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Abstract

Background

A risk-stratified approach to colorectal cancer (CRC) screening could result in a more acceptable balance of benefits and harms and be more cost-effective.

Aim

To determine the effect of a consultation in general practice using a computerised risk assessment and decision support tool (CRISP) on risk-appropriate CRC screening.

Design and setting

RCT in 10 general practices in Melbourne, Australia.

Methods

Intervention consultations included CRC risk assessment using the CRISP tool, and discussion of CRC screening recommendations. Control group consultations focused on lifestyle CRC risk factors. Participants were recruited from a *c*onsecutive sample of patients aged 50-74 attending their general practitioner. Primary outcome: Risk-appropriate CRC screening at 12-months.

Results

734 participants (65.1% of eligible patients) were randomised (369 intervention, 365 control); the primary outcome was determined for 722 (362 intervention, 360 control). There was a 6.5% absolute increase (95% CI: -0.28 to 13.2%) in risk-appropriate screening in the intervention compared to control group [71.6% vs 65%; OR: 1.36 (95% CI: 0.99 to 1.86) p = 0.057]. In those due CRC screening during follow-up, there was a 20.3% (95% CI:10.3 to 30.4%) increase [intervention 59.8% vs control 38.9%; OR: 2.31 (95% CI 1.51 to 3.53) p < 0.001] principally by increasing faecal occult blood testing in those at average risk.

Conclusions

A risk assessment and decision support tool increases risk-appropriate CRC screening in those due screening. The CRISP intervention could commence in people in their fifth decade to ensure people start CRC screening at the optimal age with the most cost-effective test.

Trial registration

Australian and New Zealand Clinical Trial Registry ACTRN12616001573448p.

Keywords

General practice; colorectal neoplasms; early detection of cancer; clinical decision support.

How this fits in

Using risk models that account for family history, lifestyle and medical history could tailor CRC screening and determine starting age and screening test. This could be more cost-effective than population screening.

In this RCT, we showed that using the CRISP risk tool in general practice can increase risk-appropriate CRC screening in those due screening. Its effect is more uncertain in patients who are up-to-date with screening.

The CRISP intervention could be used in people in their fifth decade to ensure people start CRC screening at the optimal age with the most cost-effective screening test.

Background

Australia has one of the highest incidence rates of colorectal cancer (CRC) worldwide. (1, 2) A range of screening tests can reduce CRC mortality including faecal occult blood testing (FOBT), (3, 4) and flexible sigmoidoscopy.(5) A recently reported trial of colonoscopy demonstrated reduced risk of CRC but an uncertain effect on CRC mortality. (6) An Australian microsimulation model found that biennial immunochemical FOBT (iFOBT) was the most cost-effective approach relative to other tests.(7)

Risk-stratified approaches to CRC screening have been proposed where those at higher CRC risk have more invasive tests, and commence screening at a younger age.(8, 9) The Australian National Health and Medical Research Council (NHMRC) recommends biennial iFOBT screening from 50-74 years for those at average risk of CRC.(10) For those at moderately increased risk, iFOBT-based screening is recommended from age 40 and colonoscopy screening from age 50; for individuals at higher familial risk, iFOBT-based screening commences from age 35 and then colonoscopy from age 45.(11)

There are discrepancies between Australian recommendations and actual screening behaviours. Approximately 18% of people at average risk are being screened by colonoscopy, while 62% at moderate risk and 56% at high risk of CRC are receiving no screening at all.(12) Within the Australian National Bowel Cancer Screening Program (NBCSP) participation rates are only 43.5%.(13)

Internationally there are guidelines which apply family history criteria for risk-stratified CRC screening, with colonoscopy for those at increased risk, (14) but family history alone is a poor discriminator of CRC risk. (15) Risk-prediction models exist which incorporate multiple risk factors and have better discrimination.(16) To translate these models into practice requires risk assessment tools to tailor CRC screening, (17) but whether such tools offer a cost-effective approach to implement risk-stratified screening is uncertain.(18)

The CRISP Trial aimed to test the effect of a health consultation in Australian general practice using a risk assessment and decision support tool (The CRISP Tool (Colorectal cancer RISk Prediction)) on risk-appropriate CRC screening.

Methods

The trial protocol has been published. (19) Ethics approval was granted by the University of Melbourne Human Research Ethics Committee (ID 1647804).

Trial design

A stratified RCT in 10 general practices in Melbourne, Australia with patient randomisation.

Participants

Eligible participants were aged 50-74 years, able to comprehend written English and give informed consent. Exclusion criteria were: previous diagnosis of CRC or inflammatory bowel disease; current rectal bleeding; known genetic predisposition to CRC.

Patients aged 50-74 attending a general practitioner (GP) were recruited consecutively from the waiting room and taken into a private room to confirm eligibility and obtain informed consent. An online baseline questionnaire was completed before randomisation.

