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ORIGINAL ARTICLE

The role of defensive information processing in population-based colorectal cancer screening uptake

Linda Sharp PhD²

Nicholas Clarke PhD¹ Louise Haves PhD² Amy McQueen PhD^{3,4} Pamela Gallagher PhD¹ | Patricia M. Kearney MD⁵ | Deirdre McNamara MD⁶ Colm A. O'Morain MD⁷ | Christian von Wagner PhD⁸ | Therese Mooney PhD⁹ |

Correspondence

Nicholas Clarke, School of Psychology, Dublin City University, Glasnevin, Dublin 9, Ireland. Email: nicholas.clarke@dcu.ie

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Abstract

Background: Internationally, colorectal cancer screening participation remains low despite the availability of home-based testing and numerous interventions to increase uptake. To be effective, interventions should be based on an understanding of what influences individuals' decisions about screening participation. This study investigates the association of defensive information processing (DIP) with fecal immunochemical test (FIT)-based colorectal cancer screening uptake.

Methods: Regression modeling of data from a cross-sectional survey within a population-based FIT screening program was conducted. The survey included the seven subdomains of the McQueen DIP measure. The primary outcome variable was the uptake status (screening user or nonuser). Multivariable logistic regression was used to estimate the odds ratio (OR) for screening nonuse by DIP (sub)domain score, with adjustments made for sociodemographic and behavioral factors associated with uptake.

Results: Higher scores (equating to greater defensiveness) on all DIP domains were significantly associated with lower uptake in the model adjusted for sociodemographic factors. In the model with additional adjustments for behavioral factors, the suppression subdomains of "deny immediacy to be tested" (OR, 0.53; 95% confidence interval [CI], 0.43-0.65; p < .001) and "self-exemption" (OR, 0.80; 95% CI, 0.68–0.96; p < .001) independently predicted nonuse of FIT-based screening.

Conclusions: This is the first study outside the United States that has identified DIP as a barrier to colorectal cancer screening uptake, and it is the first focused specifically on FIT-based screening. The findings suggest that two suppression barriers,

See editorial on pages 000-000, this issue.

The first two authors contributed equally to this article.

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¹School of Psychology, Dublin City University, Dublin, Ireland

²Population Health Sciences Institute, Newcastle University, Newcastle Upon Tyne, UK

³Health Communication Research Laboratory, Brown School, Washington University in St. Louis, St. Louis, Missouri, USA

⁴Division of General Medical Sciences, School of Medicine. Washington University in St. Louis, St. Louis, Missouri, USA

⁵School of Public Health, University College Cork, Cork, Ireland

⁶Department of Clinical Medicine, Adelaide and Meath Hospital, Dublin, Ireland

⁷Faculty of Health Science, Trinity College Dublin, Dublin, Ireland

⁸Department of Epidemiology and Public Health, University College London, London, UK

⁹National Screening Service, Dublin, Ireland

namely denying the immediacy to be tested and self-exempting oneself from screening, may be promising targets for future interventions to improve uptake.

KEYWORDS

colorectal cancer screening, defensive information processing, fecal immunochemical test, participation, uptake

INTRODUCTION

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Stool testing has been the frontline screening method within population-based colorectal cancer screening programs for more than a decade.¹⁻⁴ The fecal immunochemical test (FIT), with improved sensitivity and uptake over its predecessor, the fecal occult blood test, is recommended as the test of choice.^{5,6} However, despite the availability of effective home-based tests, uptake remains low (<50%) in many settings.⁷⁻⁹

Considerable potential exists for reducing cancer mortality through increased screening uptake. Internationally, various strategies to improve uptake have been tested. Some studies report increases for interventions related to screening processes (e.g., advance notification letters and postal mailing of home-based testing kits), 10,11 and others have found increases when home tests are sent with physician endorsements or reminders. 12 A review of intervention trials based in the United States found that patient navigation and fecal blood test outreach were the most frequent and promising interventions to increase uptake, 13 whereas another review observed significant but small effect sizes for interventions to increase colorectal cancer screening uptake. 14 Notably, the majority of studies in the latter review were also based in the United States, where the health care system was found to moderate intervention effectiveness. 14 An important limitation of existing studies, however, is the widespread failure to design interventions based on evidence of what influences individuals' decision-making about screening participation and/or relevant theory, with both considered prerequisites for effective interventions.15

