Behavioural challenges associated with Risk-Adapted Cancer Screening

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Ethical Statement

This commentary did not involve any primary data collection or any other involvement by human participants.

Abstract

Cancer screening programmes have a major role in reducing cancer incidence and mortality. Traditional internationally-adopted protocols have been to invite all 'eligible individuals' for the same test at the same frequency. However, as highlighted in Cancer Research UK's 2020 strategic vision, there are opportunities to increase effectiveness and cost-effectiveness, and reduce harms of screening programmes, by making recommendations on the basis of personalised estimates of risk. In some respects, this extends current approaches of providing more intensive levels of care outside screening programmes to individuals at very high risk due to their family history or underlying conditions. However, risk-adapted colorectal cancer screening raises a wide range of questions, not only about how best to change existing programmes but also about the psychological and behavioural effects that these changes might have. Previous studies in other settings provide some important information but remain to be tested and explored further in the context of colorectal screening. Conducting behavioural science research in parallel to clinical research will ensure that risk-adapted screening is understood and accepted by the population that it aims to serve.

Main body

Cancer screening programmes have a major role in reducing cancer incidence and mortality. Traditional internationally-adopted protocols have been to invite all 'eligible individuals' for the same test at the same frequency. However, as highlighted in Cancer Research UK's 2020 strategic vision, there are opportunities to increase effectiveness and cost-effectiveness, and reduce harms of screening programmes, by making recommendations on the basis of personalised estimates of risk.[1] In some respects, this extends current approaches of providing more intensive levels of care outside screening programmes to individuals at very high risk due to their family history or underlying conditions.

The Bowel Cancer Screening Programme (BCSP) in England currently invites all men and women aged 60 to 74 years old to complete a biennial Faecal Immunochemical Test (FIT) followed by a referral for colonoscopy for the small proportion of participants with a positive result.[2,3] As an example of how a risk-adapted approach may work in practice, the quantitative result from FIT allows the threshold for referral for colonoscopy or interval between FIT tests to be adjusted based on the specific result or the result in combination with past screening history and/or other personal characteristics.[4] For example, compared with a single FIT threshold, using a neural network model that combines age, sex, level of deprivation and previous screening history with FIT results to determine whether individuals are offered colonoscopy, is estimated to result in 586 additional advanced adenomas being detected for every 1 million people invited to screening.[5] On-going work focusing on surveillance has similarly demonstrated that the probability of adenoma detection at first post-polypectomy surveillance colonoscopy varies with individual level characteristics, highlighting the potential to improve the efficiency of surveillance within the programme by harnessing this additional data.[6]

Determining initial eligibility for screening based on estimates of risk may also have the potential to deliver a more favourable ratio of costs and harms to benefits than fixed ages. A recent modelling study estimated that using a risk model with an area under the receiver operating characteristic curve (AUROC) of 0.72 and a threshold for starting invitations for biennial FIT screening set such that the population mean screening start age was approximately age 60 would result in fewer CRC cases and fewer CRC deaths compared with inviting all individuals at age 60 without using significant additional screening resources.[7] That approach is also estimated to have a 96% probability of being more cost-effective than inviting all individuals at age 60, in part because it could maximise diagnostic yield within the limits of a finite colonoscopy resource by utilising additional information, some of which is routinely available. The benefits of such a risk-adapted approach are reduced with

risk models with poorer discrimination and lower AUROCs, with an AUROC of 0.65 appearing to be the threshold above which benefits are seen both in terms of cost-savings and health outcomes. Less benefits is also seen when the threshold for further testing after the FIT test is higher and when compared with inviting all individuals at younger ages. While the uptake of screening for individuals was considered to vary by age, sex, sociodemographic deprivation and prior response to screening, no effect of the risk stratified approach on uptake was incorporated. That analysis also did not include the additional cost of performing the risk assessment, instead estimating that up to £114 could be spent on risk assessment and the risk-adapted approach remain cost-effective. This cost of risk assessment is important, with other modelling studies demonstrating that the cost-effectiveness of risk-adapted approaches is highly dependent on the cost of determining risk[8] In a modelling study based on the screening programme in Australia, for example, personalised screening was only cost-effective when these costs were less than $AUD 48 (£26), considerably less than the likely costs in practice. In that analysis though, the population was only categorised into five risk groups and in Australia a positive FIT requires a consultation with a primary care provider to discuss test results and obtain a referral for colonoscopy so the costs are not directly comparable to other bowel cancer screening programmes, such as the programme in England, where referral for colonoscopy is handled within the screening programme at marginal additional cost. A similar analysis based on a US cohort estimated that risk-adapted screening could become cost-effective if the AUROC value was greater 0.65, the cost of risk assessment less than $141 (£102), or the introduction of risk-adapted screening would lead to a 5% increase in screening participation.[9]

