Radiology

Detection of Extracolonic Pathologic Findings with CT Colonography: A Discrete Choice Experiment of Perceived Benefits versus Harms[1]

Andrew A. Plumb, MA, MRCP, FRCR
Darren Boone, MBBS, MRCS, FRCR
Heather Fitzke, BSocSci
Emma Helbren, MBChB, FRCR
Susan Mallett, DPhil
Shihua Zhu, MSc, PhD
Guiqing L. Yao, MSc, PhD
Nichola Bell, BSc
Alex Ghanouni, MSc
Christian von Wagner, PhD
Stuart A. Taylor, MBBS, MD, MRCP, FRCR
Douglas G. Altman, DSc
Richard Lilford, PhD, FRCOG, FRCP, FFPH
Steve Halligan, MBBS, MD, FRCP, FRCR

Purpose: To determine the maximum rate of false-positive diagnoses that patients and health care professionals were willing to accept in exchange for detection of extracolonic malignancy by using computed tomographic (CT) colonography for colorectal cancer screening.

Materials and Methods: After obtaining ethical approval and informed consent, 52 patients and 50 health care professionals undertook two discrete choice experiments where they chose between unrestricted CT colonography that examined intra- and extracolonic organs or CT colonography restricted to the colon, across different scenarios. The first experiment detected one extracolonic malignancy per 600 cases with a false-positive rate varying across scenarios from 0% to 99.8%. One experiment examined radiologic follow-up generated by false-positive diagnoses while the other examined invasive follow-up. Intracolonic performance was identical for both tests. The median tipping point (maximum acceptable false-positive rate for extracolonic findings) was calculated overall and for both groups by bootstrap analysis.

Results: The median tipping point for radiologic follow-up occurred at a false-positive rate greater than 99.8% (interquartile ratio [IQR], 10 to >99.8%). Participants would tolerate at least a 99.8% rate of unnecessary radiologic tests to detect an additional extracolonic malignancy. The median tipping-point for invasive follow-up occurred at a false-positive rate of 10% (IQR, 2 to >99.8%). Tipping points were significantly higher for patients than for health care professionals for both experiments (>99.8 vs 40% for radiologic follow-up and >99.8 vs 5% for invasive follow-up, both $P < .001$).

Conclusion: Patients and health care professionals are willing to tolerate high rates of false-positive diagnoses with CT colonography in exchange for diagnosis of extracolonic malignancy. The actual specificity of screening CT colonography for extracolonic findings in clinical practice is likely to be highly acceptable to both patients and health care professionals.

© RSNA, 2014

Online supplemental material is available for this article.

Radiology

Diagnostic tests used for cancer screening programs usually target a specific organ. However, when screening for colorectal cancer (CRC) by using computed tomographic (CT) colonography, extracolonic abdominal and pelvic tissues are imaged unavoidably, which potentially detects disease in organs other than the primary target. For example, a systematic review of 24 studies (1) estimated that approximately 20% of indeterminate renal masses detected with CT colonography ultimately were malignant. While some of these findings are clinically important, the majority are not. For example, the same systematic review (1) estimated false-positive diagnoses of extracolonic malignancy with CT colonography in 4.6% of men and 6.8% of women. Clarification often requires further investigations, including biopsy and even surgery, which may be worrisome, costly, and occasionally harmful, all for no ultimate benefit in most patients. Balancing benefit and

harm is important because further tests precipitated by extracolonic findings are common, occurring in 7%–11% of people who are screened after CT colonography (2–9). One series estimated average costs for additional tests at just under $100 per patient screened (6). However, evidence suggests that more asymptomatic cancers are detected beyond the colon than within it: a retrospective study (10) of 10 286 screened patients found that CT colonography depicted extracolonic malignancies in 0.35% versus CRC in 0.21%.

The benefits or otherwise of extracolonic imaging has been debated widely (11,12), and neither clinicians (13) nor policy makers (14) are clear about whether it is helpful or not for population screening. Furthermore, little research has investigated whether clinicians or their patients regard extracolonic imaging as desirable. Specifically, it is unclear how individual patients and health care professionals balance the possibility of detecting life-threatening extracolonic pathologic findings against the larger chance of fruitless (or even harmful) testing precipitated by extracolonic findings. While qualitative studies have found that screening-age patients generally view the ability of CT colonography to visualize extracolonic organs as advantageous (15), we do not know at what point (if at all) perceived benefit is outweighed by the inconvenience, worry, and risks of unnecessary further investigation. We therefore aimed to determine the maximum rate of false-positive diagnoses that patients and health care professionals were willing to accept in exchange for detection of extracolonic malignancy by using CT colonography for CRC screening.

Advances in Knowledge

- Patients and health care professionals were highly tolerant of false-positive diagnoses that led to additional, unnecessary radiologic testing subsequent to CT colonography, up to a median false-positive rate greater than 99.8% (interquartile ratio [IQR], 10 to >99.8%).

- Patients and health care professionals were highly tolerant of false-positive diagnoses that led to additional, unnecessary invasive testing (eg, biopsy, endoscopy, and surgery) subsequent to CT colonography, up to a median false-positive rate of 10% (IQR, 2 to >99.8%).

