: $32,440/LYS-$36,967/LYS) but the predicted lifetime CRC mortality reduction would decrease to 30% and 25% (vs no screening), respectively, from the baseline estimates (32% and 28% respectively). For the benefit of lowering the screening start age to be realised, it is important to engage Aboriginal and Torres Strait Islander peoples in a consultation process to assess its acceptability and have culturally appropriate communication to promote NBCSP participation for people in the targeted age range and awareness of CRC.

Published studies have shown that CRC incidence rates have been increasing in people aged under 50 years in Australia from mid-2000s [51,52]. The increases in CRC incidences are partially due to changes in exposure to lifestyle risk-factors, such as obesity, red and processed meat, and alcohol consumptions etc. [51]. No study to date has analysed the CRC incidence trends for Aboriginal and Torres Straits Islander peoples. If CRC incidence rates has been increasing in Aboriginal and Torres Straits Islander peoples aged under 50 years, lowering screening start age would result a higher health benefit and be more cost-effective than this study's estimates.

4.3. Comparisons with previous study findings

Although this is the first study to focus on Aboriginal and Torres Strait Islander peoples, previous studies have assessed the health and economic outcomes of the NBSCP for the general population [13,14]. These outcomes for the two populations differ given differences in the life-expectancy and burden of CRC. This is illustrated in the cost-effectiveness (ICER: $11,927/LYS vs <$3000/LYS) and benefits-and-burden balance (51 NNC vs 35 NNC per CRC death prevented) of the NBCSP (vs no screening) for Aboriginal and Torres Strait Islander peoples and the general population, respectively.

Previous studies have also provided benefits-and-burden balance estimates for other national cancer screening programmes (e.g. the National Cervical Screening Program in Australia with 95–145 number-needed-to-colposcope per cervical cancer death prevented, and the national breast cancer screening programme in Australia with 62 number-needed-to-undergo-diagnostic assessment per breast cancer death prevented [53]). The benefits-and-burden balance estimates between screening programmes for different cancer types should not be compared directly due to the significant differences between target populations of each programme and the differences in diagnostic tests which utilise different technologies with differing potential burden, harms, and invasiveness.

There was one other study that evaluated the cost-effectiveness of CRC screening for an Indigenous population, in this case for the Māori population of New Zealand [54]. Aboriginal and Torres Strait Islander peoples and Māori people have a similar pattern of lower CRC incidence, worse CRC survival, and lower CRC screening participation rate than /their non-Indigenous counterparts [55,56]. In our study, CRC screening was predicted to be cost-effective for Aboriginal and Torres Strait Islander peoples but associated with a higher ICER compared with non-Indigenous Australians. This is consistent with the findings of the study that estimated the cost-effectiveness of CRC screening for Māori and non-Māori peoples in New Zealand [54].

4.4. Strengths and limitations

A strength of this study is that it is the first to use a comprehensive and calibrated microsimulation model to evaluate the health benefits, costs and burden of CRC screening for Aboriginal and Torres Strait Islander peoples. Existing economic evaluations of CRC screening are primarily focused on the average-risk population [15,28,38]; more research focused on Aboriginal and Torres Strait Islander peoples is needed to reduce the significant health disparities. Another strength of this study is that we used a comprehensive calibrated and validated microsimulation model, *Policy1-Bowel*, which incorporated the latest evidence of CRC natural history (including the adenoma-carcinoma and serrated pathway in CRC development) and real-world data on screening participation and outcomes to estimate the impact of CRC screening for Aboriginal and Torres Strait Islander peoples.

A limitation for this study is the scarcity of data available for Aboriginal and Torres Strait Islander peoples to inform model assumptions and calibration. Additionally, where data are available for Aboriginal and Torres Strait Islander peoples, the sample size of the study is often small and/or contains insufficient completeness of Indigenous status, and/or the data used in analyses are dated. Furthermore, as the corrected national CRC mortality rate estimate for Aboriginal and Torres Strait Islander peoples has not been published, the model could not compare the CRC mortality predictions with the observed CRC mortality rates for Aboriginal and Torres Strait Islander peoples [8,42]. These limitations increase uncertainty and could lead to a potential underestimate or overestimate of outcomes for Aboriginal and Torres Strait Islander peoples. Despite these limitations, the model incorporated the best available data identified for Aboriginal and Torres Strait Islander peoples, and assumptions were based on findings in the general population and expert advice when data were not available.

Furthermore, we assessed a comprehensive list of parameters with alternative assumptions in the sensitivity analyses to assess the potential impact of uncertainties. The model-predicted reduction in lifetime CRC deaths for the screening strategies were found to be most sensitive to alternative assumptions for the screening participation rate and compliance to follow-up colonoscopy after positive iFOBT. This highlights the importance of the National Cancer Screening Registry in collecting and reporting detailed and reliable screening participation data for Aboriginal and Torres Strait Islander peoples to capture more accurate estimates of NBCSP effectiveness for this target population. The cost-effectiveness of lowering the screening start age from 50 to 40 or 45 was found to be robust under a range of parameter values assessed in the sensitivity analyses.

Another limitation of the study is that the quality-adjusted-life-years (QALY) was not considered in the cost-effectiveness analysis as setting-specific bowel cancer screening, diagnosis and cancer treatment related quality-of-life data for the Aboriginal and Torres Strait Islander peoples are not available. Therefore, this study could potentially underestimate the cost-effectiveness of the NBCSP by not taking into account the improvement in the quality of life associated with disability prevented by preventing CRC. *Policy1-Bowel* has been adapted and calibrated for Aboriginal and Torres Strait Islander peoples. The model will be refined continually as more detailed data become available and be used to estimate long-term health outcomes, resource utilisation and cost-effectiveness of a range of crucial policy questions for NBCSP screening for Aboriginal and Torres Strait Islander peoples. These estimates can be used to aid ongoing discussions, research, and planning for interventions to improve health outcomes and equity for Aboriginal and Torres Strait Islander peoples via CRC screening.

The NBCSP is now fully implemented in Australia and provides free biennial iFOBT screening for people aged 50–74 years in Australia. Evidence has shown that the NBCSP is effective in preventing CRC deaths [57]. However, Aboriginal and Torres Strait Islander peoples participate at a low rate which contributes to health inequities. This study estimated that increasing NBCSP participation rates and/or extending the target CRC screening age range for Aboriginal and Torres Strait Islander peoples could improve health outcomes and equity. The findings highlight a need to increase NBCSP participation and explore the feasibility and acceptability of lowering the NBCSP start age for Aboriginal and Torres Strait Islander peoples. Any interventions to promote awareness and NBCSP participation will need to be co-designed, community-led, culturally appropriate and consider the identified barriers to screening for Aboriginal and Torres Strait Islander peoples.

Authors' contributions

J-BL led the development of the *Policy1-Bowel* model, natural history calibration, and was responsible for the collation and integration of cost and epidemiological data into the model, performed model analysis, and drafted the manuscript. EF, JW, and KCfl participated in model development and drafted the manuscript. JW conducted the sensitivity analyses. All authors participated in the model natural history calibration and sourcing of data and assumptions. KD conceived the study; EF, KD, and KC oversaw the project and all aspects of the analysis. All authors reviewed the study's findings and read and approved the final manuscript.

Ethical approval

This model-based study did not involve human participants, so ethics approval was not required.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jcpo.2022.100325.

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