Which Test Is Best? A Cluster-Randomized Controlled Trial of a Risk Calculator and Recommendations on Colorectal Cancer Screening Behaviour in General Practice

Lyndal J. Trevena\textsuperscript{a}  Bettina Meiser\textsuperscript{b}  Llewellyn Mills\textsuperscript{b}  Timothy Dobbins\textsuperscript{c}  Danielle Mazza\textsuperscript{d}  Jon D. Emery\textsuperscript{e}  Judy Kirk\textsuperscript{f}  Annabel Goodwin\textsuperscript{g}  Kristine Barlow-Stewart\textsuperscript{h}  Sundresan Naicker\textsuperscript{a,i}

\textsuperscript{a}Faculty of Medicine and Health, School of Public Health, University of Sydney, Sydney, NSW, Australia; \textsuperscript{b}Psychosocial Research Group, Prince of Wales Clinical School, UNSW, Sydney, NSW, Australia; \textsuperscript{c}School of Population Health, UNSW, Sydney, NSW, Australia; \textsuperscript{d}Department of General Practice, Monash University, Melbourne, VIC, Australia; \textsuperscript{e}Department of General Practice, Centre for Cancer Research, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Melbourne, VIC, Australia; \textsuperscript{f}Faculty of Medicine and Health, Western Clinical School, University of Sydney, Sydney, NSW, Australia; \textsuperscript{g}Royal Prince Alfred Hospital, Sydney, NSW, Australia; \textsuperscript{h}Faculty of Medicine and Health, Northern Clinical School, University of Sydney, Sydney, NSW, Australia; \textsuperscript{i}Australian Centre for Health Services Innovation (AusHSI), Centre for Healthcare Transformation, Queensland University of Technology (QUT), Brisbane, QLD, Australia

Keywords
Cluster-randomized controlled trial · Colorectal cancer · Cancer screening · General practice

Abstract
Introduction: This cluster-randomized controlled trial aimed to assess the effect of the "Which test is best?" tool on risk-appropriate screening (RAS) and colorectal cancer (CRC) screening uptake. Methods: General practices in Sydney and Melbourne, Australia, and a random sub-sample of 460 patients (aged 25–74 years) per practice were invited by post. Clusters were computer randomized independently of the researchers to an online CRC risk calculator with risk-based recommendations versus usual care. Primary and secondary outcomes were RAS and screening uptake via self-reported 5-year screening behaviour after 12 months follow-up. The usual care group (UCG) also self-reported 5-year CRC screening behaviour at 12 month post-randomization. Results: Fifty-six practices were randomized (27 to the intervention and 29 to the control, 55 practices participated) with 818 intervention and 677 controls completing the primary outcome measure. The intervention significantly increased RAS in high-risk participants compared with UCG (80.0% vs. 64.0%, respectively; OR = 3.14, 95% CI: 1.25–7.96) but not in average-risk (44.9% vs. 49.5%, respectively; OR = 0.97, 95% CI: 0.99–1.12) or moderate-risk individuals (67.9% vs. 81.1%, respectively; OR = 0.40, 95% CI: 0.12–1.33). Faecal occult blood testing uptake over 12 months was increased compared with the UCG (24.9% vs. 15.1%; adjusted OR = 1.66, 95% CI: 1.24–2.22), and there was a non-significant increase in colonoscopies during the same period (16.6% vs. 12.2%; adjusted OR = 1.42, 95% CI: 0.97–2.08). Conclusion: An online CRC risk calculator with risk-based screening recommendations
Colorectal cancer (CRC) is the third most common cancer and the fourth most common cause of cancer death worldwide [1]. There are, however, several effective options for CRC screening, each with varying levels of efficacy, supporting evidence, cost, invasiveness, and complication rates. The US Preventive Services Taskforce and others have suggested that risk-stratified screening may be one way of reducing the harms and costs of more invasive screening tests such as colonoscopy in lower risk individuals while also recommending targeting higher risk individuals for whom the benefit-to-harm ratio will be greater [2, 3]. For example, 10-yearly screening colonoscopies in 1,000 people may avert 24 CRC deaths in a lifetime but may cause 15 gastrointestinal or cardiovascular complications [2]. Faecal occult blood testing (FOBT) using the immunochemical test annually may avert 22 deaths in a lifetime for 1,000 people screened with 10 being harmed through complications of testing and follow-up [2]. In the UK, faecal immunochemical tests (FITs) have recently superseded FOBT in the UK’s national screening program [4]. A FIT test is similar to an FOBT but has a better diagnostic performance than the FOBT [5]. Furthermore, modelling has also suggested that a risk-stratified approach to CRC screening would consistently reduce the harms of screening, even though it may not substantively affect the benefits [3, 6], and that it is highly cost-effective [7].

Australia has for some time had clinical practice guidelines for CRC screening, which adopt this approach [8]. People are classified into one of three categories depending on their family history. Category 1 (average or slightly increased risk) accounts for around 98% of the population, who are recommended to consider FOBT every 2 years from the age of 50 years. Category 2 (moderately increased risk) accounts for 1–2% population, who have first-degree relatives diagnosed at a younger age with CRC or two first- and/or second-degree relatives on the same side of the family; they are recommended colonoscopy every 5 years. Category 3 (high risk) accounts for <1% population, who may require specialist genetic screening and colonoscopy from age of 25 years. Minor changes have been made to some of these definitions in the new guideline [9], but the risk-based approach has been maintained. Similar risk-stratified screening programs are available in other countries. For example, in the UK, for people at average risk for CRC, FIT every 2 years is recommended from the age of 50 to 74 years [4, 10]. For people at moderate risk, UK guidelines recommend a one-off colonoscopy at age of 55 years, with subsequent colonoscopic surveillance determined by post-polypectomy surveillance guidelines [11]. For individuals at high risk, UK guidelines recommend that yearly colonoscopy be performed from age of 40 years until age of 75 years [11].

Implementation of this stratified approach has been variable, with wide variation in colonoscopy rates noted nationally, the highest rates being in high socioeconomic urban areas [12]. This variation and potential “overscreening” sits alongside underscreening with low (although improving) uptake of FOBT [13] and low awareness and detection of younger individuals potentially at high risk for Lynch Syndrome and other genetic syndromes [14, 15]. We know that some of the barriers to risk-stratified screening include a lack of awareness of CRC risk by patients, sub-optimal family history records in general practice, and a lack of awareness of strata-level recommendations for CRC screening by general practitioners (GPs) [15–17].