- Patients were significantly more tolerant of false-positive diagnoses of extracolonic malignancy by CT colonography than were health care professionals, for both those that generated subsequent radiologic tests and those that generated subsequent invasive tests.

Implication for Patient Care

- The false-positive rate of screening CT colonography for extracolonic findings in current clinical practice is likely to be highly acceptable to both patients and health care professionals.

Materials and Methods

Ethical committee approval was granted. All participants gave written informed consent. Opinions were elicited by using a discrete choice experiment where participants chose between two alternatives. Each alternative has characteristics (ie, attributes: sensitivity or discomfort) that are presented at different levels (eg, sensitivity 80%, 85%, 90%) during the experiment. Repeating the choice task with systematic variation of the levels allowed the relative importance of each attribute to be quantified (16). Since discrete choice experiments are difficult to administer via postal questionnaires (17), we used face-to-face interviews primarily, providing background information for participants via interactive laptop presentation.

Recruitment

Consecutive adults of CRC screening age (55–69 years) who were scheduled to attend for unrelated ultrasonographic (US) investigations were identified by using a booking system. A research assistant mailed information and consent forms beforehand, and responders were interviewed on their appointment day. Individuals with a history of CRC or who underwent investigations for possible CRC were excluded to avoid bias (18). Additionally,

radiologists, colorectal surgeons, gastroenterologists, specialist nurses, and radiographers who requested, performed, or interpreted colorectal imaging were recruited via hospital e-mail. Participants were offered a £10 voucher. Because a previous study found no difference for health care professionals between online and face-to-face completion (19), this group could complete the experiment online. All patient participants were interviewed in person by either radiology research fellows (A.A.P., D.B., E.H.), or research assistants (H.F., N.B.).

Attributes

The focus of this study was extracolonic false-positive diagnosis with CT colonography at CRC screening, described to participants as false alarms. While some extracolonic findings are fully characterized by using additional imaging (eg, US for indeterminate renal lesions), others require invasive tests (endoscopy, biopsy, or surgery). To address both situations, participants undertook two separate experiments. In the first experiment (radiologic testing), participants were told that false-positive extracolonic diagnosis would precipitate unnecessary further imaging. Participants were instructed to assume the rates of such imaging to be 50% US, 45% CT, and 5% magnetic resonance (MR) imaging, per published literature (6). Disadvantages of imaging were explained as follows: US and MR imaging were described as safe, but might cause inconvenience and anxiety. Noise and claustrophobia were described for MR imaging. CT was described as including a very small chance of cancer induction several years afterward (20). In the second experiment (invasive testing), false-positive diagnoses led to biopsy, endoscopy, or surgery. Participants were instructed to assume that approximately 50% of invasive tests would be surgical, 25% would be needle biopsy (either fine-needle aspiration or core), and 25% would be endoscopy (6). Pain, bleeding, perforation, and a small risk of death were mentioned as possible complications.

Participants were told that tests for false alarms were unnecessary because the patient derived no benefit from the ultimate diagnosis, the hypothetical population being tested was asymptomatic, and the focus was purely on findings outside the colon.

We presented two hypothetical tests: unrestricted CT colonography evaluated both the colon and extracolonic organs, and restricted CT colonography was confined to the colon. Participants were told that diagnostic accuracy for colonic neoplasia was identical for both tests (5). Unrestricted CT colonography was assumed to depict extracolonic malignancy at an early and curable stage in one in 600 cases (a conservative estimate derived from the literature [10]), whereas restricted CT colonography did not. Participants were told that the impact of early diagnosis on overall survival was unknown, and that even by using unrestricted CT colonography, many extracolonic malignancies would remain undetected by a one-off screening examination (ie, detection did not necessarily result in cure). Across the scenarios presented, the specificity (depicted as a false-positive rate) of unrestricted CT colonography varied from 100% to 0.17%, corresponding to a rate of additional testing that ranged from none to 599 extra tests to diagnose one extracolonic malignancy per 600 patients (Table 1). The invasive testing experiment included a scenario where the chance of death was directly equivalent to the chance of extracolonic malignancy diagnosis, and it had the additional disadvantage of the near-certainty of an unnecessary invasive procedure.

Experiment Format

Background information regarding CRC, screening, CT colonography, and risk was presented by using a multimedia presentation. Consequences of false-positive results were described in terms of need for additional imaging or biopsy (eg, resection of indeterminate ovarian cysts). We explained the nature of needle, endoscopic, and surgical excision biopsy. The chance of requiring an extra test was presented graphically

and by using text and included both absolute risks and natural frequencies to maximize patient understanding (21,22) (Fig 1). Patients were told to assume they were asymptomatic and at average risk of both intracolonic and extracolonic pathologic findings and to pick the test they would choose for themselves or a close friend or relative, with no opt-out. Health care professionals were asked to pick the test they felt was best suited to population screening (rather than for their own care). The radiologic testing experiment was performed first, followed by the invasive testing experiment.

