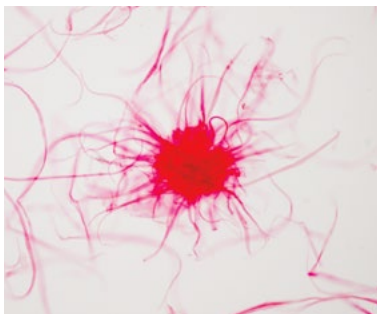

'Why don't I need a colonoscopy?'

A novel approach to communicating risks and benefits of colorectal cancer screening

CPD

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Background and objectives
There is significant growth in demand for colonoscopies, with over 700,000 performed in Australia in 2012–13. For every one million Australians aged 50 years and older, 80,000 people at average risk of colorectal cancer are being over-screened with colonoscopy, and 29,000 people at increased risk are not having the colonoscopy they need.

Methods
Using monitoring data from the Australian National Bowel Cancer Screening Program and published data on colonoscopic screening, we have developed expected frequency trees (EFTs) to demonstrate projected outcomes of different colorectal cancer screening options for participants at different levels of colorectal cancer risk in Australia.

Results
The EFTs highlight the overall balance in favour of faecal occult blood screening for those at average risk in terms of fewer deaths and complications.

Discussion
This novel method of risk communication can be used to promote appropriate patient choice of colorectal cancer screening modality and potentially reduce the number of referrals for colonoscopy in patients who are not at increased risk of colorectal cancer.

AUSTRALIA AND NEW ZEALAND together have the highest incidence of colorectal cancer worldwide. Colorectal cancer is the second most common non-cutaneous malignancy in Australia (16,682 projected cases in 2017) and second only to lung cancer in terms of cancer mortality (4114 projected deaths in 2017).[1] Currently, over 40% of colorectal cancers are diagnosed at Stage 3 or Stage 4 in Australia. Screening is an effective method to reduce the burden of colorectal cancer. Randomised controlled trials (RCTs) of faecal occult blood testing (FOBT) using the older guaiac-based test have shown a 15–33% reduction in colorectal cancer mortality.[2] Biennial FOBT using the more sensitive immunochemical test (iFOBT) from age 50 years is cost effective, estimated at a range from $25,000 to $41,667 per year of life saved.[3] On the basis of this evidence, many countries, including Australia, are implementing nationally organised screening programs, predominantly using iFOBT.[4]

There is considerable international debate about the use of other methods of screening for colorectal cancer. Four RCTs have shown that a single flexible sigmoidoscopy can reduce colorectal cancer mortality by 22–31%;[5] in some countries, including England and Italy, flexible sigmoidoscopy is being implemented into national programs as an addition to FOBT screening.[4] No RCTs have evaluated the effect of colonoscopy on colorectal cancer mortality, although trials are in progress in Europe and the US. Despite this absence of RCT evidence, the US Preventive Services Taskforce recommendations support the use of any of the following as the primary screening test: FOBT, FOBT plus flexible sigmoidoscopy or colonoscopy; it is acknowledged that the risks and benefits of each test vary.[6]

People are not at an equal risk of colorectal cancer. Lifetime risk of colorectal cancer is not normally distributed; a large proportion of the population is below the average 5% risk and a smaller proportion is at higher levels of risk.[7] National Health and Medical Research Council (NHMRC)-endorsed guidelines, which were published in 2017, recommend biennial iFOBT screening for people at or slightly above the average risk of colorectal cancer, from age 50 to 70 years, and limiting colonoscopy only to those who are at increased risk of colorectal cancer.[8] Table 1 presents a summary of the family history criteria that define individuals as having an average, moderately increased or potentially high risk of colorectal cancer. Colonoscopy is only recommended as a screening test for individuals who have an increased risk of colorectal cancer. This risk-stratified approach to screening is increasingly recognised as a means to optimise the benefit–harm ratio, especially given the cost-effectiveness of cancer screening programs using FOBT and the known risks of colonoscopy (perforation, haemorrhage and, rarely, death).[3]

There is significant growth in demand for colonoscopies, with over 700,000 performed in Australia in 2012–13, of which approximately 80% are at least partly funded through the Medicare