In Australia, previous studies have examined the factors associated with risk-appropriate CRC screening in primary care [18, 19]. The observations of these studies are consistent with the few US and UK studies specifically evaluating risk-appropriate CRC screening within primary care, which observed that GP endorsement is a significant predictor of uptake of CRC screening, but that, by itself, it is not sufficient to increase the uptake of risk-appropriate screening [20–23]. Nonetheless, the impact of GP screening invitations and electronic reminders and prompt systems on increasing the uptake of CRC screening across all modalities are well documented and have been shown to increase the rate of FOBT uptake by as much as 10–15% [24–28]. Given the barriers to risk-stratified screening and the critical role of primary physicians in increasing the uptake of CRC screening, our study, therefore, aimed to evaluate whether an online risk calculator administered in the general practice setting with recommendations designed to address barriers to CRC screening would increase risk-appropriate CRC screening over a 12-month follow-up period. It was hypothesized that patients receiving the online risk calculator would have had higher rates of risk-appropriate CRC screening during the previous 12 months compared to the usual care group.
Materials and Methods

Design
The study design is a cluster-randomized controlled trial with the unit of randomization (i.e., cluster) being a general practice located in urban Sydney or Melbourne, Australia. These are the largest two cities in Australia with populations of 5 million and 4.5 million people, respectively. Both cities have sizeable GP workforces – 7,500 and 6,200, respectively – and have reasonable access to services such as colonoscopies and familial cancer services. We did not include regional and rural practices in order to avoid rural-specific access issues, which were not part of our hypothesis. It was decided that the unit of randomization should be the general practice, not the individual patient, in order to minimize contamination between patients attending the same GP, whose behaviour might change due to exposure to the intervention output reports.

Participants
The study only enrolled general practice clinics that had the necessary software to extract patients by study eligibility criteria and the ability to receive automated patient CRC risk reports via email or fax. Letters of invitation were sent using contact details from publicly available online telephone listings and through research networks affiliated with the University of Sydney and Monash University. In addition, the study was publicized through educational workshops, newsletters, websites, and GP-orientated publications. GPs were offered continuing medical education points for their participation in the study.

Patients of each participating clinic had to meet the following criteria: aged between 25 and 74 years; had visited the practice within the last 12 months from date of extraction; not having been diagnosed with CRC, the inflammatory bowel diseases ulcerative colitis or Crohn's disease; not living in a residential aged care facility; and absence of abnormal cognition and serious illness. Exclusion criteria were: individuals under 25 or over 74 years of age, a previous/current diagnosis of CRC, no internet access, and inability to read or write in English at a year 8 level. There were no differences in time spent and level of academic detailing between the intervention or control practices. Recruited practices received academic detailing face-to-face by one of the researchers, and physicians were given a 30-min overview of the study rationale by the attending researcher. This followed a standardized script summarizing the importance of guideline-based CRC screening and the role of family history as adapted from the screening recommendations at the time. The recruiting researchers worked with staff to generate random lists of up to 460 patients per practice who met the eligibility criteria mentioned above. GPs were asked to check these lists of randomly selected patients and further exclude those who would not be suitable (e.g., cognitive impairment, severe illness); letters of invitation by their GP were prepared for those deemed suitable.

Description of the Intervention
The intervention, called the “Which test is best?” tool, was developed by the authors, who had expertise in general practice, psychology, statistics, clinical genetics, genetic counselling, and public health. The tool was designed to overcome a number of identified barriers to risk-appropriate screening. First, the incompleteness of family history information was addressed through an online questionnaire based on the Amsterdam Criteria and a locally successful campaign to encourage family health history discussions [29]. The tool was designed to be completed at home in consultation with relatives, if required. The “Which test is best?” website was developed to achieve ease of use, good accessibility of information, and effective communication of an individual’s familial risk of developing CRC and the related screening recommendations. Navigation tabs provided access to information about CRC and links to other resources, a summary of the current National Health and Medical Research Council (NHMRC) guidelines, and an explanation of each of the risk categories. The risk algorithm was presented in the form of a questionnaire, which was laid out vertically as shown in Figure 1. Each of the content tabs was positioned on top of the website from left to right, allowing users to browse through that information as they saw fit. This provided participants with a sense of control over their browsing experience, a feature which has been shown to increase user satisfaction [30, 31]. Five content tabs ensured users could easily navigate to a welcoming homepage, information about the study, a consent page (which they would be redirected to and asked to read as a requirement for study registration), general information about CRC, and a page with the researchers’ contact details. Since many people are unsure of their family’s history of cancer, we also included a design feature that encouraged people to check with their relatives in case they were unsure about answers to any of the questions [32]. A login and registration tab was embedded in the website for users to click on when they felt ready to register. At registration, they were required to enter their first and last names, email address (for website activation), date of birth, post code, and educational status. A pilot study (n = 26 users) was conducted prior to the implementation of the tool within the RCT. The results of this pilot study were used iteratively to refine and update the website to meet user expectations and enhance the perceived value of the online risk tool.

After completing their family history questionnaire, users were sent an activation email allowing them to access the CRC family history details in the form of a questionnaire, which was laid out vertically as a series of risk categories. Each of the risk categories was presented with a risk assessment tool allowing users to specify if they had a positive family history of CRC and the related screening recommendation in lay terms and a section explaining the classification of the risk category assigned, which could be saved as a PDF file and/or printed. The report described the familial phenotype categories and the category-specific screening recommendation in lay terms (see Fig. 2). The report also advised participants to consult with their GP if they had not yet had risk-appropriate screening. In addition, the report was designed to be shared with the GP, who received a copy immediately after the participant completed the questionnaire. This occurred via an “automated forward” programmed into the website, which either emailed or faxed the report to the GP’s practice depending on the GP’s nominated method of receipt.

Recruitment of Participants
Inviting the Intervention Group at Time = 0
A random sample of eligible patients from intervention GP clinic clusters was mailed invitation letters in addition to a participant information sheet at time = 0 (t = 0) (Fig. 3), with a sequential rollout to all clusters randomized to the intervention group occurring over a period of 12 months. The invitation letter asked eligible patients to complete the “Which test is best?” tool at home and provided the participant with access to the study website and a unique access code with which to register. Study consent was obtained online at the point of registration. To register for the study, participants were required to enter their first and last names, an active email address, and their date of birth, postcode, gender, and educational attainment. Once successfully registered, participants were sent an activation email allowing them to access the CRC fa-
They could login as many times as required to complete answering the relevant questions until they were ready to confirm their responses by selecting “submit,” which in turn generated an automated CRC risk report with the appropriate screening information for them and their GP. If participants had not completed the tool within a month of registering, they were sent a reminder email to do so. The research team could monitor participant logins and completion through tracking cookies once participants successfully registered. A telephone number at the researchers’ office was also provided, if additional technical support was required. Reminder letters were sent out 1 month later to non-responders from 17 clusters, while 11 clusters opted not to send out reminder letters.