For each experiment, the different false-positive rates for unrestricted CT colonography were presented in a nonsequential order (ie, the rate did not increase or decrease incrementally). One choice was repeated to test consistency. If inconsistent, the response was clarified with the participant; the second response was used for online participants. Unrestricted CT colonography was also presented with a zero false-positive rate, and those who chose restricted CT colonography in this scenario were labeled as irrational responders. If this occurred, the reason for choosing restricted CT colonography was recorded after qualitative exploration, but the response was retained for the subsequent analysis. Participants who preferred unrestricted CT colonography despite a false-positive rate of 599 of 600 cases in the invasive testing scenario were presented with additional information that emphasized potential harms (including death) that could arise from this situation. The risk of death was stated as one in 600 cases (23); participants were therefore choosing between a one-in-600 chance of early extracolonic malignancy diagnosis versus an equivalent risk of death plus the near certainty of unnecessary additional invasive procedures.

Pilot Testing

To confirm comprehensibility, estimate completion time, and inform sample size, 15 individuals (10 professionals and five patients) were piloted (data

Radiology

Table 1

Attributes and Levels Presented in the Radiologic Testing and Invasive Testing Experiments

A: Radiologic Testing Experiment

Radiologic Testing Question No.	False-Positive Rate, Unrestricted CT Colonography (%)	False-Positive Rate, Restricted CT Colonography (%)	No. of Curable Extracolonic Cancers Detected with Unrestricted CT Colonography Per 600 Screening Examinations	No. of Additional False-Positive Detections with Unrestricted CT Colonography Per 600 Screening Examinations
Question 1r	0	0	1	0
Question 2r	0.17	0	1	1
Question 3r*	4	0	1	24
Question 4r*	4	0	1	24
Question 5r	10	0	1	60
Question 6r	20	0	1	120
Question 7r	40	0	1	240
Question 8r	60	0	1	360
Question 9r	80	0	1	480
Question 10r†	99.8	0	1	599

B: Invasive Testing Experiment

Invasive Testing Question No.	False-Positive Rate, Unrestricted CT Colonography (%)	False-Positive Rate, Restricted CT Colonography (%)	No. of Curable Extracolonic Cancers Detected with Unrestricted CT Colonography Per 600 Screening Examinations	No. of Additional False-Positive Detections with Unrestricted CT Colonography Per 600 Screening Examinations
Question 1i	0	0	1	0
Question 2i	0.17	0	1	1
Question 3i*	1	0	1	6
Question 4i*	1	0	1	6
Question 5i	2	0	1	12
Question 6i	4	0	1	24
Question 7i	10	0	1	60
Question 8i	20	0	1	120
Question 9i	40	0	1	240
Question 10i	60	0	1	360
Question 11i	80	0	1	480
Question 12i	99.8	0	1	599
Question 13i‡	99.8	0	1	599§

Note.—Unrestricted CT colonography shows the inside and outside of the colon, while restricted CT colonography only shows the inside of the colon.

* Questions are identical to test for internal consistency.

† Participants who chose unrestricted CT colonography in response to question 10 were considered nontraders.

‡ Participants who chose unrestricted CT colonography in response to question 13 were considered nontraders.

§ One death.

not included in the final analysis). This confirmed that attributes and levels, and the concept of choosing between two scenarios (ie, trading test benefits vs harms) were comprehensible. However, simultaneous consideration of false-positive diagnoses that led to both radiologic follow-up and invasive testing was judged as too confusing, which explained why these were presented ultimately as separate experiments (see Appendix E1 [online]).

Analysis

The primary outcome measure was the maximum false-positive rate that the average participant was willing to accept in exchange for a one-in-600 chance of diagnosing an extracolonic malignancy, or the so-called tipping point. The pilot suggested a mean acceptable false-positive rate of 11% for invasive testing with a standard deviation of 0.23. To determine the mean tipping point with 95% confidence intervals at a two-sided α level of .05 and 90% power required 81 participants and used the following equation: $[n = 4\sigma^2(z_{crit})^2/D^2]$ where D = 0.10, σ = 0.23, and z_{crit} = 1.960 (24). Because pilot data were not normal, we aimed to recruit a further 15% of participants (ie, $81 + 0.15 \times 81$ = minimum of 93 participants in total). A prespecified secondary outcome to compare subgroups of patients versus health care professionals required 56 participants each for 90% power to detect a 20% difference in the maximum false-positive rate.
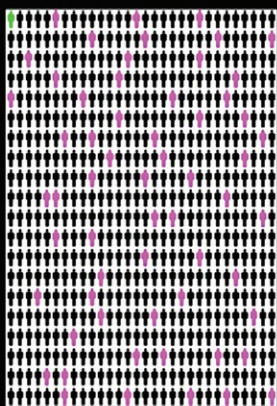
The overall median tipping point for participants was calculated for each experiment, and it was calculated individually for patients and professionals. Because numbers of patients and professionals differed, the overall tipping point was calculated by using 2000 bootstrap estimates of medians and interquartile ranges with equally sized samples from each group (n = 50 participants in each sample). Tipping points were nonnormal and were therefore summarized with medians and interquartile ranges. Nontraders were defined as participants who consistently chose one test over the alternative across all of the scenarios presented. Nontraders were therefore regarded as requiring higher tipping-points than were offered in the experiment, but responses were still included. The Mann-Whitney U test and Wilcoxon signed rank sum test were used for unpaired and paired comparisons respectively. Data were collated by using software (Microsoft Excel 2011 for Mac v14.3.4; Microsoft, Redmond, Wash) and analyzed with statistical software (R version 2.15.1; R Foundation for Statistical Computing, Vienna, Austria) (25).