Various emotional and attitudinal barriers to colorectal cancer screening participation, including fatalism, a fear of cancer, a desire not to know if one has cancer, disgust, embarrassment, and beliefs that screening will be uncomfortable or inconvenient, have been identified. Other potential emotional and behavioral responses are emerging but have received less attention; one example is defensive information processing (DIP).

DIP is defined as a means by which individuals reduce negative psychological affect when they are faced with real or imagined threats (e.g., cancer risk), including information or behavior that is inconsistent with their preferred view of the self.²⁰ A DIP measure developed by McQueen et al.²⁰ comprises seven subscales reflecting four domains or stages of DIP: (1) attention avoidance (reducing risk awareness by avoidance), (2) blunting (active mental disengagement through avoidance and accepted denial), (3) suppression (acknowledging others' risk but avoiding personal inferences through self-

exemption beliefs), and (4) counterargumentation (arguing against the evidence). Among US adults, greater defensive processes were consistent and strong predictors of lower participation in opportunistic colorectal cancer screening by colonoscopy, sigmoidoscopy, or fecal occult blood testing. Using a theoretically informed qualitative investigation within a population-based colorectal cancer screening program, we previously identified DIP as a possible explanation for resistance to, and rejection of, FIT-based screening.²¹ Our finding was coherent with growing evidence suggesting that defensive reactions to health messages (messages primarily aimed at improving health and healthy behaviors) may lead to rejection of these messages when someone is faced with a potential cancer diagnosis.²²

DIP may be culturally or contextually specific, but to date, the roles of all four domains of DIP in colorectal cancer screening uptake have not been investigated outside the United States, within organized screening programs, or in relation to FIT-based screening.

We undertook a comprehensive quantitative investigation of the role of DIP in uptake in a FIT-based population-based screening program with a particular focus on identifying which DIP domains may be most influential.

MATERIALS AND METHODS

The methods have been described in detail previously. ¹⁶ Briefly, we conducted a cross-sectional survey of individuals systematically invited to participate in a population-based FIT screening program in Dublin (Tallaght Hospital/Trinity College Dublin Colorectal Cancer Screening Programme [TTC-CRC-SP]) in 2008–2012. The TTC-CRC-SP was performed in a relatively deprived area of Dublin. Questionnaires were mailed to 7476 individuals in September 2015. The sample comprised all individuals who had been invited to participate in the screening program (over two screening rounds) but had declined (nonusers; n = 3738) and a random sample, stratified by sex, of individuals who had participated (users; n = 3738). After two reminders, 2299 individuals (1988 users [a 53% response rate] and 311 nonusers [an 8% response rate]) completed questionnaires. The study was approved by the research ethics committee of St James/Adelaide and Meath Hospital (REC Reference 2013/12/05).

The questionnaire, informed by the Theoretical Domains Framework²³ and our previous qualitative study,²¹ was designed to elicit respondents' views of factors shown to be associated with FIT uptake. We have previously reported that, in addition to sex and deprivation, stronger fatalistic beliefs, the belief that the test was

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disgusting or was tempting fate, and disagreement that cancer can be cured (among those younger than 65 years) were associated with lower uptake.¹⁶ In the analyses presented here, we explore the potential additional explanatory role for DIP in uptake.

Survey measures

The DIP measure contains seven subscales, with each measured on a five-point Likert scale (from 1 [strongly disagree] to 5 [strongly agree]): (1) opt-out informational (five items; e.g., "I avoid watching TV programs about cancer"), (2) opt-out behavioral (five items; e.g., "I don't go to a doctor unless it's really serious"), (3) blunting (three items; e.g., "I tend to avoid thoughts of bowel cancer"), (4) suppression (deny immediacy; four items; e.g., "I will wait to get tested for bowel cancer when I am not as busy"), (5) suppression (self-exemption; five items; e.g., "I don't need to be screened for bowel cancer because I have regular bowel movements"), (6) counterarguing (message rejection; eight items; e.g., "Few people get bowel cancer"), and (7) counterarguing (normalize the risk; three items; e.g., "I can't do everything that you're supposed to do for your health; it'd be a full time job").