Inviting and Following Up the Usual Care Group at Time = 1, 12 Months Later

Usual care group clusters invited eligible participants to participate in the study 12 months from the date of extraction at their GP clinic (t = 1) (see Fig. 3). The invitation letter provided them access to a usual care version of the website using a registration procedure identical to that of the intervention group. However, they were given access to the online CRC survey collecting the primary outcome data instead of the CRC familial risk tool. Please see below a list of measures included in the CRC survey. Once they had completed the survey, they were able to access the online CRC familial risk tool, which provided them and their GP with an automated risk report for developing CRC with the appropriate screening information attached. Participants in the usual care group were also sent a reminder letter.
At or slightly above average risk

Your chance of developing bowel cancer is about the same as the general population. Most people will fall into this category.

Which test is best for you?
A faecal occult blood test (FOBT) every two years from the age of 50 is recommended for people in your risk category. Please speak with your GP if you are over 50 and have not had (or are unsure about) whether you have had a FOBT in the last two years.

Moderately increased risk

Your chance of developing bowel cancer may be higher than average. Less than 10% of people are in this category but the vast majority (70-90%) will never develop bowel cancer.

Which test is best for you?
A colonoscopy every five years starting at age 50 OR starting five years before the earliest age of bowel cancer diagnosis in your family, if your affected relative was diagnosed before age 50. Please speak with your GP if you are in this age group and have not had (or are unsure about having) a colonoscopy in the past 5 years.

Potentially high risk

Your chance of developing bowel cancer may be high when compared to the general population. Fewer than 5% of people are in this category.

Which test is best for you?
Your more complex family history needs a more detailed assessment than we can provide with this tool. Please speak to your GP who can assist with referral to a Familial Cancer Service or specialist where this can be done.

Fig. 2. Risk-appropriate screening recommendations from “Which test is best?” tool.
Following Up the Intervention Group at Time = 1, 12 Months Later

Participants in the intervention group were followed up 12 months after completion of the "Which test is best?", when they were asked to complete the online self-reported CRC survey. Consequently, screening behaviours were measured during the same time for both the intervention and control groups.

Randomization and Blinding
Practices were consented, and the patient list was extracted from participating practices. The allocation schedule for randomly assigning each consenting GP cluster clinic was computer generated using a block randomization method and monitored by the NHMRC Clinical Trials Centre, which was an external organization independent from the study team. Block randomization by state was undertaken to ensure that there are roughly the same proportion of intervention and control clinics at each location and about equal numbers of clinics randomized to each arm for the overall study. As soon as a GP practice consented, a list of eligible patients were extracted. When this extraction was complete, a form eliciting practice demographic details (number of GPs, billing arrangement, and presence of a full time practice manager) was emailed to the NHMRC Clinical Trials Centre. This allowed the NHMRC Clinical Trials Centre to assess any selection bias in the randomization and adjust appropriately through further demographic stratification as required and appropriate. GP clusters were blinded to their intervention assignment in that they were told that the study was about the role of family history and improving the prevention of bowel cancer. All outcome data were collected online ensuring that allocation concealment remained.

Outcomes
Cluster Data
A brief survey collected data on the number of GPs in the practice, postcode, and practice billing arrangements.

Primary Outcome
The online CRC patient survey assessed the primary outcome for the trial, which was risk-appropriate screening. The survey contains 24 screening and 9 patient demographic items and was hosted on LimeSurvey. The screening questions assessed participants’ screening behaviours for the past 5 years and the frequency of their CRC screening regimen. These questions were designed with a branching algorithm, such that participants only answered questions relevant to their previous responses. This questionnaire was adapted from similar types of surveys conducted within Australia and internationally and used standard phrasing, which has been previously validated for screening studies.

Table 1 shows how risk-appropriate screening was defined using family history risk category and 5-year screening behaviour based on the Australian guidelines [8]. Since some debate remains about what contribution extended family history makes to CRC risk [33], we formed a clinician panel from within the team of investigators (one GP and two cancer genetics specialists). Data on family history and screening behaviour were extracted for all participants who had been identified as being at "potentially high risk" by the “Which test is best?” tool. These cases were independently reviewed by all three clinicians, and the majority classification of risk-appropriate screening was accepted. This process best reflects current practice in Australia, where patients who may be at high risk of CRC (based on their family history) are recommended to have expert assessment by cancer geneticists.

Five-year screening behaviour was measured in all participants at $t = 1$ (12 months after randomization). CRC risk using the “Which test is best?” tool was measured at $t = 0$ in intervention clusters and at $t = 1$ in usual care group clusters, thus allowing for any effect of the intervention to be assessed at the 12-month follow-up.

Sample Size Calculations
The study was powered to detect a change in risk-appropriate screening behaviour in category 2 and category 3 risk patients.

Fig. 3. Overview of study timeline.
Initial Sample Size Calculations

Originally, it was estimated that category 2 and 3 would comprise 6% of the population. In this group, it was assumed that 30% of patients would follow risk-appropriate screening [34]. In order to detect a change in the rate of risk-appropriate screening to 65% in the intervention group as statistically significant at the 0.05 level with 80% power, a minimum of 6,154 completed patient follow-up responses would be required. This sample size would result in more than 85% power to detect a difference of 10% in risk-appropriate screening in category 1 patients, regardless of the control rate of risk-appropriate screening.

Revised Sample Size Calculations

However, these calculations were revised because the percentage of participants who fell into categories 2 and 3 was much higher than anticipated (11.6%), and the rate of risk-appropriate screening in categories 2 and 3 was much higher than expected (73.5%). From 55 GP practices that completed the trial, there were a total of 170 category 2 and 3 participants. The study had 80% power to detect a change of risk-appropriate screening from 74 to 91% in the intervention group as statistically significant at the 0.05 level.

There were 1,325 category 1 participants. This provided 80% power to detect a difference of 11% or lower in risk-appropriate screening as statistically significant at the 0.05 level in category 1 participants, regardless of the control rate of risk-appropriate screening. We assumed an intracluster correlation coefficient of 0.05, consistent with intracluster correlation coefficients observed for pathology test ordering (0.046) and imaging test ordering (0.029) in patient encounters in Australian general practice [35].

Statistical Analysis

Descriptive statistics were used to characterize the GP and patient samples in terms of sociodemographic and family history data and uptake of each screening modality. Participants were classified as either risk-appropriate screeners (RAS; those who met screening criteria appropriate for their risk level) or non-risk-appropriate screeners (non-RAS; encompassing both underscreeners and overscreeners). For a detailed description of the criteria for risk-appropriate-, under-, and overscreening, see Table 1. Contingency tables were generated to represent the proportions of RAS and non-RAS in each treatment arm, risk category, age group, and sex. Age was dichotomized into 25–49 and 50–75 age brackets for the purpose of these tables.