Figure 1

Test A:
Looks inside and outside the bowel.

For every 600 patients going for bowel cancer screening, one will have cancer outside the bowel which will be picked up at an early stage by this test.

But 60 patients get worrying test results and need to go for extra tests such as biopsy or surgery.

Test B:
Does not look outside the bowel.

For every 600 patients going for bowel cancer screening, one will have an early cancer outside the bowel which cannot be picked up by this test.

But no patient gets worrying test results or needs to go for extra tests such as biopsy or surgery.
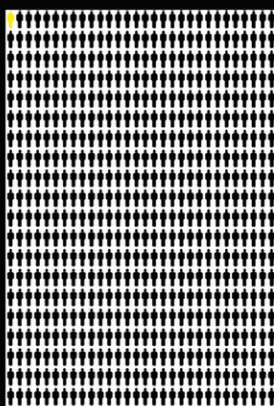
Figure 1: Example from the invasive testing experiment. A hypothetical screening population of 600 individuals was presented and participants were invited to choose between a test that generated a variable rate of false-positive diagnoses (pink) with a one-in-600 chance of finding an early-stage extracolonic malignancy (green) or a test that generated no false-positive diagnoses but had no chance of finding an extracolonic malignancy (yellow). Participants were informed that their chance of receiving any particular result could not be predicted in advance and was essentially random. Relative and absolute percentages were presented. This image corresponds to the median tipping point for patients and professionals combined: on average, unrestricted CT colonography (Test A on the Figure) was preferred to this level of false-positive invasive tests, but not beyond.

Results

We invited 318 patients and 96 health care professionals. Of these, 79 patients participated (24.8%) but only 52 were interviewed because of scheduling conflicts. Fifty health care professionals participated (a response rate of 52.1%), 21 (42.0%) were interviewed face to face, and 29 (58.0%) responded online. On average, patients were older than professionals (median, 64.5 years vs 29.5 years; *P* < .001) and had discontinued education earlier (50.0% educated to at least bachelor's degree level vs 94.0%; *P* < .001; Table 2). There were no significant differences in sex ratio (*P* = .54) or ethnicity (*P* = .14).

Nontraders

For the radiologic testing experiment, 61 of the 102 participants interviewed (59.8%; 41 patients, 20 professionals) were deemed nontraders (ie, they always chose unrestricted CT colonography), 24 of whom (23.5% overall; 23 patients, one professional) were also nontraders for the invasive testing experiment. These 24 nontraders felt unable to choose restricted CT colonography despite that one scenario for unrestricted CT colonography presented a risk of death equivalent to the chance for detection of an extracolonic malignancy. Conversely, a single patient participant never chose unrestricted CT colonography (even for the zero false-positive scenario), stating a firm opinion that CRC screening should examine the colon alone. On average, nontraders were significantly older (median age, nontraders vs traders, 64.5 years vs

29.5 years, respectively; *P* < .001), significantly more likely to be patients (41 patients [67.2%] vs 20 professionals [32.8%]; *P* < .001), and were less educated than traders (at least bachelor's degree–level education, nontraders vs traders, 38 of 61 [62.3%] vs 35 of 41 [85.4%] respectively; *P* < .01). There was no significant difference in sex (men, nontraders vs traders, 32 of 61 [52.5%] vs 24 of 41 [58.5%] respectively; *P* = .55) or ethnicity (whites, nontraders vs traders, 48 of 61 [78.7%] vs 28 of 41 [68.3%] respectively, *P* = 0.24).

Radiologic Testing Discrete Choice Experiment

When the consequence of extracolonic findings was radiologic testing, the median tipping point occurred at a false-positive rate of greater than 99.8% (interquartile range [IQR], 10 to >99.8%; Table 3). Thus, the average participant was prepared to tolerate at least a 99.8% rate of unnecessary additional radiologic tests to diagnose a single additional extracolonic malignancy. The median tipping point was significantly higher for patients than professionals at greater than 99.8% (IQR, >99.8% to >99.8%) versus 40% (IQR, 10% to >99.8%; *P* < .001; Table 3). Overall, at a prevalence of one in 600 for potentially curable extracolonic malignancy, this corresponds to more than 599 unnecessary additional radiologic tests (IQR, 60 to >599) to find one curable extracolonic malignancy. Patients were prepared to accept a significantly higher number of false-positive diagnoses (median, >599; IQR, >599 to >599; Table 3, Fig 2a) than were professionals (median, 240; IQR, 60 to >599; *P* < .001; Table 3, Fig 2b).