Intervention

The intervention occurred before the participant's consultation with their GP and involved a standardised consultation delivered by a research assistant in which the participant's risk of CRC was assessed using the CRISP tool; risk-appropriate CRC screening recommendations were discussed and a report provided to the participant and their GP. This was designed to model the role of a practice nurse, the most likely method of implementation of the CRISP tool in general practice, based on our previous developmental studies.(20)

The CRISP tool is a web-based application that calculates an individual's five-year and lifetime risk of developing CRC, (http://crisp.org.au/crisp-clinic) and recommends CRC screening (see Supplementary text).

Participants were encouraged to discuss the CRISP report with their GP. Those due an iFOBT test were shown how to complete the test, and their GP who was expected to order an iFOBT. Participants due iFOBT screening received an SMS reminder at one month to complete the test. If the participant reported a history of polyps, the GP received a summary sheet about NHMRC polyp surveillance guidelines, asking them to arrange colonoscopic surveillance. These components were part of a complex intervention to improve risk-appropriate CRC screening.(21)

Control

Those randomised to the control were directed to an online presentation of the Cancer Council Victoria *Cut your Cancer Risk* brochure. The research assistant discussed the information using a standardised script; the focus was on modifiable lifestyle factors to reduce cancer risk. Participants received a copy of the brochure and continued with usual care.

Outcomes and measures

The *primary outcome* was the proportion of participants who had completed risk-appropriate CRC screening at 12-months follow-up. In the intervention group, risk category was defined using the CRISP-calculated five-year CRC risk; for the control group, it was determined by their family history in accordance with the NHMRC-endorsed guidelines that were current at the time of recruitment (see Supplementary text).(10, 22) Appropriateness of screening for both groups was determined by an assessment of previous screening and concordance with the recommended mode and frequency of screening for each risk group (see Supplementary text).

CRC screening was obtained from multiple sources: self-report; GP record audit; Medicare Benefits Schedule (MBS); the NBCSP; and the Victorian Admitted Episodes Dataset (VAED). We used self-reported data only where objective data from these clinical and administrative sources were unavailable.

A Clinical Sub-Committee reviewed blinded screening data for cases where there were discrepancies between data sources or to review participants with complex polyp histories (see Supplementary text).

Additional measures included:

1. Demographics and clinical variables at baseline.
2. Secondary outcomes:
    a. Risk perception, absolute and comparative risk. (23, 24)

b. State-Trait Anxiety Inventory (STAI) scale.(25)

c. Cancer-specific anxiety.(26, 27)

d. Intentions to have CRC screening.

e. Clinical outcomes of screening tests (to be reported with five-year follow-up).

f. Healthcare service utilisation and healthcare costs related to CRC screening at 12 months obtained from GP records, MBS, VAED and NBCSP data. (see Supplementary text).

Participant-completed measures (a-d) were collected at baseline, one, six- and 12-months post-randomisation.

Sample size

Our original sample size was 278 per group, based on historic estimates of risk-appropriate screening of less than 5%. (28) The Trial Steering Committee met in February 2018 and reviewed blinded self-reported CRC screening in 397 participants, suggesting that risk-appropriate screening at baseline was as much as 25%. The Committee recommended an increase in the sample size to 366 per group. Allowing for 10% attrition over 12 months, this gave at least 80% power with a two-sided 5% level of significance to detect a minimum 10% difference in the proportion who were risk-appropriately screened, assuming 25% of control participants received risk-appropriate screening at 12 months.

Randomisation and masking

Participants were automatically randomised after the baseline questionnaire. The random allocation sequence, stratified by general practice, was computer-generated by the trial statistician (PC) with a 1:1 allocation ratio using random permuted block sizes of four, six and eight within each stratum. This randomisation sequence was incorporated into the online platform used to collect baseline data and redirect the browser to the CRISP tool or the control presentation. Participants were told the trial was about bowel cancer prevention and therefore blinded to allocation.

Blinding

For telephone follow-up of non-responders, and extraction and analysis of health service utilisation data, research staff were blinded to group assignment. All statistical analyses were performed blinded to group assignment.

Statistical methods

All randomised participants who did not withdraw their data were included in the primary analysis. Those who died before the 12 months' follow-up were excluded for the primary outcome, but we included their survey responses for secondary outcomes. For the primary outcome, we used logistic regression to estimate the odds ratio. We used a generalised linear model with the identity link function and binomial family to estimate the absolute difference in the proportion of risk-appropriate screening between groups. All regression models included the randomisation stratification factor of general practice as a fixed effect. The absolute (between-group difference in the proportions) and relative (odds ratio) estimated effect sizes were presented with their respective 95% confidence interval (CI), and the p-value estimated using logistic regression.

Comparisons between groups on continuous secondary outcomes used a linear mixed-effects model that included trial group, general practice and time (baseline, one, six and 12 months) as fixed effects and individuals as random effects, with two-way interactions between group and time,

except for baseline where study group means were constrained to be equal. Comparisons between groups on binary secondary endpoints with repeated outcome measures were performed using logistic regression, using generalised estimating equations with robust standard errors, with general practice as the covariate.