An incremental approach was used to test the effect of the intervention, risk category, and any potential effect on screening behaviour using likelihood ratio tests. All models were multilevel logistic regressions with the binary screening behaviour (i.e., RAS vs. non-RAS) variable as the outcome measure and practice ID as the random factor. The first model (unadjusted model) included treatment group as the sole fixed predictor. The second model (adjusted model) added risk category, gender, age (in decades to generate more interpretable estimates), and socioeconomic status (SES) of the practice location (based on Socioeconomic Index for Areas, Australian Bureau of Statistics scores) [36] to the unadjusted model. The final model (effect modification model) added the interaction between treatment group and risk category to the adjusted model to test whether the effect of the intervention was modified by risk category.

### Table 1. Primary outcome categorization

| Risk category                      | Not risk appropriate/overscreening | Risk-appropriate screening | Not risk appropriate/underscreening |
|-----------------------------------|-----------------------------------|---------------------------|-----------------------------------|
| At or slightly above average risk | No FOBT in previous 2 years if over 50 years old | From 50 years old, FOBT every 2 years | Any FOBT if under 50 years old OR more than 2 FOBT in previous 2 years if over 50 years old OR any colonoscopy |
| Moderately increased risk          | No colonoscopy if over 50 years old, or if within 10 years before earliest bowel cancer diagnosis in first-degree relatives | One colonoscopy if over 50 years old, or if older than 10 years before earliest bowel cancer diagnosis in first-degree relatives | Any colonoscopy if ≤50 years old or greater than 10 years before age of earliest bowel cancer diagnosis in first-degree relatives OR more than one colonoscopy in past 5 years if over 50 years old or within 10 years before earliest age of bowel cancer diagnosis in first-degree relatives |
| Potentially high risk              | Assessment by familial cancer service (or similar) OR colonoscopy at a frequency consistent with family history (as assessed by a panel of clinicians) | Colonoscopy at a frequency greater than recommended for family history | Colonoscopy for screening purpose only |

FOBT, faecal occult blood testing. a Colonoscopy for screening purpose only.
If model 3 demonstrated significant effect modification, post hoc tests of simple effects were performed within this model, testing the effect of the intervention on screening behaviour at each level of risk. All comparisons involving categorical predictors with more than two levels were corrected using the Westfall method, a step-down form of error correction that offers similar protection against type I error as traditional single-step methods such as the Bonferroni procedure but is less conservative and, therefore, less likely to overinflate $p$ values and conceal genuine effects [37].

To test the effect of the intervention on general screening behaviour (i.e., leaving aside whether this behaviour was risk appropriate or not), two binary variables were created, the first indicating whether or not participants had had an FOBT in the previous 12 months, and the second indicating whether they had had a colonoscopy. An iterative model comparison approach was also undertaken with these variables, with a multilevel logistic regression with experimental group as the sole predictor and practice ID as the random factor as model 1, risk category, gender, age, and SES added as fixed predictors in model 2, and the interaction added to model 3. Likelihood ratio tests were once again performed to test which model best fitted the data.

**Patient Involvement**

An expert consumer group from the PC4 cancer clinical trials group provided feedback on the protocol for this study at the time of the funding application. The funder also includes consumer engagement and review as part of their assessment process.
Public Health Genomics 2022;25:193–208
DOI: 10.1159/000526628

Trial Registration
The study was registered with the Australian and New Zealand Clinical Trials Group (Registration No: ACTRN12611000534987).

Adverse Events
One of the participants, who had been randomly selected from the GP records, died around that time, and the GP did not check the patient’s status prior to mailing out the invitation letter. The patient’s wife opened letter and contacted the Human Research Ethics Committee to complain. We wrote a letter of apology to the patient’s wife.

Results
Written consent was obtained for both physicians and patients. Fifty-six clusters were enrolled between March 2012 and February 2013 with final outcome data collected in April 2014. One cluster withdrew from the study without specifying a reason for doing so. The flow of participants in the trial is outlined in Figure 4.

The baseline characteristics at the cluster and individual level are shown in Tables 2 and 3. Eighty-nine percent (88.6%) of the sample were at or slightly above average risk, 4.3% at moderately increased risk, and 7.0% at potentially high risk. Fifty-nine percent (59.1%) of the sample were female. Overall, the study sample was highly educated, with 55.0% of the sample having attained an undergraduate or postgraduate degree. There were no substantial differences in practice- or patient-level characteristics between the two treatment arms.

Table 4 shows the number and percentages of RAS versus non-RAS participants by randomization, risk category, age group, and sex. Across the entire sample, the proportion of RAS appeared to be distributed approximately evenly across the groups, with 48.0% RAS in the intervention group, compared to 52.3% in the usual care group. There appeared to be a higher proportion of RAS in the higher risk categories, with 49/65 (75.4%) and 76/105 (72.4%) in the moderate- and high-risk categories, respectively, compared with 622/1325 (46.9%) in the average-risk category. There was a higher proportion of RAS in the lower age bracket (25–49 years: 330/455, 72.5%) than in the older age bracket (50+ years: 417/1040, 40.1%), where a greater proportion underscreened compared with the younger age brackets (17.6% compared with 3.5%, respectively) and overscreened (42.3% compared with 24.0%, respectively). There was a slightly higher proportion of RAS among females (469/883, 53.1%) than males 278/612 (45.4%).

Table 2. Baseline information for each trial arm at the GP (cluster) level

| Variables | Intervention group (N = 27) | Usual care group (N = 28) | Total sample (N = 55) |
|-----------|----------------------------|---------------------------|-----------------------|
| Mean number of participating GPs per cluster | Mean (SD) | Mean (SD) | Mean (SD) |
| Range: 1, 8 | 2.22 (1.3) | 2.71 (2.1) | 2.47 (1.8) |
| Level | N (%) | N (%) | N (%) |
| Full-time practice manager | | | |
| Yes | 25 (93) | 24 (86) | 49 (89) |
| No | 2 (7) | 4 (14) | 6 (11) |
| Billing arrangements | | | |
| Private billing all patients | 4 (15) | 5 (18) | 9 (16) |
| Concession bulk billing | 16 (59) | 15 (54) | 31 (56) |
| Bulk billing all patients | 7 (26) | 8 (28) | 15 (27) |
| SES of practice locationa | | | |
| SEIFA rank (in quartiles) | | | |
| 75–100 | 20 (74) | 19 (68) | 39 (71) |
| 50–75 | 1 (4) | 5 (18) | 6 (11) |
| 25–50 | 6 (22) | 2 (7) | 8 (15) |
| 1–25 | 0 (0) | 2 (7) | 2 (4) |