Invasive Testing Discrete Choice Experiment

When the consequence of extracolonic findings was invasive, the median tipping point occurred at a false-positive rate of 10% (IQR, 2% to >99.8%). Thus, the average participant was prepared to tolerate a 10% rate of unnecessary additional invasive tests in exchange for diagnosis of a single

Radiology

Table 2

Demographic Characteristics of Patient and Professional Participants

Characteristic	Patients*	Professionals†	No. of Participants‡
Sex			
Male	27 (52)	29 (58)	56 (55)
Female	25 (48)	21 (42)	46 (45)
Age (y)			
<25	0 (0)	1 (2)	1 (1)
25–34	0 (0)	31 (62)	31 (30)
35–54	0 (0)	18 (36)	18 (18)
55–59	1 (2)	0 (0)	1 (1)
60–69	51 (98)	0 (0)	51 (50)
Ethnicity			
White	42 (81)	34 (68)	76 (75)
Other	10 (19)	16 (32)	26 (25)
Education level			
≥ Bachelor's degree	26 (50)	47 (94)	73 (72)
Other	26 (50)	3 (6)	29 (28)

Note.—Data in parentheses are percentages.

* n = 52.

† n = 50. Professionals consisted of 10 radiologists, five gastroenterologists, four surgeons, 19 registrars in these specialties, two specialist colorectal nurses, and 10 radiographers.

‡ n = 102.

Table 3

Tipping Points and Number of False-Positive Diagnoses Deemed Acceptable in Each Scenario for Patients, Professionals, and the Two Groups Combined

Parameter	Tipping Point (%)		Average No. Additional False-Positive Diagnoses Tolerated Per Additional Extracolonic Cancer Found	
	Median	IQR	Median	IQR
Patients				
Scans	>99.8	>99.8 to >99.8	>599	>599 to >599
Invasive tests	>99.8	20 to >99.8	>599	120 to >599
Professionals				
Scans	40	10 to >99.8	240	60 to >599
Invasive tests	5	2–10	30	12–60
Combined				
Scans	>99.8	10 to >99.8	>599	60 to >599
Invasive tests	10	2 to >99.8	60	12 to >599

extracolonic malignancy. The median tipping point was significantly higher for patients than professionals at greater than 99.8% (IQR, 20% to >99.8%) versus 5% (IQR, 2%–10%; $P < .001$; Table 3), respectively. Overall, at population prevalence of one in 600, this corresponds to 60 (IQR, 12 to > 599) additional invasive tests per extracolonic malignancy. Again, patients were prepared to tolerate higher numbers of false-positive diagnoses (median > 599, IQR 120 to > 599 plus risk of death; Table 3, Fig 3a) than professionals (median 30, IQR 12–60, $P < .001$; Table 3, Fig 3b).

The median number of false-positive diagnoses tolerated per extracolonic malignancy was significantly higher for the radiologic testing than the invasive testing experiment ($P < .001$), which demonstrated that additional imaging tests were deemed more acceptable than additional invasive tests.

There was no significant difference in the median tipping points for patients interviewed by either radiologists or research assistants ($P = .57$) or between professionals who gave their responses online as opposed to face-to-face interviews ($P = .81$).

Discussion

Extracolonic findings at CT colonography present a clinical dilemma: Early diagnosis of important pathologic findings might be curative, but unnecessary investigation of ultimately irrelevant findings has physical, psychologic, and financial costs. How patients and health care professionals balance these costs is not known with precision, hence our decision to conduct these experiments. We found that patients were prepared to tolerate an extremely high rate (>99.8%) of unnecessary additional imaging or invasive tests subsequent to screening CT colonography to reap the potential benefits of finding early-stage extracolonic malignancy. While health care professionals were less tolerant of unnecessary follow-up testing than patients, nevertheless we were surprised by the very high rates they accepted; on average, 40% was deemed acceptable for radiologic follow-up. Invasive tests were deemed less acceptable by health care professionals, with the median tipping point at 5%. Nevertheless, these rates are substantially greater than occur in published series, where approximately 7%–11% of individuals required further diagnostic testing after CT colonography, and only 1%–2% required an invasive test (6). Therefore, our data suggest that the specificity of screening CT colonography for extracolonic malignancy in current clinical practice is likely to be highly acceptable to both patients and health care professionals.
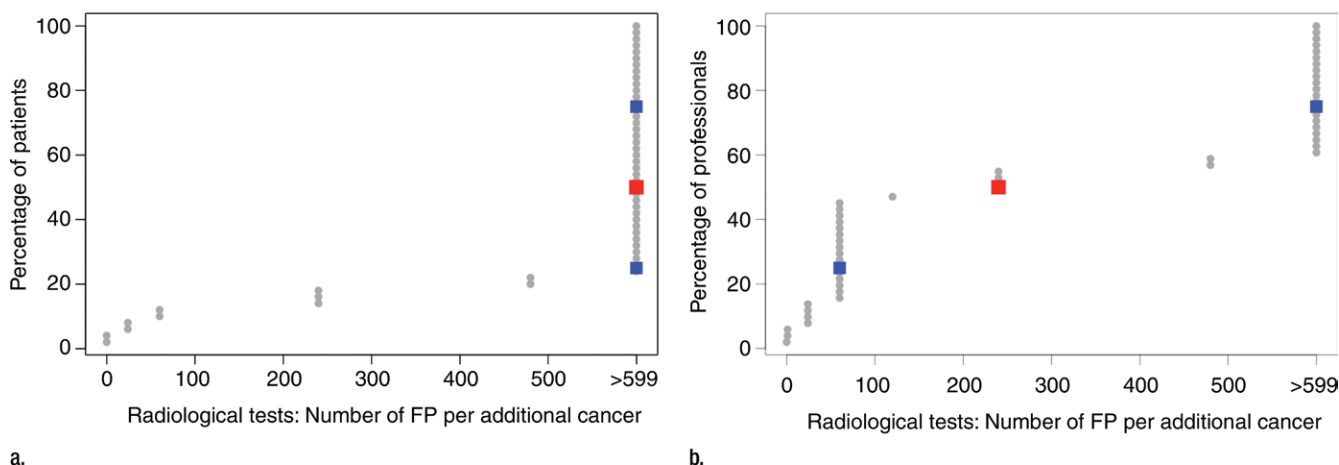
Figure 2