Based on review of the blinded data, the Trial Steering Committee agreed to conduct an explanatory analysis using a statistical test for interaction to examine if the intervention effect was modified by whether participants were due CRC screening during follow-up.(29) To assess for potential contamination, we examined the number of iFOBTs ordered by GPs at two and four weeks after recruitment. Planned sensitivity analyses are described in the Supplementary methods. Analyses were conducted in Stata 15.

Costs for delivering the intervention and associated with screening utilisation were expressed as the mean expenditure and associated 95% CI for iFOBT and colonoscopy over the period of the trial for each group, including over-screening. We calculated the cost per appropriately screened individual for the CRISP intervention compared to usual care based on the primary outcome measure and for those due screening at baseline.

Results

Between 9th May 2017 and 4th May 2018, we approached 1,610 patients of whom 1,128 were eligible. Seven hundred and thirty-four (65.1%) consented and were randomised (Figure 1). Of these, six (1.6%) in the intervention and 4 (1.1%) in the control group withdrew all data post-randomisation. One participant in each group died during the 12 months' follow-up. All participants received the allocated interventions as intended. Age and gender were similar between those recruited and who declined to participate (Supplementary Table 2). Participant characteristics were balanced between groups (Table 1). The distribution of socio-economic advantage of the trial cohort was comparable to the population of Melbourne. The majority of participants (95%) were in an

average CRC risk category based on the CRISP risk prediction model or NHMRC criteria.(10, 22) (Table 1).

Objective CRC screening information was ascertained for 98.4% (722/725) participants; three control participants had self-reported data only. Of these 722 participants 71.6% (259/362) had risk-appropriate screening in the intervention group compared to 65.0% (234/360) in the control group, a 6.5% absolute increase between groups. We are 95% confident that the true between-group difference lies between -0.28% and 13.2%, which includes our hypothesised minimally important value of 10% (Table 2 and Figure 2). Estimates adjusted for risk group remained relatively unchanged (data not shown). The sensitivity analyses demonstrated similar patterns to the primary analysis (Figure 2).

In the intervention group 50.8% (184/362) of participants were due CRC screening at baseline or within the next 12 months of follow-up, and 50.0% (180/360) in the control group. There was strong evidence for effect modification ($p<0.001$); of those who were due CRC screening, 59.8% (110/184) in the intervention group compared to 38.9% (70/180) in the control group had risk-appropriate screening at 12-months (estimated absolute group-difference in proportions: 20.3%, 95% CI: 10.3% to 30.4%, $p<0.001$). (Table 2 and Figure 2) In those who were not due screening, the intervention was associated with reduced risk-appropriate screening at 12-months (intervention group 83.7% (149/178) vs control group 91.1% (164/180), estimated absolute group-difference in proportions -7.2% 95% CI: -13.5% to -0.92% $p = 0.042$).

More participants were over-screened in the intervention group compared to the control group. Thirty-six intervention group participants (9.9%) were over-screened at 12-months [17 iFOBT (47.2%) and 19 colonoscopies (52.8%)], compared with 18 (5.0%) in the control group [6 iFOBT (33.3%) and 12 colonoscopies (66.7%)].

GPs ordered an iFOBT in 11.6% and 14.6% of intervention participants at two and four weeks respectively, compared with 0.3% and 1.1% of control participants, demonstrating minimal

contamination between groups. These process data were consistent with the intervention acting mainly through GPs ordering more iFOBT tests in those at average risk of CRC.

At one-month follow-up those in the intervention group were more likely than the control group to intend completing an iFOBT in the next three months (27% vs 14.8% OR 2.16 (95% CI for OR 1.46 to 3.21) p<0.001) (Table 3). There were no observed effects on participants' intentions to have a colonoscopy or modify their lifestyle. There were no differences between groups at any timepoint on general or cancer-specific anxiety or absolute risk perception (Table 4).

The total average incremental cost per participant (CRISP less usual care) was $223 (Supplementary Table 3). Based on the primary outcome including all participants, this resulted in an average cost per appropriately screened participant of $3,436. This effect ranged from being dominated (costlier and resulting in fewer screened individuals) to an incremental cost per appropriately screened individual of $1,718 using the 95% CIs of the efficacy endpoint. When analysis was restricted to those individuals due screening at baseline, the cost per appropriately screened individual was $1,990 ($1,326 to $3,979 using the 95% CIs of the efficacy endpoint) (Supplementary Table 4).

Discussion

Summary

Using a risk assessment and decision support tool in patients attending general practice increased risk-appropriate CRC screening by 6.5% in the whole intervention cohort. Although the 95% CI includes a true effect size of no difference, we cannot preclude a clinically important true intervention effect since the CI includes the possibility of a 13% increase in risk-appropriate screening, higher than originally hypothesised. In an explanatory analysis, the intervention effect was more evident in people who were due CRC screening, with a 20% absolute increase in risk-appropriate screening over 12 months compared to the control group.