SEIFA, Socioeconomic Index for Areas. a Based on percentile ranks within NSW contained in the 2011 Socioeconomic Index for Areas (SEIFA) published by the Australian Bureau of Statistics. Higher ranks indicate higher socioeconomic status.
Table 5 shows the results of the logistic regression modelling RAS versus non-RAS screening, and the effect of the intervention by risk category. There was little evidence of an effect of the intervention in either model 1 (unadjusted OR 0.83; 95% CI: 0.64–1.06, \( p = 0.13 \)) or model 2 (adjusted OR 1.01; 95% CI: 0.78–1.30, \( p = 0.95 \)). The addition of risk category, age, sex, and SES to model 2 significantly improved model fit (\( \chi^2(5) = 193.71, p < 0.001 \)). In model 2, there were significant effects of risk category level, with participants in the moderate-risk category an estimated 3.89 times more likely to screen risk-appropriately than those in the average-risk category (95% CI: 2.12–7.93, \( p < 0.001 \)), and participants in the high-risk category an estimated 3.27 times more likely than those in the average-risk category (95% CI: 2.05–5.20, \( p < 0.001 \)), and no significant difference in likelihood of RAS between the high- and moderate-risk categories. Model 3 showed a significant experimental group \( \times \) risk category interaction (\( \chi^2(2) = 8.52, p = 0.014 \)), suggesting that the intervention might have had differing effects on RAS at different levels of risk. When examining the simple effects of the intervention at each level of risk (Table 5; Fig. 5), only in the high-risk category was the intervention associated with significantly greater odds of risk-appropriate screening than the usual care group. In particular, the intervention significantly increased RAS in high-risk participants compared with UCG (80.0% vs. 64.0%, respectively; OR = 3.14, 95% CI: 1.24–7.96, \( p = 0.0047 \)) but not in average-risk (44.9% vs. 49.5%; OR = 0.97, 95% CI: 0.75–1.27, \( p = 0.83 \)) or moderate-risk individuals (67.9% vs. 81.1%; OR = 0.40, 95% CI: 0.12–1.33, \( p = 0.25 \)). Consistent with the proportions of RAS versus

| Table 3. Demographic and family history variables of each trial arm at the patient (individual) level |
| Variables | Intervention group (\( N = 818 \)) Mean (SD) | Usual care group (\( N = 677 \)) Mean (SD) | Total sample (\( N = 1,495 \)) Mean (SD) |
| Age Range: 26, 75 | | | |
| Level n (%) | n (%) | n (%) |
| Age | | | |
| 25–49 years | 215 (26.3) | 240 (35.8) | 455 (30.4) |
| \( \geq 50 \) years | 603 (73.7) | 437 (64.5) | 1,040 (69.6) |
| Gender | | | |
| Male | 342 (41.8) | 270 (39.9) | 612 (40.9) |
| Female | 476 (58.2) | 407 (60.1) | 883 (59.1) |
| Highest education level achieved\( ^a \) | | | |
| Some high school | 15 (1.9) | 15 (2.3) | 30 (2.0) |
| Year 10 | 79 (9.9) | 57 (8.6) | 136 (9.3) |
| Year 12 | 95 (11.8) | 79 (11.9) | 174 (11.9) |
| Vocational college | 176 (21.9) | 144 (21.7) | 320 (21.8) |
| Degree/postgraduate degree | 437 (54.5) | 369 (55.6) | 806 (55.0) |
| Marital status | | | |
| Married/living as married | 661 (80.8) | 595 (87.9) | 1,216 (81.3) |
| Never married/divorced/widowed | 157 (19.2) | 82 (12.1) | 279 (18.7) |
| Children | | | |
| Yes | 653 (79.8) | 548 (80.9) | 1,201 (80.3) |
| No | 165 (20.2) | 129 (19.1) | 294 (19.7) |
| Health insurance | | | |
| Yes | 736 (90.0) | 595 (87.9) | 1,331 (89.0) |
| No | 82 (10.0) | 82 (12.1) | 164 (11.0) |
| Family history risk category | | | |
| At or slightly above average risk | 735 (89.9) | 590 (87.1) | 1,325 (88.6) |
| Moderately increased risk | 28 (3.4) | 37 (5.5) | 65 (4.3) |
| Potentially high risk | 55 (6.7) | 50 (7.4) | 105 (7.0) |

\( ^a N = 1,466 \) due to incomplete answers.
non-RAS observed in each age group, age was a significant negative predictor of the odds of RAS, with each decade predicting a 45% reduction in odds of having screened risk appropriately (95% CI: 0.50–0.61, \( p < 0.001 \)).

Table 4. Percentages of participants who underscreened, screened risk appropriately, and overscreened\(^a\) based on self-reported 5-year screening behaviour

| Variable                        | Total N | RAS\(^b\) N (%) | Underscreeners N (%) | Overscreeners N (%) | Non-RAS\(^c\) N (%) |
|---------------------------------|---------|----------------|----------------------|---------------------|---------------------|
| **Allocation**                  |         |                |                      |                     |                     |
| Intervention                    | 818     | 393 (48.0)     | 101 (12.3)           | 324 (39.6)          | 425 (52.0)          |
| Usual care group                | 677     | 354 (52.3)     | 98 (14.5)            | 225 (33.2)          | 323 (47.7)          |
| **Risk category**               |         |                |                      |                     |                     |
| Average risk                    | 1,325   | 622 (46.9)     | 164 (12.4)           | 539 (40.7)          | 703 (53.1)          |
| Moderate risk                   | 65      | 49 (75.4)      | 7 (10.8)             | 9 (13.8)            | 16 (24.6)           |
| High risk                       | 105     | 76 (72.4)      | 28 (26.7)            | 1 (1.0)             | 29 (27.6)           |
| **Age group**                   |         |                |                      |                     |                     |
| 25–49 years                     | 455     | 330 (72.5)     | 16 (3.5)             | 109 (24.0)          | 125 (27.5)          |
| 50–74 years                     | 1,040   | 417 (40.1)     | 183 (17.6)           | 440 (42.3)          | 623 (59.9)          |
| **Sex**                         |         |                |                      |                     |                     |
| Male                            | 612     | 278 (45.4)     | 89 (14.5)            | 245 (40.0)          | 334 (54.6)          |
| Female                          | 883     | 469 (53.1)     | 110 (12.5)           | 304 (34.4)          | 414 (46.9)          |
| \(^a\)Patients who responded that they were “unsure” whether they had a particular screening test were not included in the analyses. \(^b\)RAS, risk-appropriate screeners. \(^c\)Non-RAS, non-risk-appropriate screeners (underscreeners and overscreeners).
The results of these two models are presented in Table 7. There was no evidence of effect modification for either outcome ("Had FOBT in last 12 months": $\chi^2(1) = 0.00$, $p = 1.000$; "Had colonoscopy in last 12 months": $\chi^2(1) = 2.11$, $p = 0.15$).