a.

b.

Figure 2: Cumulative plot of tipping points expressed as absolute numbers of additional unnecessary tests for **(a)** patients and **(b)** professionals in the radiologic testing experiment. Each gray dot shows an individual's tipping point. Large red square shows the median value, corresponding to an average participant. Blue squares show 25 and 75 percentage points. *FP* = false positive.
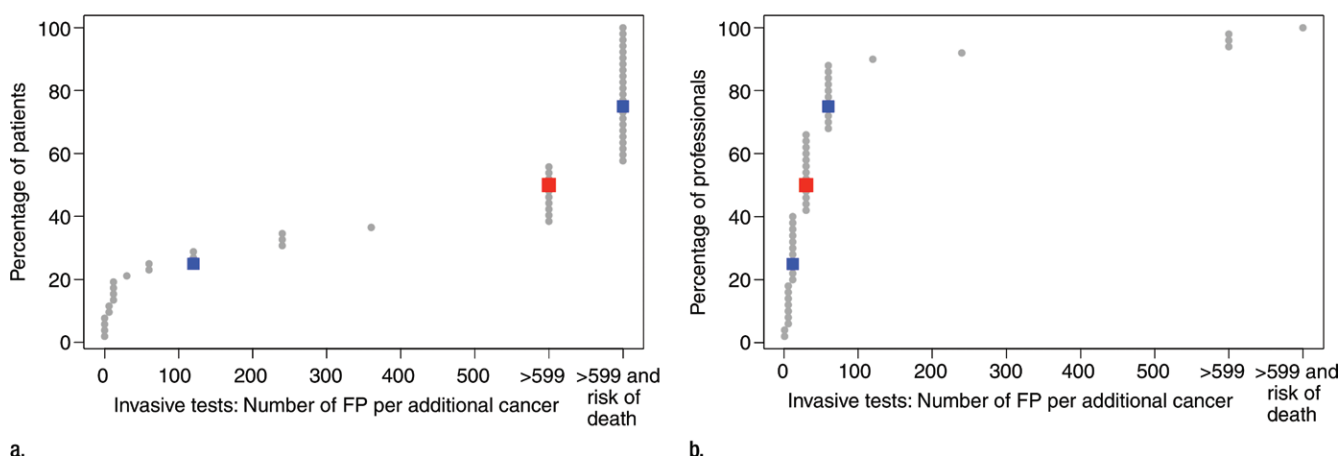
Figure 3

a.

b.

Figure 3: Cumulative plot of tipping points expressed as numbers of additional unnecessary tests for **(a)** patients and **(b)** professionals in the invasive testing experiment. Each gray dot shows an individual's tipping point. Large red square shows the median value, corresponding to an average participant. Blue squares show 25 and 75 percentage points. *FP* = false positive.

Previous studies that quantified patients' perceptions of false-positive diagnoses have shown an overwhelming preference for improved sensitivity despite the costs of diminished specificity. When considering breast cancer screening with mammography, one study (26) found that 63% of women were prepared to accept 500 or more additional false-positive mammograms to save a single life by early breast cancer diagnosis. Similarly, a study of CT

colonography for CRC screening found patients would tolerate over 4000 false-positive diagnoses to avoid a single missed CRC (19); the issue of extracolonic malignancy was not examined. We found patients equally tolerant in the context of extracolonic malignancy, which confirmed that potentially life-saving detection of pathologic findings outweighs the perceived disadvantages of subsequent testing irrespective of the organ being evaluated.

