Population screening for colorectal cancer by colonoscopy

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BURDEN OF COLONOSCOPY COMPARED TO NON-CATHARTIC CT COLONOGRAPHY IN A COLORECTAL CANCER SCREENING PROGRAM: RANDOMIZED CONTROLLED TRIAL


* equal contributions

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ABSTRACT

Objective: CT colonography has been suggested to be less burdensome for primary CRC screening than colonoscopy. We compared the expected and perceived burden of both in a randomized trial.

Design: 8,844 Dutch citizens aged 50-74 were randomly invited for CRC screening with colonoscopy (n=5,924) or CT colonography (n=2,920). Colonoscopy was performed after full colon lavage, CT colonography after limited bowel preparation (non-cathartic). All invitees were asked to complete the expected burden questionnaire (EBQ) before the procedure. All participants were invited to complete the perceived burden questionnaire (PBQ) 14 days afterwards. Mean scores were calculated on five-point scales.

Results:
Expected burden: 2,111 (36%) colonoscopy and 1,199 (41%) CT colonography invitees completed the EBQ. Colonoscopy invitees expected the bowel preparation and screening procedure to be more burdensome than CT colonography invitees: mean scores 3.0±1.1 versus 2.3±0.9 (p<0.001) and 3.1±1.1 versus 2.2±0.9 (p<0.001).

Perceived burden: 1,009/1,276 (79%) colonoscopy and 801/982 (82%) CT colonography participants completed the PBQ. The full screening procedure was reported as more burdensome in CT colonography than in colonoscopy: 1.8±0.9 versus 2.0±0.9 (p<0.001). Drinking the bowel preparation received a higher burden score in colonoscopy (3.0±1.3 versus 1.7±1.0, p<0.001) while related bowel movements were scored more burdensome in CT colonography (2.0±1.0 versus 2.2±1.1, p<0.001). Most participants would probably or definitely take part in a next screening round: 96% for colonoscopy and 93% for CT colonography (p=0.99).

Conclusion: In a CRC screening program, colonoscopy invitees expected the screening procedure and bowel preparation to be more burdensome than CT colonography invitees. In participants, CT colonography was scored as more burdensome than colonoscopy. Intended participation in a next screening round was comparable.
STUDY HIGHLIGHTS

What is already known about this subject?
• Population screening for colorectal cancer (CRC) should lead to a reduction in CRC-related mortality.
• Colonoscopy and CT-colonography are both accurate methods for the detection of colorectal neoplasia and can be used for population-based CRC screening.
• CT colonography has been shown to be superior in terms of overall patients’ preference in tandem-studies.

What are the new findings?
• Colonoscopy invitees expected the screening procedure to be more burdensome than CT colonography invitees.
• CT colonography participants perceived the screening procedure as more burdensome than colonoscopy participants.
• Intended participation in a future screening round was comparable.

How might it impact on clinical practice in the foreseeable future?
• Results may attenuate some of the advantages of CT colonography compared to colonoscopy in a screening setting.
• Although CT colonography participants perceived the screening procedure as more burdensome, it remains to be seen whether this will result in a difference in actual participation to future screening rounds, as intended participation was comparable.
BACKGROUND

Each year, more than 400,000 persons are diagnosed with colorectal cancer (CRC) and half of them die from the disease. (1) CRC incidence can be decreased by timely detection of CRC and removal of colonic adenomatous polyps. (2) Early detection of adenomas and CRC is possible through population screening programs, which should lead to a reduction in CRC-related mortality and maybe also incidence. (3;4)

The population health gain of a screening program is affected not only by the accuracy of the screening test, but also by the corresponding participation rate. Initial participation can be influenced by the expected burden of the screening test. Those who anticipate the screening procedure to be burdensome may be less likely to take part. The actually perceived burden of the procedure, from beginning to end, could play a role in future program adherence.

Colonoscopy and CT colonography are both accurate methods to visualize the entire colon. Colonoscopy is considered as the reference standard for detection of colonic neoplasia while CT colonography has a high estimated per-patient sensitivity (88%) for large adenomas. (5) CT colonography has been shown to be superior in terms of overall patient preferences. (6-9) Previous CT colonography studies were non-randomized and used a tandem design, in which CT colonography was performed prior to colonoscopy. This gives participants the opportunity to compare the perceived burden of both techniques but suffers from having a fixed sequential order. To our knowledge no studies have been published comparing both the expected and perceived burden of colonoscopy and CT colonography.

Within a randomized controlled trial we compared the expected burden of a population-based colorectal cancer screening using either primary colonoscopy or CT colonography, as well as the perceived burden and participants’ willingness to return in future screening rounds. One would expect that colonoscopy invitees would anticipate the procedure to be more burdensome than CT colonography invitees. In addition, CT colonography participants can be expected to perceive the screening as less burdensome, especially because of the limited bowel preparation used in CT colonography, compared to the extensive bowel preparation needed for colonoscopy. (8) A lower patient burden may be reflected in a larger proportion of CT colonography participants expressing a willingness to return in future screening rounds.

METHODS

Patients and settings

Between June 2009 and July 2010, a total of 8,844 Dutch citizens aged 50-74 years were invited by mail for population-based CRC screening in the regions of Amsterdam and Rotterdam. The trial protocol has been described in detail elsewhere. (10) Invitations were randomly allocated 2:1 to colonoscopy (n=5,924) or CT colonography (n=2,920) by a computerized randomization program (ALEA Randomization Service). (11) Invitees within a single household were invited to the same modality. Allocation was stratified for age, sex and socio-economic status based
on data of Statistics Netherlands. Invitees could not opt for the alternative screening strategy. At the time of the trial, the Netherlands did not have population-based CRC screening programs. Ethics approval was obtained from the Dutch Health Council (2009/03WBO, The Hague, The Netherlands). The trial was registered in the Dutch Trial Register: NTR1829 (www.trialregister.nl).