Strengths and limitations

We recruited our intended sample size, with a high accrual rate; participants were representative of the local population. We applied a hierarchical approach to define the primary outcome using objective health services data in preference to self-report and relied on self-reported information for only three participants for the primary analysis. To maintain blinding, we defined risk-appropriate screening based on the risk assessment method specific to each trial group. We had complete data for the primary outcome for 98% of trial participants. Our sensitivity analyses showed our findings were robust to different assumptions. Including participants who were not due CRC screening during follow-up diluted the observable effect of the intervention. They were included because we were interested in effects on risk-appropriate screening, both under- and over-screening in average and increased risk groups. The rate of risk-appropriate screening in the control group who were due screening was only 39%, similar to rates of participation in the national screening program. It was not possible to confirm whether someone was genuinely due screening in the 12-month follow-up until we obtained the objective screening data from health records and knew their baseline risk. Our preliminary estimates of baseline risk-appropriate screening, on which our original and revised sample sizes were based, could not adequately account in advance that only 50% of our sample were due CRC screening during our follow-up period. Although guidelines recommend CRC screening in those at increased risk from age 40, we chose to recruit a sample aged 50-74. If we had recruited a younger cohort, we would have included an even larger proportion of participants who were not due screening during follow-up.

Comparison with existing literature

Our previous systematic review of cancer risk assessment tools found that they increase intentions to screen but the effects on risk-appropriate screening were unclear. (30) Our results provide new evidence that this type of intervention could increase risk-appropriate screening, especially in those who are due screening. Our systematic review also highlighted methodological limitations in

previous trials including cluster randomised designs and low recruitment rates. (30) Our trial had a high recruitment rate with a broad range of educational and sociodemographic backgrounds making our results more generalisable. We randomised at patient level and demonstrated no evidence of contamination; this design minimised selection bias between groups and allowed us to obtain patient reported outcomes.(31)

Two trials of CRC risk assessment tools have reported since our systematic review.(32, 33) One showed no effect on CRC screening;(32) the other trialled a self-completed tool which resulted in a threefold relative increase in CRC screening. (33) We tested a tool for application in a consultation, based on clinician feedback recommending it be used by practice nurses. (20) In a study of a self-completed version of the CRISP tool, people who were older, less educated or who spoke English as a second language found the tool difficult to complete .(34)

Our complex intervention was more than computerised risk assessment or a simple reminder to complete screening of any kind. It included a discussion about bowel cancer, demonstration of the iFOBT kit and prompting GPs to order the risk-appropriate screening test. Our 'attention control' was designed to account for the non-specific effects of the intervention. This was an efficacy trial to test whether delivery of the CRISP intervention in a standardised way could improve risk-appropriate screening.(35) We conducted a parallel implementation study of the CRISP intervention in which practice nurses used the CRISP tool, taking between five to ten minutes to conduct the risk assessment.(36) We recognise that further implementation-effectiveness research is required to understand whether similar results would be achieved if delivered in routine care.

The intervention led to higher rates of over-screening in those who were not due screening, mainly through over-ordering iFOBT tests. With the implementation of the National Cancer Screening Register, it should be possible to reduce this over-screening by determining when someone is due their next iFOBT. This information in the Register could also be used to determine when a CRISP risk assessment should be performed. Our intervention aimed to reduce colonoscopies in people at

average risk of CRC. We will report five-year follow-up data on potential reductions in colonoscopies in average risk patients and the longer-term cost-effectiveness of the CRISP tool.

Implications for research and practice

Risk-stratified screening targets more intensive screening to populations with higher rates of cancer, and, if fully implemented, would reduce screening intensity in those at lower risk.(37) Modelling studies show this is cost-effective (12, 38) and there are calls to move away from population-based to risk-based approaches to CRC screening.(8) The incidence of CRC in people below 50 years of age is rising, due to risk factors such as obesity, smoking, low physical activity and diet.(39) This has led to changes in American guidelines to commence CRC screening from age 45. (40) Risk-based screening which accounts for these risk factors, as well as family history would require implementation using tools like CRISP. (17) However, there remain substantial implementation challenges for countries with CRC screening programs which mail kits to people based on age, such as in Australia and the UK. A risk-based approach would require greater engagement with primary care and integration with the NBCSP to identify those in their forties at increased risk of CRC. Nearly 90% of Australians aged 45-54 attend a GP each year,(41) and most several times, creating opportunities to assess cancer risk. The CRISP intervention could commence in people in their fifth decade as part of a risk-based screening program to ensure people start CRC screening at the optimal age and with the most cost-effective screening test.

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Conflict of interests: none declared.

Author contributions

JDE, MJ, FM, IW, PC, JM, JD, RDAL, GF, LF, FW, AB, DAO, MP, LT contributed to the design of the trial and obtained funding for the trial. JDE, JM, PC, SS, JO, SM, KN, PN, EH, AB, MC, MP contributed to the implementation of the trial protocol and acquisition of the data. PC and SS verified the trial data. PC led the statistical analyses and RDAL and AC the health economic analyses. All authors contributed to the interpretation of the analyses. All authors contributed to the drafting of the manuscript and have approved the final version. JDE is guarantor.