Further variables included in this analysis were from the final model in our previous analysis. ¹⁶ The sociodemographic variables were age at survey completion (<65 years/≥65 years), sex, and arealevel deprivation category (each individual was assigned to a deprivation quintile based on the characteristics of his or her area of residence ²⁴). Relationship status was divided into two categories for analysis: cohabiting relationship or not.

Cancer fatalism was measured with the 15-item Powe Fatalism Inventory²⁵ (the belief that death is inevitable when cancer is present) and was amended to refer to colorectal cancer. Item responses (agree [1]/disagree [0]) were summed; higher scores indicated greater cancer fatalism ($\alpha=0.86$). A single belief about cancer was included from the Awareness and Beliefs About Cancer questionnaire²⁶ ("Cancer can often be cured"); this was rated on a four-point response scale, which was reduced to two categories for analysis (agree/disagree). Negative emotional attitudes toward screening included two items²⁷: "doing the test was disgusting" and "doing the test was tempting fate." These were rated on a four-point scale which were then reduced to two categories (agree/disagree) for analysis.

Statistical analysis

The construct validity of the DIP subscales has previously been reported in a US population. 20,28 We conducted a confirmatory factor analysis to verify the factor structure in our data set. We used Pearson correlation to explore associations between subscales. The Cronbach α was computed as a measure of internal reliability for each subscale. Mean DIP subscale scores for FIT users and nonusers were compared with t-tests. We conducted logistic regression analyses to assess associations between each DIP subscale (individually

and together) and FIT use, with adjustments made for age, sex, and deprivation. To investigate the additional influence of the DIP subscales on uptake beyond previously identified determinants, we tested the effect of adding those DIP subscales that remained statistically significant when we adjusted for other DIP subscales to our previous multivariable model (which included sex, area-level deprivation, the influence of a partner, fatalistic beliefs, an interaction between the belief that the test was disgusting and the belief that taking the test was tempting fate, and an interaction between the belief that cancer could not be cured and age). Likelihood ratio tests were used to assess whether the DIP variables made a significant contribution to the model. Model fit was assessed with the Hosmer and Lemeshow test, and variable inflation factors were obtained to check for collinearity.

RESULTS

The characteristics of the survey respondents are shown in Table 1. Overall, approximately equal proportions of men and women responded, although a higher proportion of nonusers who responded were men (59%) rather than women (41%). The proportion of nonusers aged 65 years or older who responded was lower than the proportion who responded in the <65-year age group. Overall, 87% of the respondents were from relatively deprived socioeconomic backgrounds.

Our confirmatory factor analysis verified that the seven-factor structure of the DIP measure fit the data well in our study population ($\chi^2(df)=3616,\ p<.001,$ comparative fit index = 0.930, root mean square error of approximation = 0.063 [95% confidence interval, 0.061-0.065], standardized root mean square residual = 0.034). The individual items within each DIP subscale were strongly related to the overall scores for the subscale; standardized factor loadings were between 0.67 and 1.1 (Table S1). Internal consistency was very good for each subscale (Table S1).

Mean scores for each of the DIP subscales for nonusers and users of FIT are presented in Table 1. Nonusers scored significantly higher on all subscales, and this indicated stronger agreement with the statements that compose each subscale (i.e., greater defensiveness). The individual subscales were all moderately correlated with one another (correlation coefficients, 0.26–0.65; Table S2).

Table 2 shows the results of a series of logistic regression analyses examining the association between each subscale separately and screening uptake, with minimal adjustments made for age, sex, and area deprivation. An increase in the score of each of the subscales (greater defensiveness) was associated with reduced odds of participating in FIT-based screening. The suppression subscales (deny immediacy and self-exemption) and the counterarguing message rejection subscale were most strongly associated with lower screening uptake.