While risk models with an AUROC close to 0.65 exist,[10] the cost and logistics of the risk assessment process remain uncertain and whether these hypothesised benefits will be seen in practice is yet to be demonstrated in empirical studies. In parallel, an important range of psychological questions arise, which will affect the efficacy of this modified approach to screening (Table 1). These psychological questions have in the past often been forgotten but there is increasing recognition of the importance of addressing these aspects.[1]

Acceptability of risk assessment

There is evidence that many people take for granted that risk assessment (a necessary precursor of risk-adapted screening) is advantageous. UK studies have shown that public attitudes are generally supportive towards at least some forms of cancer risk assessment and personalised screening: 85% of women stated they would be likely to take up genetic testing for ovarian cancer risk[10] and 94% would take up risk assessment for breast cancer.[11] Studies in other countries have found similar results; a majority (80%) of participants in a sample of Dutch women were interested in their breast

cancer risk[12] and an even larger majority (94%) of members of the public in Sweden stated that they were interested in knowing their risk of breast or prostate cancer.[13]

These findings suggest that applying the same principles to colorectal cancer screening would be well received. However, as well as not asking directly about risk adaptive colorectal cancer screening, in common with much survey research, these studies had low response rates (18.4 to 57%). Respondents were also often outside the age ranges for current screening[10] or from only those attending screening[11], casting some doubt about the representativeness of study samples to the relevant population.

Data on the acceptability of risk assessment within the context of colorectal cancer screening are therefore limited. Innovative alternative methods such as co-production where members of the public work together with service providers to design better healthcare may be highly relevant in trying to optimise ways in which to educate the public about risk assessment and empower people to make informed choices. Such a process which would seek out views from lesser heard groups would be instrumental in ensuring equal representation across the full range of the target population. .

Important topics of research for such studies include assessing both people's willingness to allow sharing of data already collected by the NHS and willingness to actively complete other forms of risk assessment via self-report questionnaires or genetic testing. The ecological validity of this research will depend on the ability to educate people about how information relating to them may be used, with whom it may be shared, for how long it may be stored, and how it may affect any other aspect of their healthcare or everyday life (e.g., impact on employability and life insurance). The way this information is communicated will benefit from input by key stakeholders. Careful surveillance of participation across all socioeconomic and ethnic groups will also be needed if risk assessments are implemented in order to assess whether positive attitudes expressed in hypothetical surveys are reflected in actual participation behaviour and whether these are similar across population subgroups.[14] Here it will be vital that these epidemiological analysis is supported by data being made available on peoples' background to ensure that the introduction of more personalised regimes based on more complex recommendation does not lead to a widening of the gap in uptake of CRC screening by SES and ethnicity.

Comprehension of risk assessment

It is likely to be challenging to communicate the results of risk assessment in a way that makes their meaning and implications clear to lay individuals. The general population does not easily understand

key concepts around risk, with lay perceptions often being resistant to change and differing substantially from those of experts.[15-16] One notable study assessed the effects of providing information on estimated 10-year breast cancer risk to women invited to the NHS Breast Screening Programme: 23% of participants given information on their risk erroneously believed that the results indicated that they "definitely [did] not have breast cancer" and 11% believed they were "likely to develop breast cancer" (despite being at no more than moderate risk).[17] Relatedly, a large proportion of people continue to overestimate their risk after feedback.[18] These findings highlight the complexities of explaining risk information in a way that is intelligible to the general population, and hence sufficiently meaningful to be acted upon when deciding on future screening and other health behaviours.

Discussion groups (e.g.[19]) and experimental surveys (e.g.[20]) could be used to test whether visual aids such as icon arrays may be an effective method of explaining these issues.[21] An additional complication of some potential forms of risk-adapted colorectal screening is that they may offer risk estimates for a single point in time in order to gauge suitability for subsequent colonoscopy; this contrasts with many previous studies, in which estimates are for lifetime risk of cancer. Participants may not make a clear distinction between these two forms of risk and have misperceptions about their feedback, such as misinterpreting a 'low-risk' result as having implications for future risk. A good understanding of and trust in risk assessment will be essential to ensure acceptability of and adherence with risk-adapted approaches to screening. This could be tested using a rigorous experimental medicine approach in which different ways of communicating risks could be compared using key outcome metrics such as risk perception, comprehension, ability to make an informed choice.