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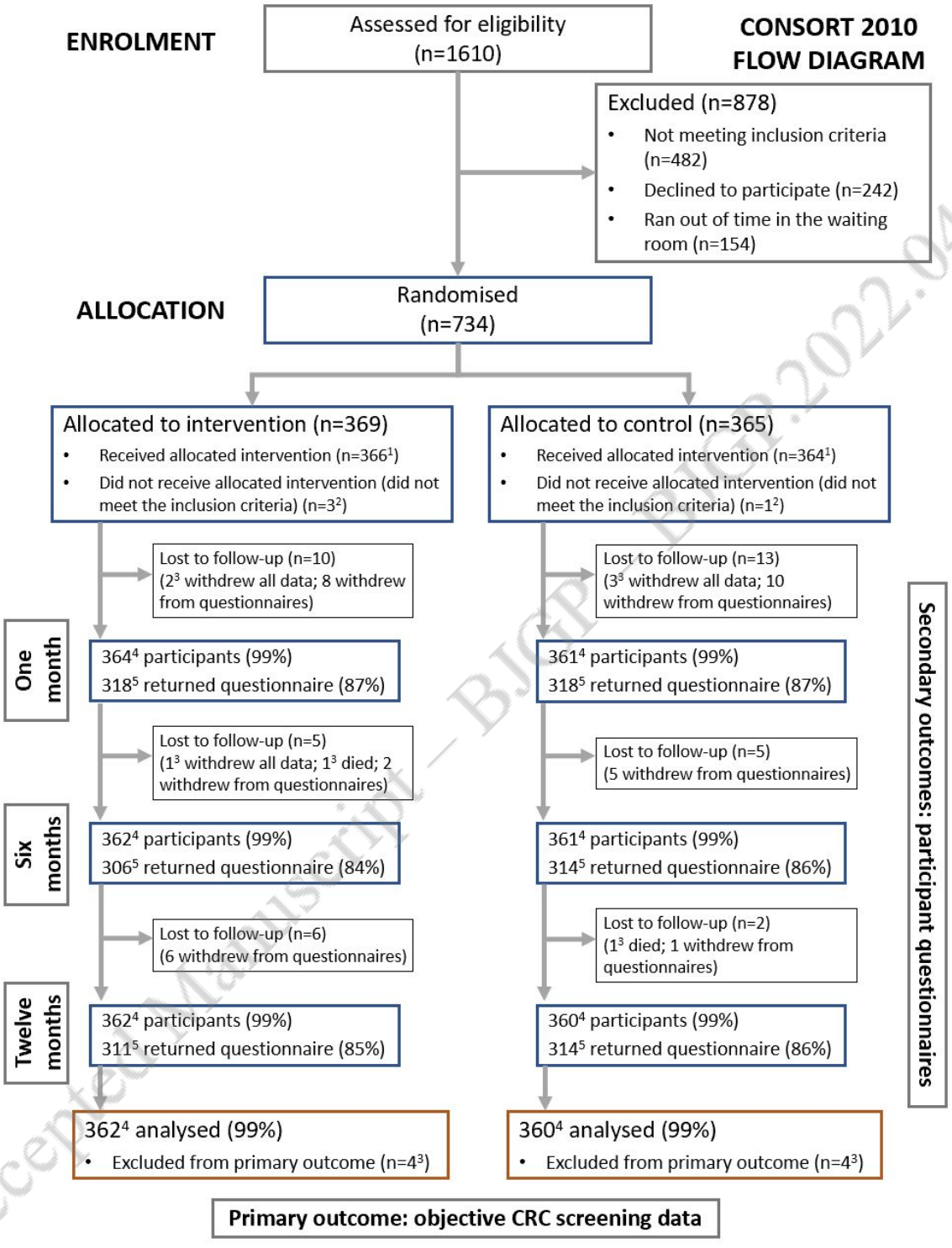

Figure 1. Consort diagram showing number of participants assessed for eligibility, randomised, and available for analysis of primary and secondary outcomes.

[1] Denominator for percentages is those who received the allocated intervention in each group (366 for intervention group, 364 for control group); [2] Participants who did not meet the inclusion criteria were excluded from all analyses; [3] Participants who withdrew all data or who deceased prior to the primary endpoint were excluded from all analyses (four in each group); [4] The number of participants remaining for analysis of the primary outcome at each timepoint; [5] The number of participants who returned questionnaires at each timepoint contributing data to the analysis of secondary outcomes.