When all of the subscales were included in the same minimally adjusted model, only the suppression subscales remained significantly associated with lower screening uptake (Table 2).

TABLE 1 Participant characteristics and mean scores for DIP subscales of users and nonusers of the FIT-based uptake survey (N = 2299)

| Characteristics | Total | | Users | | Nonusers | | |
|--------------------------|-------|-------|-------|-------|----------|-------|----------------|
| | No. | % | No. | % | No. | % | p ^a |
| Sex | | | | | | | |
| Female | 1101 | 47.90 | 974 | 49.00 | 127 | 40.80 | .007 |
| Male | 1198 | 52.10 | 1014 | 51.00 | 184 | 59.20 | |
| Age | | | | | | | |
| <65 years | 1133 | 50.10 | 948 | 48.60 | 182 | 59.50 | <.001 |
| ≥65 years | 1126 | 49.90 | 1002 | 51.40 | 124 | 40.50 | |
| Area deprivation | | | | | | | |
| Very disadvantaged | 206 | 9.00 | 161 | 8.10 | 45 | 14.50 | <.001 |
| Disadvantaged | 640 | 27.80 | 524 | 26.40 | 116 | 37.30 | |
| Marginally below average | 1156 | 50.30 | 1034 | 52.00 | 122 | 39.20 | |
| Marginally above average | 241 | 10.50 | 218 | 11.00 | 23 | 7.40 | |
| Affluent | 56 | 2.40 | 51 | 2.50 | 5 | 1.60 | |
| | Total | | Users | | Nonusers | | |
| DIP subscales | Mean | SD | Mean | SD | Mean | SD | p ^a |
| Opting out | | | | | | | |
| Informational | 2.01 | 0.99 | 1.95 | 0.95 | 2.44 | 1.10 | <.001 |
| Behavioral | 2.70 | 1.03 | 2.65 | 1.01 | 3.08 | 1.05 | <.001 |
| Blunting | | | | | | | |
| Blunting | 2.77 | 1.11 | 2.72 | 1.09 | 3.11 | 1.18 | <.001 |
| Suppression | | | | | | | |
| Self-exemption | 2.03 | 0.96 | 1.94 | 0.91 | 2.6 | 1.06 | <.001 |
| Deny immediacy | 1.91 | 0.80 | 1.83 | 0.75 | 2.44 | 0.89 | <.001 |
| Counterarguing | | | | | | | |
| Message rejection | 1.96 | 0.75 | 1.91 | 0.73 | 2.31 | 0.81 | <.001 |
| Normalize the risk | 2.68 | 1.03 | 2.64 | 1.03 | 2.92 | 1.01 | <.001 |

Abbreviations: DIP, defensive information processing; FIT, fecal immunochemical test.

The results of adding the DIP suppression subscales to our previously reported multivariable model for FIT uptake (including sex, area deprivation, fatalistic beliefs, the belief that the test was disgusting, the belief that taking the test was tempting fate, disagreement that cancer can be cured among those younger than 65 years, and the influence of a partner) are shown in Table 2. Both suppression subscales were statistically significantly associated with FIT nonuse, and this indicated that they made independent contributions to uptake. A one-unit increase in the suppression self-exemption subscale was associated with 20% lower odds of screening uptake; a one-unit increase in the suppression deny immediacy subscale was associated with 47% lower odds of screening uptake. The final model had adequate fit according to the Hosmer and Lemeshow test (p=.149), and there was little collinearity (the variance inflation factors were all below 3.4).

DISCUSSION

After accounting for sociodemographic determinants of colorectal cancer screening uptake, we found that all DIP subscales had a statistically significant negative association with screening uptake; higher defensiveness scores were associated with lower odds of FIT-based screening participation. These results support previous findings and highlight the important influence of DIP on screening participation. Once other previously identified behavioral influences on uptake were taken into account, only the two subscales of the suppression domain remained statistically significant. Our results suggest that both kinds of suppression—self-exemption (screening is not relevant or important for the individual) and denying immediacy (screening is not an immediate concern)—are independent influences on nonparticipation in FIT-based screening.