Our data, while framed in the context of CRC screening, potentially have wider implications for incidental findings discovered with other imaging modalities. Such so-called incidentalomas are common in CT urography (27), CT coronary angiography (28), thoracic CT when screening for lung cancer (29), and abdominopelvic CT and were the subject of the American College of Radiology white paper for management guidance (30). Our

results suggest that both patients and health care professionals are likely to tolerate additional work-up in these different clinical settings. We chose a prevalence of incidentally detected extracolonic malignancy of one in 600, based on available data for CT colonography screening populations (10); we would expect tipping points to differ if this prevalence changed. For example, our 10% invasive test rate deemed acceptable overall might be unacceptably high if the chance of uncovering an unexpected malignancy decreased to one in 2000 (as was found in a large lung cancer screening trial [31]).

When patients complete simple rank-order preferences, they choose the most accurate, comfortable, convenient, and cheapest test (32). However, discrete choice experiments reflect so-called real-world choices, where different attributes must be traded against one other (16,17,32). These experiments are complex to comprehend, so we interviewed patient participants face to face, provided extensive background information by using laptops and graphic aids, and were available to answer questions. Despite this, many patients made the (apparently irrational) decision to choose unrestricted CT colonography when the scenario was presented alongside a risk of death from unnecessary further investigations equal to the chance of detecting extracolonic malignancy, and the near certainty of an unnecessary invasive procedure. Such counter-intuitive behavior may arise from prior belief (33); many patients could not deviate from their conviction that early cancer diagnosis is always preferable, regardless of associated risks. Others stated an unwillingness to live with the uncertainty of not knowing whether an equivocal extracolonic lesion was clinically significant or not, apparently by overlooking the fact that such uncertainty could be avoided entirely by choosing restricted CT colonography, which was unable to image beyond the colon.

Limitations of our study include the necessary simplifications required to render discrete choice experiments comprehensible. For example, attributes of intracolonic performance, bowel preparation, discomfort during the examination, and radiation dose were not included other than as background information; an increase in the number of attributes and their levels renders the experiment impracticable in terms of both cognitive complexity and the number of individual scenarios required to achieve statistical power. Our piloting confirmed this, so we examined radiologic and invasive follow-up by using separate experiments whereas, in reality, a false-positive result might generate both. Also, responses from participants may not reflect their real-life behavior, a limitation of all stated-preference study designs. We could not estimate an upper boundary to patients' tolerance of false-positive diagnoses because the nontrade rate was so high; higher than suggested by the pilot. Consequently, estimates of the median tipping point had a broader IQR than anticipated.

Future researchers should consider treating patients and professionals as separate groups from the outset and power accordingly. For example, health care workers who request screening tests will tend to be younger than the patients who receive them; Table 2 shows that all professionals were 54 years or younger while all patients were older (because we wished to reflect screening age). It is possible that as professionals age and become more susceptible to cancer themselves their opinions might converge with those of patients. However, we believe the reason that professionals were less tolerant of false-positive diagnoses was influenced more by their superior medical knowledge than by their younger age. Our current sample reflects the demographics of the two groups, but it would be interesting in the future to solicit the views of older or retired health care professionals who are themselves of screening age, to see if their opinion has changed. It may also be informative to test community physicians because our health care professionals were all hospital based. The response rate for patients was also lower than expected, perhaps because of cognitive complexity. Costs that arose from additional testing were not investigated, and it is possible that responses may have been different if patients were responsible for these costs; the experiments were performed in the English National Health Service where patients do not bear costs directly. Finally, we studied outpatients attending hospital for unrelated investigations, who may not fully represent an unselected screening population.

In summary, by using discrete choice experiments we found that both patients and health care professionals believe diagnosis of extracolonic malignancy with screening CT colonography greatly outweighs the potential disadvantages of subsequent radiologic or invasive investigation precipitated by false-positive diagnoses. This belief was held more strongly by patients than health care professionals. The specificity of CT colonography for extracolonic malignancy in clinical practice is likely to be highly acceptable to both patients and health care professionals.

References

1. Wernli KJ, Rutter CM, Dachman AH, Zafar HM. Suspected extracolonic neoplasms detected on CT colonography: literature review and possible outcomes. Acad Radiol 2013; 20(6):667–674.

2. Gluecker TM, Johnson CD, Wilson LA, et al. Extracolonic findings at CT colonography: evaluation of prevalence and cost in a screening population. Gastroenterology 2003; 124(4):911–916.

3. Yee J, Kumar NN, Godara S, et al. Extracolonic abnormalities discovered incidentally at CT colonography in a male population. Radiology 2005;236(2):519–526.

4. Chin M, Mendelson R, Edwards J, Foster N, Forbes G. Computed tomographic colonography: prevalence, nature, and clinical significance of extracolonic findings in a community screening program. Am J Gastroenterol 2005;100(12):2771–2776.

5. Kim DH, Pickhardt PJ, Taylor AJ, et al. CT colonography versus colonoscopy for the detection of advanced neoplasia. N Engl J Med 2007;357(14):1403–1412.

6. Pickhardt PJ, Hanson ME, Vanness DJ, et al. Unsuspected extracolonic findings at screening CT colonography: clinical and economic impact. Radiology 2008;249(1):151–159.