In both model 1 and model 2, participants in the intervention group were significantly more likely to have had an FOBT in the last 12 months (model 1 unadjusted OR 1.86; 95% CI: 1.37–2.53, $p < 0.001$; model 2 adjusted OR 1.66; 95% CI: 1.24–2.22, $p = 0.001$) than patients in the usual care group. In model 1, patients in the intervention group were also significantly more likely to have had a colonoscopy (model 1 unadjusted OR 1.43; 95% CI: 1.00–2.03, $p = 0.047$) than those in the usual care group. However, when this effect was adjusted by the addition of the covariates in model 2, it was no longer significant (model 2 adjusted OR 1.42; 95% CI: 0.97–2.08, $p = 0.071$). Interestingly, the effect of age on simple screening behaviour (i.e., without judging its appropriateness) was opposite to its effect on RAS, with each additional decade predicting a 66% increase in the odds of having had an FOBT in the previous 12 months (95% CI: 1.45–1.89, $p < 0.001$) and a 29% increase in the odds of having had a colonoscopy (95% CI: 1.11–1.49, $p = 0.001$). Those who had an FOBT in the last year reported the following reasons: advised by their GP (35.0%), their own idea (11.7%), and completed as a result of being in the research study (36.3%). Of those who reported having had a colonoscopy in the last year, 79.8% reported having been advised to do so by their GP and 20.2% by a specialist.

### Discussion

Our study of an online risk calculator with screening recommendations did not increase risk-appropriate CRC screening overall after a 12-month follow-up period.
However, the intervention did increase the rate of risk-appropriate screening in moderate- and high-risk categories compared to usual care with a statistically significant increase among participants in the high-risk category. In particular, a high proportion of individuals with a potentially high-risk family history from the intervention group underwent a colonoscopy during the 12-month follow-up period, with all of these individuals considered to be risk appropriately screened. This may indicate that these individuals were underscreeners at baseline and that the tool was effective in changing their screening behaviour to risk appropriate. This compares very favourably to previous interventions, which aimed to improve the level of screening and surveillance for individuals with a salient family history of CRC [38, 39]. Individuals with a high-risk family history of CRC are still routinely overlooked by population screening programs across the world [40]. In fact, at the time of writing, no CRC population screening program across the globe incorporated family history into their program, and the vast majority of studies that targeted individuals with a high-risk family history of CRC did so through index cases within a tertiary health-care setting and not a population level through primary care [38, 40–43]. This is an important distinction since only the latter uses a truly preventative population level method, as approaching relatives of index cases introduces selection bias into the study population.

In general, the tool also significantly increased the uptake of FOBT screening over a 12 month period but did not increase colonoscopy screening in the adjusted model. The lack of effect of the intervention on risk-appropriate screening among average-risk participants may be due to generally high colonoscopy rates reported over the previous 5 years in this group. Since the follow-up period for this trial was only 12 months, we were not able to measure whether overscreening with colonoscopies would be reduced when rescreening would have been due for these individuals. Of those in the study population who had an FOBT in the last 12 months, a statistically significant greater proportion of participants within the intervention (25%) arm had an FOBT compared to those within the usual care group (15%). The direction and magnitude of this finding is consistent with the significant increase in CRC screening over the past 12 months observed for individuals with a potentially high-risk family history when compared to their counterparts in the usual care group. However, when stratified by the primary outcome (risk-appropriate screening), there were no significant differences between the control or intervention group. This suggests that for the majority of participants at population risk (defined as no or negligible family history of CRC), the online familial CRC risk tool was not effective at increasing the level of risk-appropriate screening for CRC when compared to the control group of usual care.
but that it increased the overall level of FOBT screening for those at population level. Taking into account the findings related to these individuals with a potentially high-risk family history, this suggests that an online family history tool with a CRC risk category calculator that notifies both patients and their primary physician of their familial CRC risk may be effective at encouraging screening with any modality, but that it is not effective at inhibiting overscreening behaviour.

Despite risk-based CRC screening guidelines being in place for more than a decade [8], there appears to have been a lack of implementation, with higher than expected screening colonoscopy rates and relatively low uptake of FOBT in average-risk individuals among our study population. This is consistent with a recent Australian study of people attending outpatient clinics, which found that 41% of people underscreened and 21% overscreened for CRC [15]. Modelling studies have asserted the cost-effectiveness of family history-based CRC screening [44], but we could not find any studies that have tested strategies to address this and thus improve the implementation of evidence into practice. To the best of our knowledge, our study is the first to do this.

Unsurprisingly, increasing age was a strong predictor of more regular screening but unfortunately not an increase in risk-appropriate screening. Younger participants were more likely to screen risk appropriately, although this was probably more due to the fact that risk-appropriate screening for younger people is achieved by simply not screening at all rather than the fact that they are better informed about their level of risk and the screening behaviour appropriate to that level risk. Older people were screening more often but less risk appropriately. Clearly, more resources need to be devoted to educating older members of the population about their personal risk level and the screening behaviour most appropriate to that level of risk. We also noted an increase in FOBT uptake with increasing SES, even within this relatively affluent population. Further exploration of strategies to address this inequity is needed.

A limitation of this study is the low uptake by GP clinics across the Melbourne and Sydney metropolitan areas and the over-representation of private billing practices. The majority of patient participants (89%) had private health insurance, which is higher than the national average (around 50%) and suggests a more affluent study population than the rest of the Australian community [45]. However, the proportion of patient participants who had completed tertiary education (55%) was similarly to the rest of the Australian population [46]. Future studies may achieve more representative samples by offering reimbursements to general practices and thereby increasing the participation from lower socioeconomic areas. This clustered RCT also had a suboptimal retention rate, as losses to follow-up of participants in the intervention arm were 54%, which may be attributable to the relatively long follow-up period of 12 months and the minimal engagement of participants during this period. Non-responders may be more or less likely to screen risk appropriately. Screening uptake was by self-report and was not verified through GP and/or other medical records. It is possible that patient recall of colonoscopies, rather than similar procedures such as flexible sigmoidoscopy, may be less accurate. In particular, the accuracy of self-report for sigmoidoscopies has been shown to be lower than for colonoscopy [47, 48]. Nonetheless, other research has shown that patients recall CRC screening tests with relative accuracy (Partin, 2008; Madlensky, 2003; Khoja, 2007). Another limitation relates to the fact that patients had to have visited the practice within the last 12 months, and this may have introduced a bias to those who are more conscious of their health. Finally, since this trial has been completed, the national Australian guidelines on CRC screening have been updated [9]. This study assessed the utility of an online tool that was developed based on the guidelines current at the time. However, such tools need to be updated as evidence and recommendations change, and it is the advantage of an online tool that it can adapted as necessary.

In conclusion, CRC risk calculators with recommendations are likely to be a useful mechanism for improving the uptake of screening in underscreened people of average risk, as well as increasing risk-appropriate screening in those at higher risk. Further evaluation of the impact of such tools on overscreening is warranted. The clinically complex algorithms for family history-based CRC screening can be feasibly delivered via a web-based tool, which can be completed by patients prior to visiting their GP. Such tools can, therefore, enhance existing screening programs and the implementation of guidelines into clinical practice.