 $^{^{}a}p$ values were obtained from χ^{2} tests and t-tests for differences between users and nonusers.

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TABLE 2 Adjusted ORs for FIT screening participation in FIT-based colorectal cancer screening by DIP subscales with 95% CIs and p values

| | Outcome: FIT-based colorectal cancer screening | | | | | | | | | | |
|-------------------------|--|-----------|----------------|--|-----------|----------------|--|-----------|----------------|--|--|
| Predictors | Each subscale considered individually ^a | | | Subscales mutually adjusted ^b | | | Subscales mutually adjusted and added to previous multivariable model ^c | | | | |
| Defensiveness subscales | Adjusted OR | 95% CI | p ^d | Adjusted OR | 95% CI | p ^d | Adjusted OR | 95% CI | p ^d | | |
| Opting out | | | | | | | | | | | |
| Informational | 0.65 | 0.58-0.73 | <.001 | 0.89 | 0.76-1.05 | .163 | _ | _ | - | | |
| Behavioral | 0.69 | 0.61-0.78 | <.001 | 0.90 | 0.76-1.06 | .201 | _ | | _ | | |
| Blunting | | | | | | | | | | | |
| Blunting | 0.74 | 0.66-0.84 | <.001 | 1.17 | 0.99-1.39 | .064 | _ | _ | - | | |
| Suppression | | | | | | | | | | | |
| Self-exemption | 0.55 | 0.49-0.62 | <.001 | 0.70 | 0.59-0.82 | <.001 | 0.80 | 0.68-0.96 | <.001 | | |
| Deny immediacy | 0.44 | 0.38-0.51 | <.001 | 0.54 | 0.43-0.66 | <.001 | 0.53 | 0.43-0.65 | <.001 | | |
| Counterarguing | | | | | | | | | | | |
| Message rejection | 0.54 | 0.46-0.63 | <.001 | 1.00 | 0.78-1.28 | .972 | _ | - | _ | | |
| Normalize the risk | 0.78 | 0.69-0.88 | <.001 | 1.06 | 0.90-1.26 | .464 | _ | _ | _ | | |

Abbreviations: CI, confidence interval; DIP, defensive information processing; FIT, fecal immunochemical test; OR, odds ratio.

Given that only the suppression domain independently predicted nonuse of FIT, we might speculate that FIT screening is perceived to be of limited relevance, or not immediately important, to invitees because they are not currently experiencing bowel issues (in the belief it will not happen to them-or consideration of future consequences). It may be that suppression is the most important DIP and should inform future intervention design, but further investigation is needed. The context in which someone learns about, is recommended to get, and is actually asked to complete a screening test may evoke different DIP. For example, it may have been harder for invitees to completely avoid the invitation (opting out) and to ignore thoughts of cancer (blunting) once they had received the FIT kit and letter in the mail. Additionally, suppression may be a more dominant response to mailed interventions, whereas counterarguing may be more influential during in-person encounters in which a patient feels pressure from health care providers, or close others, who persuasively recommend screening. Future research should investigate whether suppression is a stronger influence in comparison with other DIP or whether the dominant DIP differs across screening contexts and jurisdictions with different models of screening provision. For example, is suppression a weaker predictor of uptake in settings where health care professionals may have more opportunity to engage with patients and therefore intervene in suppression processes but perhaps prompt more counterarguing?