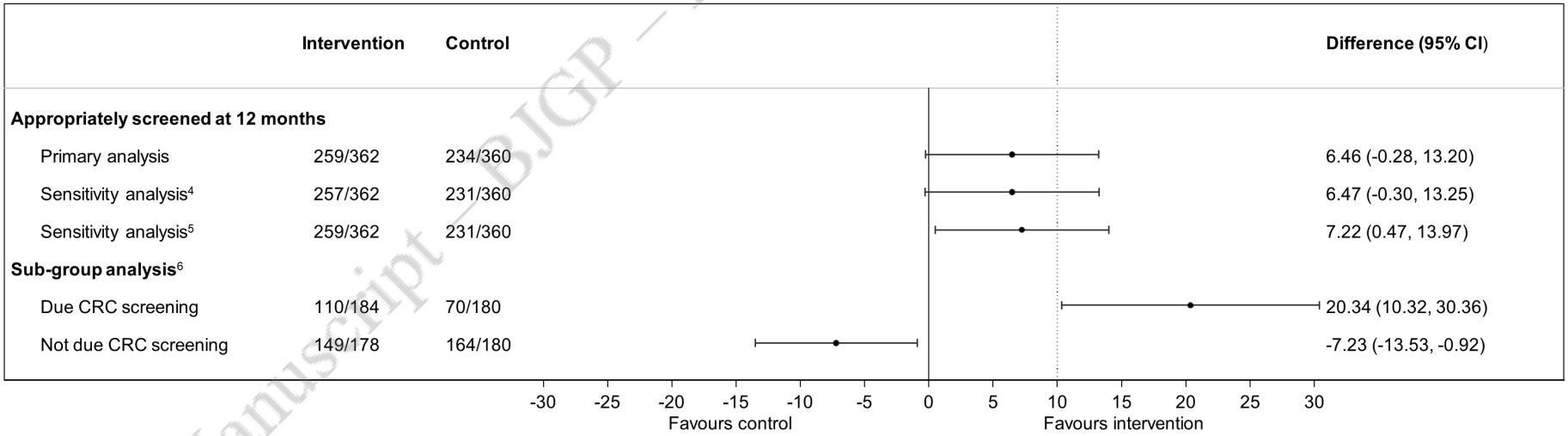

Figure 2. Forest plot showing estimated effect sizes* including planned sensitivity and sub-group analyses.

4. Accounting for data on CRC screening at baseline available to the GP to determine the type of CRC screening that was due.
5. Excluding 3 participants in control group with self-reported outcomes only.
6. Effect modification by whether participants were due CRC screening during 12-month follow-up (184 in the intervention group and 180 in the control group) or not (178 in the Intervention group and 180 in the control group); Interaction term estimated for between-group difference on the percentage scale=27.6% (95% CI: 15.7% to 39.5%), p-value for effect modification <0.001

* Difference in the percentage with appropriate colorectal cancer screening at 12-month follow-up between the intervention and control groups and respective 95% CI estimated using generalised linear model with the identity link function and binomial family adjusted for general practice

Table 1: Demographics by trial group (N=724)[1]

	Intervention (n=363)		Control (n=361)	
	n	(%)	n	(%)
Age (years) - Mean(SD)	63.28	(6.83)	63.09	(6.76)
Gender				
Female	218	(60.1)	215	(59.6)
Male	145	(39.9)	146	(40.4)
Born in Australia	250	(68.9)	246	(68.1)
Index of Relative Socio-economic Advantage and Disadvantage (Deciles[2]) for participants residence[44]				
1-3	47	(13.0)	47	(13.0)
4-7	67	(18.5)	67	(18.6)
8-10	249	(68.6)	247	(68.4)
English spoken at home	336	(92.6)	336	(93.1)
Current relationship status				
Single	54	(14.9)	61	(16.9)
In a relationship	23	(6.3)	35	(9.7)
Married	218	(60.1)	209	(57.9)
Separated/divorced	38	(10.5)	32	(8.9)
Widowed	30	(8.3)	24	(6.6)
Highest level of education completed				
Never completed high school	80	(22.0)	59	(16.3)
Completed high school only	84	(23.1)	78	(21.6)
TAFE qualification or similar	55	(15.2)	81	(22.4)
University degree or similar	144	(39.7)	143	(39.6)
Risk category based on NHMRC family history criteria (2005)				
Average Risk	347	(95.6)	342	(94.7)
Moderate Risk	11	(3.0)	15	(4.2)
High Risk	5	(1.4)	4	(1.1)
Risk category based on NHMRC family history criteria (2017)[3]				
Average Risk	348	(96.4)	340	(95.0)
Moderate Risk	11	(3.0)	15	(4.2)
High Risk	2	(0.6)	3	(0.8)
Risk category based on CRISP model				
Average	342	(94.2)	NA	
Moderate	16	(4.4)		
High	5	(1.4)		

Counts (n) and percentages (%) presented unless otherwise stated; NA - Not applicable

1 One person in each arm deceased prior to the primary endpoint (12 months) so are excluded from the primary outcome. Their survey responses are included for the secondary outcomes

2 Decile 1 is the most disadvantaged and 10 is the most advantaged decile

3 Two participants in the intervention group and three in the control group could not have their family history category determined for the 2017 guidelines due to incomplete data; their family history meant that they were at least moderate risk.