Acknowledgements

We thank the patients who generously participated in this study. We also gratefully acknowledge the assistance of the general practitioners and other staff who were involved at each practice and who were integral to the success of this trial. We thank Brandy Baylock and Angela O’Brien for research assistance.
Statement of Ethics

This study was approved the University of Sydney Human Research Ethics Committee (Ref 2012/916), and participants gave written informed consent to participate in this study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

This trial was funded by a Priority-Driven Collaborative Research Grant from Cancer Australia (632887). The sponsors had no role in the design, conduct, and analysis or involvement in the preparation or submission of the manuscript for publication. Bettina Meiser was supported by an NHMRC Senior Research Fellowship Level B (1078523).

Author Contributions

Lyndal J. Trevena led the design and conduct of this work. Bettina Meiser, Sundresan Naicker, Lyndal J. Trevena, and Timothy Dobbins were responsible for data integrity and analyses for the study. Lyndal J. Trevena, Bettina Meiser, Llewellyn Mills, Timothy Dobbins, Danielle Mazza, Jon D. Emery, Judy Kirk, Annabel Goodwin, Kristine Barlow-Stewart, and Sundresan Naicker contributed to the study concept and design. Lyndal J. Trevena, Bettina Meiser, Judy Kirk, Annabel Goodwin, Kristine Barlow-Stewart, and Sundresan Naicker designed the intervention tested in this trial. Lyndal J. Trevena and Sundresan Naicker were responsible for data acquisition. Lyndal J. Trevena, Bettina Meiser, Sundresan Naicker, and Timothy Dobbins were responsible for statistical analysis and interpretation. Lyndal J. Trevena, Bettina Meiser, Sundresan Naicker and Timothy Dobbins drafted the manuscript. Lyndal J. Trevena, Bettina Meiser, Llewellyn Mills, Timothy Dobbins, Danielle Mazza, Jon D. Emery, Judy Kirk, Annabel Goodwin, Kristine Barlow-Stewart, and Sundresan Naicker contributed to the critical revision of the manuscript for intellectual content. Lyndal J. Trevena is the guarantor.

Data Availability Statement

The investigators will share data used in the data analysis reported in this manuscript on request (from L.J.T., lyndal.trevena@sydney.edu.au). Anonymized record-level data can be made available on request to investigators, who have submitted a publicly available proposal for analysis, and who have received ethical clearance from their host institution.

References

1 Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359–86.
2 US Preventive Services Task Force; Grossman DC, Curry SJ, Davidson KW, Epling JW Jr., Garcia FAR, et al. Screening for colorectal cancer: US preventive services task force recommendation statement. JAMA. 2016; 315(23):2564–75.
3 Subramanian S, Bobashev G, Morris RJ, Hoover S. Personalized medicine for prevention: can risk stratified screening decrease colorectal cancer mortality at an acceptable cost? Cancer Causes Control. 2017;28(4):299–308.
4 Cardoso R, Guo F, Heisser T, Hackl M, Ihle P, De Schutter H, et al. Colorectal cancer incidence, mortality, and stage distribution in Europe in the colorectal cancer screening era: an international population-based study. Lancet Oncol. 2021;22(7):1002–13.
5 Brenner H, Tao S. Superior diagnostic performance of faecal immunochromatographic tests for faecal occult blood test in a head-to-head comparison with guaiac based faecal occult blood test among 2,235 participants of screening colonoscopy. Eur J Cancer. 2013;49(14):3049–54.
6 Lew JB, St John DJB, Macrae FA, Emery JD, Ee HC, Jenkins MA, et al. Evaluation of the benefits, harms and cost-effectiveness of potential alternatives to iFOBT testing for colorectal cancer screening in Australia. Int J Cancer. 2018;143(2):269–282.
7 Dillon M, Flander L, Buchanan DD, Macrae FA, Emery JD, Winship IM, et al. Family history-based colorectal cancer screening in Australia: a modelling study of the costs, benefits, and harms of different participation scenarios. PLoS Med. 2018 Aug 15;15(8):e1002630.
8 National Health and Medical Research Council. Clinical practice guidelines for the prevention, early detection and management of colorectal cancer: a guide for general practitioners. 2008.
9 Cancer Council Australia Colorectal Cancer Guidelines Working Party 2018. Clinical practice guidelines for the prevention, early detection and management of colorectal cancer. 2017. Available from: https://wiki.cancer.org.australia/Guidelines: Colorectal_cancer (accessed July 15, 2022).
10 UK National Screening Committee. Available from: https://view-health-screening-recommendations.service.gov.uk/bowel-cancer/ (accessed July 15, 2022).
11 Monahan KJ, Bradshaw N, Dolvani S, Desouza B, Dunlop MG, East JE, et al. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG)/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/United Kingdom Cancer Genetics Group (UKCCG). Gut. 2020;69(3):411–44.
12 Australian Commission on Safety and Quality in Health Care 2015. Australian Atlas of Healthcare Variation. In: National Health Performance Authority, editor. Available from: https://www.safetyandquality.gov.au/our-work/healthcare-variation/atlas-2015 (accessed July 15, 2022).
13 Todorov K, Wilson C, Sharplin G, Corsini N. Faecal occult blood testing (FOBT)-based colorectal cancer screening trends and predictors of non-use: findings from the South Australian setting and implications for increasing FOBT uptake. Austr Health Rev. 2018;42(1):45–52.
14 Patel SG, Ahnen DJ, Kinney AY, Horick N, Finkelstein DM, Hill DA, et al. Knowledge and uptake of genetic counseling and colonoscopic screening among individuals at increased risk for Lynch syndrome and their endoscopists from the family health promotion project. Am J Gastroenterol. 2016;111(2):285–93.
15 Dodd N, Mansfield E, Carey M, Oldmeadow C. Prevalence of appropriate colorectal cancer screening and preferences for receiving screening advice among people attending outpatient clinics. *Aust N Z J Public Health*, 2018 Aug;42(4):334–9.

16 Carroll JC, Campbell-Scherer D, Permaul JA, Myers J, Manca DP, Meaney C, et al. Assessing family history of chronic disease in primary care: prevalence, documentation, and appropriate screening. *Can Fam Physician*. 2017;63(1):e58–67.

17 Walker JG, Bickerstaffe A, Hewabandu N, Maddumachchi S, Dovetty JG, Jenkins M, et al. The CRISP colorectal cancer risk prediction tool: an exploratory study using simulated consultations in Australian primary care. *BMJ Med Inform Decis Mak*. 2017;17(1):13.

18 Courtney RJ, Paul CL, Sanson-Fisher RW, Macrae FA, Carey ML, Attia J, et al. Colorectal cancer risk assessment and screening recommendation: a community survey of healthcare providers’ practice from a patient perspective. *BMCFamily Pract*. 2012;13(1):17.

19 Courtney RJ, Paul CL, Sanson-Fisher RW, Macrae FA, Carey ML, Attia J, et al. Individual- and provider-level factors associated with colorectal cancer screening in accordance with guideline recommendation: a community-level perspective across varying levels of risk. *BMCPublic Health*, 2013;13(1):248.