It was noteworthy that both suppression subscales were statistically significantly associated with uptake when fitted into the same model. Although correlated, the domains are distinct from one another, in that denying the immediacy to be tested focuses on putting the test off (i.e., "I will wait to get tested for colon cancer until..."), whereas self-exemption focuses specifically on refusal (i.e., "I don't need to be tested because..."). Although suppression defenses may act simultaneously in individuals, it is also possible that they may act separately; there may be distinct groups of nonscreeners in whom suppression operates in somewhat different ways. This has implications for the development and targeting of interventions to improve screening uptake. For example, future invitations could specifically target suppression beliefs to determine whether undermining one and/or both is sufficient to increase screening uptake or change the pattern of results observed in this study. Future measures of DIP could also attempt to categorize participants by their more dominant

The suppression self-exemption domain measures whether individuals endorse personal characteristics that exempt them from risk.²⁸ It specifically focuses on health and lifestyle-related items (not eating too much red meat, eating enough vegetables, getting regular exercise, and having regular bowel movements). The association of self-exemption with nonparticipation concurs with our previous qualitative work in that some nonusers reported that

^aAdjusted for sex, age, and deprivation.

^bMutually adjusted for all other DIP subscales and for sex, age, and deprivation.

^cMutually adjusted for included DIP subscales and further adjusted for sex, age (within an interaction term with the belief that cancer can be cured), deprivation, and significant covariates from our previous analyses: fatalistic beliefs, an interaction term between the belief that the test was disgusting and the belief that taking the test was tempting fate, an interaction term between age and disagreement that cancer can be cured, and the influence of a partner.

dLikelihood ratio tests for the contribution of the subscale to the relevant model.

screening was not essential for them because they had a healthy lifestyle or had no family history of bowel cancer. In the current study, the specific item "I don't need to be tested because I have regular bowel movements" (odds ratio, 0.69; 95% confidence interval, 0.54–0.86; p=.002) was associated with the lowest odds of FIT completion within the self-exemption subscale; again, this echoes our qualitative work in which nonusers believed that their risk was lower because they had frequent bowel motions. It may be worthwhile to consider this specific item in the context of message development.

In terms of denying immediacy, others have reported that those who take a short-term view of life, or think less about the future, may engage in more negative health behaviors. Our findings align with these observations and suggest that nonusers more often fail to consider future consequences of not taking part in screening. Wardle and Steptoe²⁹ found that both thinking less about the future and unhealthy lifestyle behaviors were linked to lower socioeconomic status. It is worth noting that our study was conducted in a relatively deprived population, our analysis was adjusted for deprivation as a measure of socioeconomic status, and deprivation was significantly related to lower uptake in this population.²⁴ In agreement with our findings regarding "denying immediacy," in Australia's bowel cancer screening program, rural residents were less likely to be adherent to screening; Goodwin et al. 30 reported that this was exacerbated by minimization of symptoms and a lack of consideration of future consequences of behavior in terms of preventative health measures. These observations suggest that encouraging consideration of future consequences of one's health may encourage greater uptake among those who may not perceive any urgency to screen for colorectal cancer. Additionally, messages sent with FIT that create a sense of urgency (e.g., highlighting the often asymptomatic nature of colorectal cancer) may prompt more timely completion and reduce tendencies to procrastinate.

Other recent studies have found associations between defensiveness and nonadherence to other types of cancer screening. In Norway (where population-based mammography screening programs exist), a survey (using a convenience sample) examining how psychological factors influence defensive avoidance of breast screening reported that women with a greater fear of breast cancer were more likely to engage in defensive processing to rationalize why they did not need mammography screening.31 In the United States, Lipkus et al.³² studied the reactions of participants nonadherent to screening, who were recruited via an online network panel. They found that these participants did not repeat back their risk estimate accurately immediately after receiving it and that those who were informed that they were at higher estimated risk were more likely to report a lower risk. This suggests that participants were using defensive strategies such as blunting, suppression, unrealistic optimism, and counterarguing to reduce a cancer diagnosis threat. Our study, therefore, adds to growing evidence of the importance of DIP in the rejection of health messages and cancer screening.