Table 2. Appropriate colorectal cancer screening at 12-month follow-up between trial groups (N=722) [1]

Appropriately screened at 12 months	Intervention (n=362)		Control (n=360)		Difference (95% CI)[2]	Odds ratio (95% CI)[3]	p-value[3]
	n	(%)	n	(%)			
Primary analysis	259	(71.6%)	234	(65.0%)	6.5% (-0.28% to 13.2%)	1.36 (0.99 to 1.86)	0.057
Sensitivity analysis[4]	257	(71.0%)	231	(64.2%)	6.5% (-0.30% to 13.2%)	1.37 (1.00 to 1.88)	0.048
Sensitivity analysis[5]	259	(71.6%)	231	(64.2%)	7.2% (0.47% to 14.0%)	1.41 (1.03 to 1.93)	0.033
Sub-group analysis[6]							
Due CRC screening	110	(59.8%)	70	(38.9%)	20.3% (10.3% to 30.4%)	2.31 (1.51 to 3.53)	<0.001
Not due CRC screening	149	(83.7%)	164	(91.1%)	-7.2 (-13.5% to -0.92%)	0.51 (0.26 to 0.97)	0.042

n – count; CI – Confidence Interval

[1] One person from each trial group was excluded because they died before the 12 months of follow-up.

[2] Difference in the percentage and respective 95% CI between the intervention and control groups estimated using generalised linear model with the identity link function and binomial family adjusted for general practice

3 Odds ratio, respective 95% CI and p-value estimated using logistic regression adjusted for general practice

4 Sensitivity analysis: Accounting for data on CRC screening at baseline available to the GP to determine the type of CRC screening that was due.

5 Sensitivity analysis: Excluding 3 participants in control group with self-reported outcomes only.

[6] Effect modification by whether participants were due CRC screening during 12-month follow-up (184 in the intervention group and 180 in the control group) or not (178 in the Intervention group and 180 in the control group); Interaction term estimated for between-group difference on the percentage scale=27.6% (95% CI: 15.7% to 39.5%), p-value for effect modification <0.001.

Table 3. Intentions and self-reported behaviours to manage risk of colorectal cancer between trial groups (N=724) [1]

	Intervention (n=363)	Control (n=361)	OR (95% CI)[2]	p-value
	n (%)	n (%)		
In the three months, I intend to:				
Look for further information[3]				
1 month	35 (11.0%)	33 (10.4%)	1.08 (0.65, 1.78)	0.769
6 months	35 (11.4%)	24 (7.7%)	1.52 (0.89, 2.61)	0.129
12 months	36 (11.6%)	29 (9.2%)	1.28 (0.76, 2.15)	0.353
Consult with a health professional about my cancer risk[3]				
1 month	36 (11.3%)	26 (8.2%)	1.43 (0.84, 2.45)	0.190
6 months	36 (11.8%)	25 (8.0%)	1.51 (0.89, 2.58)	0.130
12 months	32 (10.3%)	33 (10.5%)	0.98 (0.58, 1.65)	0.945
Complete a bowel cancer screening test using FOBT[3]				
1 month	86 (27.0%)	47 (14.8%)	2.16 (1.46, 3.21)	<0.001
6 months	75 (24.5%)	62 (19.8%)	1.32 (0.91, 1.93)	0.148
12 months	75 (24.1%)	57 (18.2%)	1.43 (0.97, 2.10)	0.069
Have a colonoscopy to screen for bowel cancer				
1 month	22 (6.9%)	23 (7.2%)	0.91 (0.49, 1.68)	0.759
6 months	25 (8.2%)	19 (6.1%)	1.39 (0.74, 2.61)	0.306
12 months	26 (8.4%)	21 (6.7%)	1.30 (0.70, 2.40)	0.402
Make changes to my diet or eating habits				
1 month	60 (18.9%)	66 (20.8%)	0.88 (0.59, 1.29)	0.506
6 months	68 (22.2%)	75 (23.9%)	0.92 (0.63, 1.34)	0.663
12 months	79 (25.4%)	76 (24.2%)	1.05 (0.73, 1.52)	0.775
Make changes to my physical activity or exercise				
1 month	103 (32.4%)	95 (29.9%)	1.15 (0.82, 1.61)	0.416
6 months	117 (38.2%)	123 (39.2%)	0.96 (0.69, 1.33)	0.804
12 months	139 (44.7%)	123 (39.2%)	1.25 (0.91, 1.72)	0.170
Ask my GP for a referral to a specialist				
1 month	11 (3.5%)	14 (4.4%)	0.75 (0.34, 1.68)	0.485
6 months	16 (5.2%)	10 (3.2%)	1.68 (0.74, 3.79)	0.211
12 months	15 (4.8%)	14 (4.5%)	1.10 (0.51, 2.35)	0.815
In the last month, I have:				
Looked for further information about bowel cancer[4]				
1 month	23 (7.4)	15 (4.7)	1.60 (0.81, 3.14)	0.176
6 months	23 (7.5)	31 (9.9)	0.73 (0.41, 1.28)	0.269
12 months	49 (15.8)	39 (12.4)	1.36 (0.86, 2.15)	0.186
Consulted with a health professional about my cancer risk				
1 month	45 (14.2)	29 (9.1)	1.60 (0.98, 2.63)	0.063
6 months	41 (13.4)	36 (11.5)	1.14 (0.71, 1.85)	0.583
12 months	57 (18.3)	45 (14.3)	1.38 (0.90, 2.10)	0.142
Found out about further test for bowel cancer				
1 month	36 (11.3)	26 (8.2)	1.42 (0.83, 2.42)	0.197
6 months	24 (7.8)	26 (8.3)	0.93 (0.52, 1.67)	0.816
12 months	51 (16.4)	35 (11.1)	1.56 (0.98, 2.47)	0.061