20 Kl bunde CN, Vernon SW, Nadel MR, Breen N, Seifl IC, Brown ML. Barriers to colorectal cancer screening: a comparison of reports from primary care physicians and average-risk adults. *Med Care*. 2005;43(9):939–44.

21 Hewitson P, Glassi ou P, Irwig L, Towler B, Watson E. Screening for colorectal cancer using the faecal occult blood test, Hemoccult, *Hemocult Cochrane Database Syst Rev*. 2007;2011(2):CD001216.

22 Felsen CB, Piasecki A, Ferrante JM, Ohman-Strickland PA, Crabtree BF. Colorectal cancer screening among primary care patients: does risk affect screening behavior? *J Community Health*. 2011;36(4):605–11.

23 Skinner CS, Halm EA, Bishop WP, Ahn C, Gupta S, Farrell D, et al. Impact of risk assessment and tailored versus nontailored risk information on colorectal cancer testing in primary care: a randomized controlled trial. *Cancer Epidemiol Biomarkers Prev*. 2015;24(10):1523–30.

24 Sarfaty M, Wender R. How to increase colorectal cancer screening rates in practice. *CA Cancer J Clin*. 2007;57(6):354–66.

25 Nease DF Jr., Ruffin MT 4th., Klinkman MS, Jimbo M, Braun TM, Underwood JM. Impact of a generalizable reminder system on colorectal cancer screening in diverse primary care practices: a report from the prompting and reminding at encounters for prevention project. *Med Care*. 2008;46(9 Suppl 1):S68–73.

26 Sequist TD, Zaslavsky AM, Marshall R, Fletcher RH, Ayanian JZ. Patient and physician reminders to promote colorectal cancer screening: a randomised controlled trial. *Arch Intern Med*. 2009;169(4):364–71.

27 Levin TR, Jamieson L, Burley DA, Reyes J, Oehrli M, Caldwell C. Organized colorectal cancer screening in integrated health care systems. *Epidemiol Rev*. 2011;33:101–10.

28 Guirguet C, Muñoz-Ortiz L, Burón A, Rivero I, Grau J, Vela-Vallespi C, et al. Alerts in electronic medical records to promote a colorectal cancer screening programme: a cluster randomised controlled trial in primary care. *Br J Gen Pract*. 2016;66(648):e843–90.

29 Dunlop K, Barlow-Stewart K. “Start the conversation”: the New South Wales (Australia) family health history campaign. *Public Health Genomics*. 2010;13(3):301–9.

30 Cuddihy E, Spyridakis JH. The effect of visual design and placement of intra-article navigation schemes on reading comprehension and website user perceptions. *Comput Hum Behav*. 2012;28(4):1399–409.

31 Sutcliffe A, Namoun A. Predicting user attention in complex web pages. *Behav Inf Technol*. 2012;31(7):679–95.

32 Giroldi E, Veldhuijzen W, Dijkman A, Rozeestraten M, Muris J, van der Vleuten C, et al. How to gather information from talkative patients in a respectful and efficient manner: a qualitative study of GPs’ communication strategies. *Fam Pract*. 2016;33(1):100–6.

33 Solomon BL, Whitman T, Wood ME. Contribution of extended family history in assessment of risk for breast and colon cancer. *BMCFam Pract*. 2016 Sep;17(1):126.

34 Cockburn J, Paul C, Tzelepis F, McElduff P, Carroll JC, Campbell-Scherer D, Permaul JA, et al. The effect of visual design and placement of intra-article navigation schemes on reading comprehension and website user perceptions. *Behav Inf Technol*. 2012;31(7):679–95.

35 Knox SA, Chondros P. Observed intra-cluster correlation coefficients in a cluster survey sample of patient encounters in general practice in Australia. *BMCMed Res Methodol*. 2004;4(1):30.

36 Australian Bureau of Statistics. Socioeconomic Index for Areas (SEIFA), 2011. In: *Statistics ABo*, editor. Available from: http://www.abs.gov.au/austats/abs@.nsf/Deta ils/2033.0.55.0012011 (accessed July 15, 2022).

37 Westfall P, Young S. Resampling-based multiple testing: examples and methods for p value adjustment. New York: Wiley; 1993.

38 Lowery JT, Horick N, Kinney AV, Finkelstein DM, Garrett K, Haile RW, et al. A randomized trial to increase colonoscopy screening in members of high-risk families in the colorectal cancer family registry and cancer genetics network. *Cancer Epidemiol Biomarkers Prev*. 2014;23(4):601–10.

39 Haas JS, Baer HJ, Eibensteiner K, Klinger EV, St Hilare S, Getty G, et al. A cluster randomized trial of a personalized multi-condition risk assessment in primary care. *Am J Prev Med*. 2017;52(1):100–5.

40 Foo W, Young JM, Solomon MJ, Wright CM. Family history? The forgotten question in high risk colorectal cancer patients. *Colorect Dis*. 2009;11(5):450–5.

41 Carey M, Sanson-Fisher R, Macrae F, Cameron E, Hill D, D’Este C, et al. Can a print-based intervention increase screening for first degree relatives of people with colorectal cancer? A randomised controlled trial. *Aust N Z J Public Health*, 2016;40(6):582–7.

42 Carey M, Sanson-Fisher R, Macrae F, Cameron E, Hill D, D’Este C, et al. Improving adherence to colorectal cancer surveillance guidelines: Results of a randomised controlled trial. *BMCCanc*. 2017;17(1):106.

43 Symonds EL, Simpson K, Coats M, Chaplin A, Saxy K, Sandford J, et al. A nurse-led model at public academic hospitals maintains high adherence to colorectal cancer surveillance guidelines. *Med J Aust*. 2018;208(11):492–6.

44 Ouar krim DA, Boussioutas A, Lockett T, Hopper JL, Jenkins MA. Cost-effectiveness of family history-based colorectal cancer screening in Australia. *BMCCancer*. 2014;14:261.

45 Australian Prudential Regulation Authority 2018. Private Health Insurance Statistical Trends 2018. Available from: https://www.apra.gov.au/sites/default/files/private_health_insurance_quarterly_statistics_december_2018.pdf (accessed July 15, 2022).

46 Australian Bureau of Statistics. *Australian census of population and housing*, 2016.

47 Madlensky L, McLaughlin J, Goel V. A comparison of self-reported colorectal cancer screening with medical records. *Cancer Epidemiol Biomarkers Prev*. 2003;12(7):656–9.

48 Schenck AP, Kl bunde CN, Warren JL, Peacock S, Davis WW, Hawley ST, et al. Data sources for measuring colorectal endoscopy use among Medicare enrollees. *Cancer Epidemiol Biomarkers Prev*. 2007;16(10):2118–27.