7. Kim DH, Pickhardt PJ, Hanson ME, Hinshaw JL. CT colonography: performance and program outcome measures in an older screening population. Radiology 2010;254(2):493–500.

8. Veerappan GR, Ally MR, Choi JH, Pak JS, Maydonovitch C, Wong RK. Extracolonic findings on CT colonography increases yield of colorectal cancer screening. AJR Am J Roentgenol 2010;195(3):677–686.

9. Stoop EM, de Haan MC, de Wijkerslooth TR, et al. Participation and yield of colonoscopy versus non-cathartic CT colonography in population-based screening for colorectal cancer: a randomised controlled trial. Lancet Oncol 2012;13(1):55–64.

10. Pickhardt PJ, Kim DH, Meiners RJ, et al. Colorectal and extracolonic cancers detected at screening CT colonography in 10,286 asymptomatic adults. Radiology 2010;255(1):83–88.

11. Fletcher RH, Pignone M. Extracolonic findings with computed tomographic colonography: asset or liability? Arch Intern Med 2008;168(7):685–686.

12. Rutter CM, Kuntz KM, Zauber AG; Colorectal Cancer Modeling Group in the Cancer Intervention and Surveillance Modeling Network. Extracolonic findings from CTC: balancing risks and benefits. AJR Am J Roentgenol 2009;193(5):W470; author reply W471.

13. Yee J, Sadda S, Aslam R, Yeh B. Extracolonic findings at CT colonography. Gastrointest Endosc Clin N Am 2010;20(2):305–322.

14. Whitlock EP, Lin JS, Liles E, Beil TL, Fu R. Screening for colorectal cancer: a targeted, updated systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2008;149(9):638–658.

15. Ghanouni A, Smith SG, Halligan S, et al. Public perceptions and preferences for CT colonography or colonoscopy in colorectal cancer screening. Patient Educ Couns 2012;89(1):116–121.

16. Ryan M. Discrete choice experiments in health care. BMJ 2004;328(7436):360–361.

17. Marshall D, Bridges JF, Hauber B, et al. Conjoint analysis applications in health - how are studies being designed and reported?: an update on current practice in the published literature between 2005 and 2008. Patient 2010;3(4):249–256.

18. von Wagner C, Ghanouni A, Halligan S, et al. Patient acceptability and psychologic consequences of CT colonography compared with those of colonoscopy: results from a multicenter randomized controlled trial of symptomatic patients. Radiology 2012;263(3):723–731.

19. Boone D, Mallett S, Zhu S, et al. Patients' & healthcare professionals' values regarding true- & false-positive diagnosis when colorectal cancer screening by CT colonography: discrete choice experiment. PLoS ONE 2013;8(12):e80767.

20. Brenner DJ, Georgsson MA. Mass screening with CT colonography: should the radiation exposure be of concern? Gastroenterology 2005;129(1):328–337.

21. Gigerenzer G. What are natural frequencies? BMJ 2011;343:d6386.

22. Ahmed H, Naik G, Willoughby H, Edwards AGK. Communicating risk. BMJ 2012;344:e3996.

23. Howlett DC, Drinkwater KJ, Lawrence D, Barter S, Nicholson T. Findings of the UK national audit evaluating image-guided or image-assisted liver biopsy. Part II. Minor and major complications and procedure-related mortality. Radiology 2013;266(1):226–235.

24. Eng J. Sample size estimation: how many individuals should be studied? Radiology 2003;227(2):309–313.

25. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. http://www.R-project.org/. Accessed April 23, 2014.

26. Schwartz LM, Woloshin S, Sox HC, Fischhoff B, Welch HG. US women's attitudes to false positive mammography results and detection of ductal carcinoma in situ: cross sectional survey. BMJ 2000;320(7250):1635–1640.

27. Song JH, Beland MD, Mayo-Smith WW. Incidental clinically important extraurinary findings at MDCT urography for hematuria evaluation: prevalence in 1209 consecutive examinations. AJR Am J Roentgenol 2012;199(3):616–622.

28. Johnson KM, Dennis JM, Dowe DA. Extracardiac findings on coronary CT angiograms: Limited versus complete image review. AJR Am J Roentgenol 2010;195(1):143–148.

29. Jacobs PCA, Mali WPTM, Grobbee DE, van der Graaf Y. Prevalence of incidental findings in computed tomographic screening of the chest: a systematic review. J Comput Assist Tomogr 2008;32(2):214–221.

30. Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR incidental findings committee. J Am Coll Radiol 2010;7(10):754–773.

31. van de Wiel JC, Wang Y, Xu DM, et al. Neglectable benefit of searching for incidental findings in the Dutch-Belgian lung cancer screening trial (NELSON) using low-dose multidetector CT. Eur Radiol 2007;17(6):1474–1482.

32. Ryan M, Scott DA, Reeves C, et al. Eliciting public preferences for healthcare: a systematic review of techniques. Health Technol Assess 2001;5(5):1–186.

33. Tversky A, Kahneman D. Judgment under Uncertainty: Heuristics and Biases. Science 1974;185(4157):1124–1131.