Implications

Population screening programs rely on high levels of participation, and facilitating easy access to tests alone (i.e., mailing FIT kits to eligible adults) has not guaranteed high completion rates. Understanding and addressing psychosocial barriers such as DIP is critical if we are to influence individuals' decisions to get screened and hence improve screening uptake. Crucially, emerging research suggests that DIP is potentially modifiable. Research has shown that narratives that temper negative influences on the intention to screen for colorectal cancer can reduce counterarguing DIP, 33 but novel messages and approaches may be needed to reduce suppression DIP. Future interventions should take into account that those who suppress the screening message may be from two distinct groups, both of which may be amenable to different behavior change-based interventions. Future interventions could, for example, prompt informed choice via educative "nudges,"34 which provide opportunities for individuals to reflect on their risk (self-exempters), their future health (immediacy deniers and self-exempters), and the benefits of screening. However, more examination is needed because some nudges may be problematic and potentially unethical.34

In an investigation of reasons for nonparticipation in a trial of colorectal cancer screening interventions, the authors reported that the most common barrier for not screening was avoidance (inattention and procrastination [both considered defensive processes]).³⁵ In the United States, Green et al.³⁵ tested the efficacy of a financial incentive to overcome screening avoidance or procrastination. Financial incentives led to increased FIT completion rates; the effect was greater among Medicaid-insured individuals, who are usually of lower socioeconomic status. These results suggest that it would be worthwhile to investigate financial (and other) incentives in order to address DIP in other settings and reduce procrastination, especially where equity in screening uptake is a concern.

There is a need to inform the public in general and higher risk groups in particular (via, perhaps, targeted information to males and those living in areas of greater deprivation) about colorectal cancer risk factors, the trajectory of the disease (typically slow-growing and asymptomatic until a late stage), and the fact that having a healthy lifestyle and regular bowel movements does not negate the need for screening. Providing colorectal cancer risk estimates to promote screening is not advised unless strategies are in place to curb defensiveness, especially among higher risk groups. Effective strategies are needed to encourage screening-eligible individuals, especially those who have never been screened, to have a broader and more open-minded perspective of the benefits of screening participation. ³²

Strengths and limitations

The strengths and limitations of this study have been described previously. ¹⁶ In brief, the major strength is that this is a theoretically

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informed investigation of factors influencing FIT uptake using verified screening records. The main limitation is the low response rate among nonusers (8%); as we have previously observed, the challenge in investigating screening participation is engaging with nonusers. We were unable to follow up with telephone reminders to non-respondents as had been done in a previous study to increase survey response rates among screening nonusers. We maximized the numbers of screening nonusers responding to the survey by approaching the entire nonuser group, but in light of the response rate, it is likely that those who took part in the survey are a self-selected group. However, comparing the survey participants and the entire screening program data set²⁴ (on age, sex, and deprivation) produced similar patterns and risk estimates.

In conclusion, DIP, particularly suppression in the form of denying immediacy or self-exemption, is a key barrier to organized FIT-based screening uptake. Suppressors who deny the immediacy to be screened may be amenable to behavioral interventions that nudge them to be screened. Suppressors who self-exempt themselves may require stronger educational and defensiveness-reducing interventions to encourage future screening participation.

AUTHOR CONTRIBUTIONS

Nicholas Clarke: Conceptualization, methodology, data curation, formal analysis, project administration, funding acquisition, writing-original draft, and writing-review and editing. Louise Hayes: Formal analysis, writing-original draft, and writing-review and editing. Amy McQueen: Writing-review and editing. Pamela Gallagher: Funding acquisition and writing-review and editing. Patricia M. Kearney: Methodology and writing-review and editing. Deirdre McNamara: Data curation and writing-review and editing. Colm A. O'Morain: Data curation and writing-review and editing. Christian von Wagner: Writing-review and editing. Therese Mooney: Writing-review and editing. Linda Sharp: Conceptualization, methodology, formal analysis, supervision, project administration, funding acquisition, and writing-review and editing.

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CONFLICTS OF INTEREST

Colm A. O'Morain reports acting as an independent contractor for Laboratorios Pfizer Ltda. Linda Sharp reports grants/contracts from Medtronic and 3D Matrix. Christian von Wagner reports intellectual property (copyright). The other authors made no disclosures.

ORCID

Nicholas Clarke https://orcid.org/0000-0001-8666-5449

Linda Sharp https://orcid.org/0000-0001-9515-1722

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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