Benefits Schedule (MBS) and 20% through state-funded public hospitals.[9] MBS-funded colonoscopies increased by 28% in the five years to 2014–15.[10] A recent Australian Commission on Safety and Quality in Health Care report showed a 30-fold variation in colonoscopy rates by local area, with a strong socioeconomic gradient. This could be interpreted either as demonstrating that more deprived populations are not receiving colonoscopy when needed, or that those who are better off are more likely to receive colonoscopy inappropriately.[9] The MBS Review Taskforce Gastrointestinal Clinical Committee released its report in August 2016, again highlighting the wide variation in colonoscopy rates in Australia.[10] The Committee expressed concern that 'asymptomatic low-risk patients are undergoing low-value colonoscopy services for bowel cancer screening' and that 'low-value testing may be compromising access to services for patients who require clinically necessary colonoscopy services'.[10]

Research within our NHMRC Centre of Research Excellence on colorectal cancer screening has demonstrated that many individuals at increased risk of colorectal cancer are not having regular colonoscopies (ie under-screening), while many at 'average' risk are being over-screened with colonoscopy rather than using FOBT.[11,12] Our previously published research estimated that for every one million Australians aged 50 years and older, 80,000 people at average risk are being over-screened with colonoscopy, and 29,000 people at increased risk are not having the colonoscopy they need.[11,12] Therefore, challenges exist in identifying people at increased risk of colorectal cancer in primary care, as well as reducing referrals for colonoscopy in average-risk individuals.

Internationally, there is growing recognition of the problem of low-value healthcare, defined as services for which the degree of benefit does not justify the harms and costs.[13] The Australian 'Choosing Wisely' initiative recently added use of colonoscopy as a screening test in patients at average risk of colorectal cancer to its list of low-value tests.[14]

Our previous research has identified that there is mistrust among clinicians about the effectiveness of FOBT screening, and limited awareness of the harm-to-benefit ratio of using colonoscopy for screening in average-risk populations.[15] Some general practitioners (GPs) may be confused about the selection of suitable tests for colorectal cancer screening because of misunderstanding of the existing evidence and the push for colonoscopic screening from patients, specialists and private endoscopy clinics.[15]

Decision aids have the potential to alter people's screening choices, but a recent trial of simple risk-communication methods to reduce use of low-value screening tests had no effect on patients' decision making.[16] It may be that more sophisticated approaches to presenting complex information about screening outcomes are necessary to influence the attitudes and behaviours of patients and clinicians. One possible method could be the use of expected frequency trees (EFTs). These are graphical summaries that aim to simplify multiple conditional probabilities and present the likelihood of specific outcomes, including potential complications from screening.[17] While there have been many studies testing other risk-communication formats, such as line graphs and icon arrays (ie groups of human icons coloured to show different outcomes), many do not include potential harms as well as benefits of screening. Increasingly, there is evidence in the healthcare and screening literature supporting the use of EFTs to improve risk communication.[17,18]

Table 1. NHMRC-endorsed criteria for quantifying risk of colorectal cancer based on family history[8]*

Near average risk (98% of Australian population)
• No first-degree or second-degree relative with colorectal cancer
• One first-degree relative with colorectal cancer diagnosed at age 55 years or older
• One first-degree and one second-degree relative with colorectal cancer diagnosed at age 55 years or older
Moderately increased risk (relative risk 3–6) (1–2% of the Australian population)
• One first-degree relative with colorectal cancer diagnosed under 55 years
• Two first-degree relatives with colorectal cancer diagnosed at 55 years or older
• One first-degree and at least two second-degree relatives with colorectal cancer diagnosed at 55 years or older
Potentially high risk (relative risk 7–10) (<1% of the Australian population)
• At least three first-degree or second-degree relatives with colorectal cancer with at least one diagnosed under 55 years
• At least three first-degree relatives with colorectal cancer diagnosed at 55 years or older

**Examples of family history and risk criteria. Full criteria is available at https://wiki.cancer.org.au/australia/Clinical_question:Family_history_and_CRC_risk*
NHMRC, National Health and Medical Research Council

Method

Development of expected frequency trees

We developed EFTs to demonstrate projected outcomes for Australians at average and moderate risk of different colorectal cancer screening options: a colonoscopy, FOBT or no screening at all. We used a relative risk of six for moderate risk, consistent with the upper limit in current NHMRC guidelines.[19] We used the following data to estimate the predicted outcomes.