	Intervention (n=363)	Control (n=361)	OR (95% CI)[2]	p-value
Made changes to my diet or eating habits				
1 month	53 (16.7%)	58 (18.2%)	0.90 (0.60, 1.36)	0.629
6 months	90 (29.4%)	97 (30.9%)	0.97 (0.69, 1.37)	0.864
12 months	108 (34.7)	105 (33.4)	1.08 (0.78, 1.50)	0.653
Asked my GP for a referral to a specialist				
1 month	23 (7.2%)	15 (4.7%)	1.44 (0.75, 2.79)	0.276
6 months	26 (8.5%)	22 (7.0%)	1.19 (0.65, 2.17)	0.578
12 months	41 (13.2%)	30 (9.6%)	1.46 (0.88, 2.42)	0.143
Been referred to a specialist familial cancer clinic to discuss my family history of cancer				
1 month	4 (1.3%)	4 (1.3%)	1.02 (0.26, 4.11)	0.973
6 months	5 (1.6%)	7 (2.2%)	0.73 (0.23, 2.32)	0.591
12 months	8 (2.6%)	4 (1.3%)	2.06 (0.61, 6.93)	0.245
Attended a familial cancer clinic to discuss my family history of cancer				
1 month	3 (0.9%)	2 (0.6%)	1.57 (0.27, 9.21)	0.616
6 months	2 (0.7%)	4 (1.3%)	0.51 (0.09, 2.88)	0.448
12 months	5 (1.6%)	5 (1.6%)	1.01 (0.28, 3.64)	0.982

n – count

[1] Total sample: 318 in intervention group and 318 in control group at 1 month; 306 in intervention group and 314 in control group at 6 months; 311 in intervention group and 314 in control group at 12 months.

[2] Odds ratio (OR) with respective 95% confidence intervals (CI) estimated using logistic regression using generalised estimating equations with robust standard errors, trial group, time (baseline, one, six and 12 months), risk group and general practice as fixed effects, with two-way interactions between trial group and time. Estimates not adjusted for risk group were similar (not shown).

[3] For this item at 6 months there was one additional person in the control group who had a missing response (n=313)

[4] For this item sample size at 1 month was 312 in intervention group and 316 in control group at 1 month.

Table 4. General and cancer-specific anxiety, and risk perception between trial groups (N=724)[1]

	Intervention (n=363)	Control (n=361)		
	Mean (SD)	**Mean (SD)**	**Difference (95% CI)** [2]	**p-value**
Generalised anxiety (STAI) (38) [3]				
Baseline	9.05 (3.68)	9.17 (3.55)	--	
1 month	9.68 (3.73)	9.77 (3.69)	-0.01 (-0.55, 0.54)	0.983
6 months	10.07 (4.10)	9.77 (3.67)	0.34 (-0.24, 0.91)	0.248
12 months	9.60 (3.44)	10.11 (4.14)	-0.53 (-1.11, 0.04)	0.068
Cancer-specific anxiety (39,40)				
Baseline	6.94 (1.57)	6.95 (1.51)	--	
1 month	7.27 (1.68)	7.20 (1.85)	0.06 (-0.18, 0.31)	0.608
6 months	7.22 (1.79)	7.16 (1.58)	0.09 (-0.15, 0.32)	0.477
12 months	7.31 (2.01)	7.27 (1.78)	0.06 (-0.21, 0.33)	0.670
Mean perceived risk of colorectal cancer (0 to 100%) (36,37)[4]				
Baseline	19.33 (19.36)	21.98 (20.45)	--	
1 month	22.86 (19.95)	25.79 (20.73)	-1.59 (-4.41, 1.22)	0.267
6 months	24.56 (20.39)	25.80 (19.75)	-0.25 (-3.05, 2.55)	0.859
12 months	28.20 (21.59)	27.78 (20.38)	1.41 (-1.49, 4.32)	0.339

n - count; SD – Standard Deviation; CI - confidence interval

[1] Total sample for mean and SD: 318 in intervention group and 318 in control group at 1 month; 306 in intervention group and 315 in control group at 6 months; 311 in intervention group and 315 in control group at 12 months.

[2] Mean in the intervention minus the mean in the control arm with respective 95% CI estimated using linear mixed effects model that included trial group, risk group, general practice and time (baseline, one, six and 12 months) as fixed effects and individuals treated as random effects, with two-way interactions between trial group and time, except for baseline where trial group means were constrained to be equal. Estimates not adjusted for risk group were similar (not shown).

[3] At 1 month one additional person in the intervention group had a missing response (n=317); At 6 months two additional people in the control group had a missing response (n=313) and at 12 months an additional person in the intervention arm had a missing response (n=310)

[4] At 6 months one additional person in the control group had a missing response (n=314)