Effects of risk-adaptive screening on uptake

Previous reviews have found evidence that, on average, personalised risk feedback has either limited or no overall effect on subsequent screening uptake.[22,23] However, few studies in those reviews reported uptake by risk status, potentially overlooking important differences. For example, a major study on uptake of risk-adapted breast screening found participation was 99% among women at high risk following their next screening invitation, higher than for women at low-risk (81%), which was comparable to that of women who did not receive risk feedback (78%).[24]

Similar findings have been reported in studies of public attitudes towards hypothetical risk-adapted kidney cancer screening: 85% reported being more likely to take up screening if at high risk whereas being given a low risk result was not associated with lower intentions to take up screening.[25] In addition, a majority of participants asked about willingness to take up colorectal screening stated

that they would accept the offer if at 1%, 3%, or 5% 15-year risk, although participants were more likely to be willing to take up an offer if at higher risks.[26]

There are also encouraging findings to suggest that receiving information on risk status does not cause large negative reactions. For example, Emmons et al.[27] found that 33% of participants reported lower worry after completing colorectal cancer risk assessment and Trevena et al.[28] found no difference in anxiety between targeted colorectal cancer risk information and generic information on colorectal cancer screening.

However, there is evidence that screening participants may have some adverse reactions: Emmons et al.[27] report that 17% experienced more worry and the parallel study by French et al.[17] described that although effects were small, women told they were at higher (i.e. moderate) risk of breast cancer reported greater anxiety, worry, perceived risk and lower satisfaction compared with women who received lower risk results. It will, therefore, be necessary to monitor patient-reported experiences to monitor the psychological consequences of risk assessment particularly to avoid negative psychological consequences that might arise from being categorised as above average risk. Relatively patient reported outcomes including subsequent health behaviours should be monitored in all groups to ensure that risk assessment of CRC does not have undesirable consequences in terms of other health behaviours. For example, it would be important to ensure that low risk groups still follow guidance on early CRC diagnosis and take up opportunities for CRC screening, and do not inadvertently increase their CRC risk through lifestyle. Early clinical cohorts would therefore benefit from regular behaviour questionnaires as part of their follow up.

Public attitudes towards risk-adaptive screening

A consistent finding from research in other screening contexts is that members of the public are generally positive towards the possibility of being offered more screening but are concerned about the possibility of less screening. For example, Meisel et al.[29] report that although 85% of women were in favour of more frequent breast screening (for those at high risk), only 59% were in favour of less frequent screening for those at low risk. Findings have been similar in the context of cervical screening[30] and in other countries (e.g. The Netherlands).[19]

In the case of screening colonoscopy in the US, 29% of participants surveyed were not comfortable with ending “low value” colorectal screening and 24% thought it unreasonable to use risk calculators to assess whether screening would be low value.[31] This stated resistance in research studies is borne out in adverse public responses to increasing the age for first screen and extending the cervical screening interval in Australia.[32] This suggests that the prospect of reducing screening frequency in

colorectal cancer screening may be received poorly: the rationale for doing so would need to be communicated carefully and the advantages of a personalised approach may need to be promoted in order to maintain uptake. A recent study assessing women's preferences for risk-adapted screening with longer breast screening intervals for women at low risk showed that participants were less likely to state a preference for a risk-adapted breast screening programme with potentially longer intervals if they rated their perceived susceptibility to breast cancer as higher. This suggests that communication strategies need to be identified that are sensitive to differences between invitees in terms of their subjective interpretation of their risk status.[33] Understanding people's preferences for different intervals, and modalities could also be explored further through in-depth interviews and more systematic discrete choice experiments which could be used to test the extent to which people are willing to trade different aspects of CRC screening e.g. convenience for other characteristics such as test sensitivity. These studies could then ensure high levels of acceptance and uptake and thereby potentially reduce the potential for widening inequalities if studies are performed with representative samples which include lesser heard groups.

Conclusion

Any changes towards risk-adapted colorectal cancer screening will raise a wide range of questions, not only about how best to change existing programme but also about the psychological and behavioural effects that these changes might have. Most of the current research suggests that risk-adapted screening would be acceptable, particularly where recommendations would lead to more frequent or more intense screening. However, current evidence is limited to surveys with low response rates and would benefit from research testing acceptability and uptake of risk adapted screening as part of early clinical studies.

Table 1 - Examples of future psychological and behavioural research areas for risk-adapted colorectal cancer screening

Topics	*Research methods*
• Ascertain uptake of real-world risk assessment and other measures of acceptability among the eligible population. • Explore the facilitators and barriers of risk assessment (e.g., concerns relating to data sharing). • Determine methods of explaining risk assessment in ways that maximise lay individuals' comprehension and capability to make informed choices about participation. • Determine methods of disseminating information on risk-adapted colorectal cancer screening that effectively explains the rationale for some individuals receiving fewer invitations screening, in order to mitigate concerns and maintain trust in the programme.	• Epidemiological analysis of uptake. • Patient-reported experience measures to assess acceptability of risk-adapted cancer screening in clinical studies • Population-representative surveys to assess attitudes towards risk adapted CRC screening • Experimental surveys to compare the effectiveness of different graphic formats on risk comprehension. • Discrete choice experiments to understand people's stated preferences for different screening intervals and modalities. • Interviews with key stakeholders and members of the public to gain in-depth understanding of perceptions and attitudes • Co-production workshops and citizen jurys to develop communication materials, and policy recommendations.

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