- The 2014 Australian Institute of Health and Welfare report on outcomes in the National Bowel Cancer Screening Program (NBCSP).[20] This report provides data on sensitivity, specificity, positive predictive values (PPVs) and negative predictive values (NPVs) to detect colorectal cancer. This report also includes mortality outcomes based on an average follow-up of

19 months, with comparative data on groups who were not invited into the screening program. We chose these data as they reflect outcomes in the 'real world' Australian context rather than estimates from RCTs and are potentially more comparable with observational data on colonoscopic screening. We applied the following values for outcomes relating to iFOBT screening: positivity rate 7.3%; sensitivity for colorectal cancer 83%; PPV for colorectal cancer 3.6%; NPV for colorectal cancer 99.9%.[20] The mortality rate for people diagnosed with colorectal cancer who had not been invited to the NBCSP was 19.6%. For screen-detected and interval cancers it was 4.6% and 14.6% respectively.[20] Of note, interval cancers (14.6%) had a lower mortality rate than cancers in the unscreened population (19.6%; Appendices 1–4). Although the NBCSP has recently published its latest monitoring report, this did not include updated analyses of comparative mortality outcomes. We therefore used the values for positivity rates, sensitivity, specificity, PPV and NPV from the 2014 report on outcomes of participants in the NBCSP.

- On the basis of recent evidence from reviews of observational data on outcomes of colonoscopy, we applied a sensitivity of 95% to detect colorectal cancer.[4,5] We assumed the same degree of benefit, in terms of reduction in mortality over the same time period, as those who were diagnosed through a positive iFOBT in the NBCSP (ie 4.6% for screen-detected and 14.6% for interval cancers).
- We meta-analysed the results from two large administrative datasets on complication rates of outpatient colonoscopy in Australia and Canada to create summary estimates of risk of perforation, haemorrhage and death.[21,22] We selected these two studies because they represented populations closer to a screening population, and by using administrative datasets they reduced potential ascertainment bias. A study by Viiala et al is the largest Australian study of colonoscopy complication rates.[22] Although conducted in a teaching hospital, the authors found no differences in complication rates between trainees and consultant endoscopists. The reported rates of complications are therefore unlikely to be elevated by any training effect. We believe these summary estimates are likely to represent the complication rates in an Australian screening population. The summary rates we applied to generate our EFTs were:
  - perforation 0.68 per 1000
  - bleeding requiring intervention 1.4 per 1000
  - death 0.08 per 1000.

Results

Figures 1 and 2 present the EFTs for populations at average and moderately increased risk (relative risk of colorectal cancer = 6). In terms of fewer deaths and complications, they highlight the overall balance in favour of iFOBT screening for those at average risk. For those at moderate risk, in terms of overall deaths, the balance is in favour of colonoscopic screening, albeit with more perforations and haemorrhages in this group. We chose not to include flexible sigmoidoscopy in these EFTs, given that the new Australian draft guidelines do not recommend its use, either instead of or as an additional screening test. Currently, we have chosen not to demonstrate the comparative financial costs in these figures because of the added complexity of including this information and uncertainty about which financial perspective to include. Costs could be incorporated from the perspective of the individual (eg out-of-pocket costs, costs of taking time off work for colonoscopy) or the overall healthcare system. Applying the same cost assumptions as those used in a cost-effectiveness study of the Australian bowel cancer screening program ($29 per iFOBT; $1300 per colonoscopy),[3] the costs alone of performing the screening and diagnostic tests would be approximately $12.5 million and $130 million per 100,000 participants for iFOBT and colonoscopic screening respectively.

Discussion

We recognise that the data we present do not account for the additional benefit of reduced incidence of colorectal cancer resulting from colonoscopic screening and adenoma excision. Equally, in the absence of trial data on colonoscopic screening, one cannot estimate the extent of 'overdiagnosis' and 'over-treatment' of adenomas detected through colonoscopic screening. We therefore chose to focus solely on outcomes relating to screening for colorectal cancer. We also recognise the limitation of using mortality outcomes from the NBCSP with a relatively short mean duration of follow-up and the statistical uncertainty around these estimates. The figures will therefore need to be revised when longer term mortality outcome data from the NBCSP are reported.

In a vignette-based study we have recently completed with over 200 patients in general practice, our EFT was more effective than icon arrays, graphical or numerical methods in promoting appropriate choice of iFOBT as a screening method for people at average risk.[23] We believe these EFTs may challenge clinician and patient attitudes about the relative harms and benefits of two different screening modalities for colorectal cancer. The large variations in colonoscopy rates in Australia suggest that many people at average risk of colorectal cancer are choosing to have colonoscopy as a screening test, mostly through GP referrals to private endoscopists and funded, at least in part, through MBS payments. But how well informed are these patients about the choices they have regarding screening for colorectal cancer? Screening decisions often reflect the outcome of discussions between a patient and a GP.

This paper presents the underlying data and assumptions made to create these EFTs. Our overall rationale is to support discussions in primary care about colorectal cancer screening, to help customise screening advice on the basis of individual risk and potentially reduce referrals for low-value colonoscopic screening in people at average risk of colorectal cancer. The EFTs may also prompt better identification of individuals

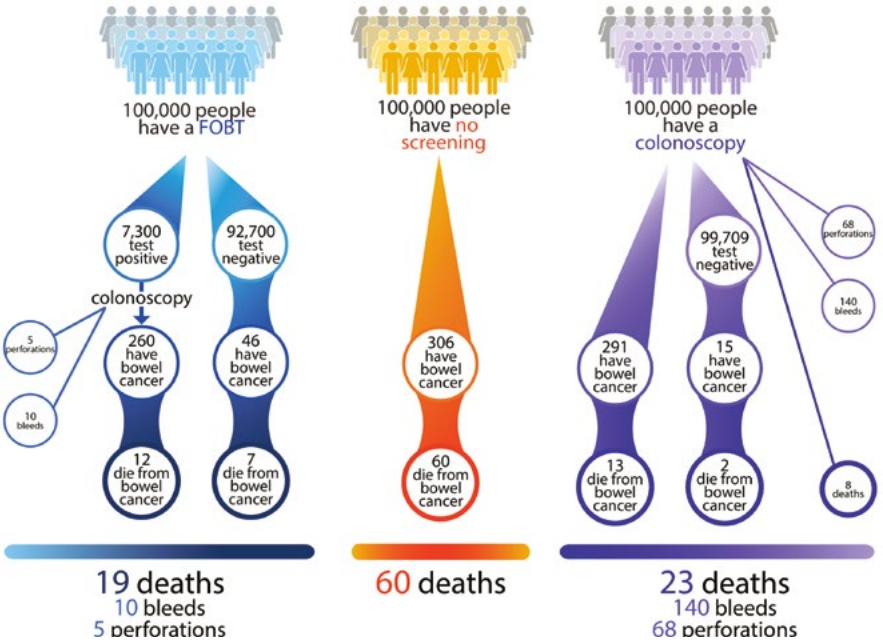

Figure 1. Expected frequency tree for population at average risk of colorectal cancer

Mortality outcomes based on data from the Australian Institute of Health and Welfare analysis of bowel cancer outcomes for the National Bowel Cancer Screening Program (2014) with an average follow-up of 19 months. Reproduced with permission from The Royal Australian College of General Practitioners, from Kim GY, Walker J, Bickerstaffe A, et al. The CRISP-Q study: Communicating the risks and benefits of colorectal cancer screening. Aust J Gen Pract 2018;47(3):139–44.

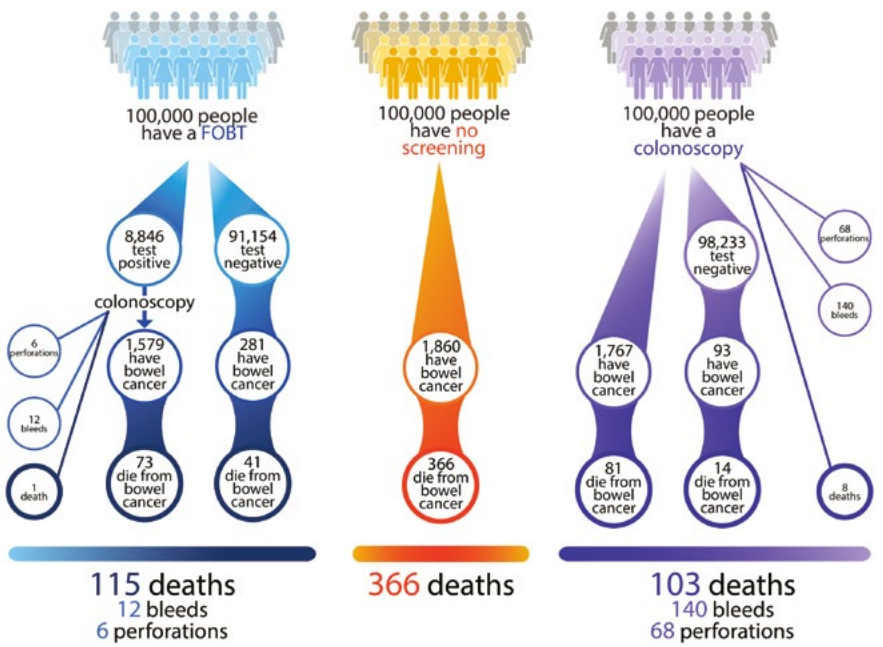

Figure 2. Expected frequency tree for population at moderately increased risk of colorectal cancer

Mortality outcomes based on data from the Australian Institute of Health and Welfare analysis of bowel cancer outcomes for the National Bowel Cancer Screening Program (2014) with an average follow-up of 19 months.

at increased risk of colorectal cancer in primary care who are more likely to benefit from colonoscopic screening. While the EFTs may not be the solution to long waiting times in the public hospital system for colonoscopy, they could help to reduce the growing demand for unnecessary MBS-funded colonoscopies.

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Appendix 1. Performance of faecal occult blood test from the Australian Institute of Health and Welfare (AIHW) analysis of bowel cancer outcomes for the National Bowel Cancer Screening Program 2014[19]

	Actual cancer outcome		
Screening result	**Cancer diagnosed**	**Cancer not diagnosed**	**Total**
Positive faecal occult blood testing (FOBT)	887 Positive predictive value 3.6%	23,899	24,786
Negative FOBT	176 0.06% false negatives	297,378 Negative predictive value 99.9%	279,554
Total	**1,063** **83.4% sensitivity**	**321,277** **92.6% specificity**	**322,340**

Appendix 2a. Estimated risks and meta-analysis for risk of bleeding from colonoscopy

	n	Bleeding risk	95% confidence intervals	% Weight
Viiala et al[22]	23,508	0.208	0.150–0.267	13.1
Rabeneck et al, Alberta[21]	11,054	0.109	0.047–0.170	11.8
Rabeneck et al, British Columbia[21]	13,999	0.079	0.032–0.125	20.7
Rabeneck et al, Nova Scotia[21]	4,406	0.295	0.135–0.455	1.8
Rabeneck et al, Ontario[21]	67,632	0.149	0.120–0.178	52.6
Pooled weighted	**120,599**	**0.140**	**0.119–0.161**	**100.0**

Appendix 2b. Estimated risks and meta-analysis for risk of perforation from colonoscopy

	n	Perforation risk	95% confidence intervals	% Weight
Viiala[22]	23,508	0.098	0.058–0.138	15.3
Rabeneck et al, Alberta[21]	11,054	0.072	0.022–0.123	9.7
Rabeneck et al, Nova Scotia[21]	4,406	0.136	0.027–0.245	2.1
Rabeneck et al, Ontario[21]	67,632	0.059	0.041–0.770	72.9
Pooled weighted	**106,600**	**0.068**	**0.052–0.084**	**100.0**

Appendix 2c. Estimated risks and meta-analysis for risk of death from colonoscopy

	n	Death risk	95% confidence intervals	% Weight
Viiala[22]	30,463	0.010	–0.001–0.021	25.3
Rabeneck et al[21]	67,632	0.007	0.001–0.014	74.7
Pooled weighted	**98,095**	**0.008**	**0.002–0.014**	**100.0**

Appendix 3. Cumulative bowel cancer deaths by screening sub-group from the Australian Institute of Health and Welfare analysis of bowel cancer outcomes for the National Bowel Cancer Screening Program 2014[20]

			Bowel cancer deaths			
			Years since diagnosis			At 23.12.2011
Screening sub-group		2006–08 diagnoses	1	2	3	
Screen-detected	n	1,352	11	34	57	62
	Proportion (%)		0.8	2.5	4.2	4.6
Interval	n	130	7	15	18	19
	Proportion (%)		5.4	11.5	13.8	14.6
Never-invited	n	10,080	766	1,350	1715	1,973
	Proportion (%)		7.6	13.4	17.0	19.6

Appendix 4. Parameters for performance and mortality outcomes for colonoscopy screening

Sensitivity	Mortality outcome (%)*	
	Screen-detected	Interval
95%[4,5]	4.6	14.6

**Based on same duration of follow-up as for the Australian Institute of Health and Welfare analysis of bowel cancer outcomes for the National Bowel Cancer Screening Program 2014[20]*

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