Information leaflet and prior consultation
Together with the invitation, all invitees received a leaflet with information on the CRC screening program in general, benefits and (complication) risks of colonoscopy or CT colonography (depending on the invitation) and on follow-up in case of a positive test result. Information leaflets were derived from previous CRC screening pilots and aimed at providing all invitees with information about the CRC screening program and the procedure itself, in order to facilitate informed decision-making on participation. Both information leaflets, as well as the invitation letters, were written and reviewed by gastroenterologists, radiologists, nurses and experts from the comprehensive cancer centers. Further, the Dutch Health Council has scrutinized this material extensively prior to giving approval for this study.

Responding invitees received a standardized prior consultation with the research staff to inform them about the bowel preparation, the procedure itself and to check on contraindications and/or exclusion criteria. Invitees were excluded from participation when they had had a full colonic examination (colonoscopy, CT colonography or double barium contrast enema) in the previous five years, were scheduled for surveillance colonoscopy (personal history of CRC, adenomatous polyps or inflammatory bowel disease (IBD)) or when they had a severe or end-stage disease with a life expectancy of less than 5 years. In addition, CT colonography responders were excluded when they had been exposed to ionizing radiation for research purposes within the previous 12 months and when they had hyperthyroidism or iodine contrast allergy.

All responders who were willing to undergo screening signed written informed consent. They were scheduled for the screening procedure within four weeks after the prior consultation. Timing of the procedure was self-selected, but within a fixed screening timetable.

Colonoscopy
All colonoscopies were performed according to the standard quality indicators defined by the Society of Gastrointestinal Endoscopy. For bowel preparation, all participants started a low-fiber diet, two days before colonoscopy. Subsequently, all participants received 2L of polyethylene electrolyte glycol solution (Moviprep; Norgine bv, Amsterdam, The Netherlands) and 2L transparent fluid, split-dose or single dose, dependent on time of procedure (morning or afternoon).

All colonoscopies were performed by experienced gastroenterologists (≥1000 colonoscopies). Forward viewing colonoscopes with variable stiffness were used (Olympus Medical Systems, Tokyo, Japan). Intravenous midazolam and fentanyl were administered if desired. Room air or carbon dioxide was used for insufflation, depending on screening location. Cecal intubation was achieved by changing positions (left lateral, right lateral, supine and prone position) during intubation if needed. At the discretion of the endoscopist,
antispasmodic medication (butylscopolamine) was given intravenously at the start of withdrawal of the endoscope and repeated if necessary. After cecal intubation, colonic mucosa was carefully inspected during withdrawal for at least 6 minutes. Detected lesions were directly removed during the same procedure, whenever possible. If not, biopsies were obtained for histopathology.

Participants were informed about the colonoscopy findings on the day of the procedure. In case of polyps or cancer, participants were informed on the definitive diagnosis by telephone or at the outpatient clinic within two weeks, followed by further staging investigations and referral for further treatment. Advice regarding surveillance colonoscopy was given according to Dutch adenoma surveillance guidelines (CBO).(14)

CT colonography
Participants received a non-cathartic bowel preparation consisting of two times 50 mL of iodinated contrast agent (Telebrix Gastro, Guerbet, Aulnay sous Bois, France) on the day prior to CT colonography and 50 mL one-and-a-half hour before the examination, combined with a low-fiber diet for one day.(15;16) We used this preparation scheme as previous studies showed that the use of a non-cathartic preparation scheme with 200 mL of iodinated contrast resulted in high per-patient sensitivities for polyps ≥6mm of 90-98% and has the advantage that participants do not have to ingest four liters of fluid or use laxatives.(15;16) However, it does not prevent the development of diarrhea, as most iodinated contrast agents are hyperosmotic. Nowadays, non-cathartic bowel preparation for CT colonography consisting of fecal tagging with barium or iodine without laxatives is increasingly used.(17)

All CT colonography examinations were performed by experienced personnel. Colonic distension was obtained with an automatic CO₂ insufflator (PROTOCO2L, Bracco, EZEM, Lake Success, USA) after intravenous administration of 1 ml butylscopolamine or (when contraindicated) 1 mg of glucagonhydrochloride intravenously. When both spasmolytica were contra-indicated, no bowel relaxants were used. The aim was to insufflate three liters (1.3 left side, 0.9 supine and 0.8 right side) or at least two-and-a-half liters within a maximum insufflation time of 5 minutes before scanning. Images were obtained in both the supine and prone position, using a low dose scan protocol. All participants were informed by telephone about the CT colonography result within two weeks.

Participants with one or more CT colonography lesions ≥10mm were referred for follow-up colonoscopy within 3 weeks, during which CT colonography findings were revealed using segmental unblinding. All participants with 1-2 lesions of 6-9 mm were recommended to undergo surveillance CT colonography after 3 years; patients with ≥3 lesions in this range were recommended follow-up CT colonography after 1.5 years. Participants with relevant extracolonic findings were invited at the outpatient clinic and referred for corresponding follow-up.

Expected Burden Questionnaire (EBQ)
All invitees received a validated questionnaire by postal mail on the expected burden of the screening procedure (expected burden questionnaire, EBQ) within four weeks before the screening procedure. They were asked to complete the questionnaire prior to the screening
procedure and to return it by mail in a prepaid envelop. All non-participants received the same questionnaire within four weeks after the initial invitation and were asked to return it by mail. The EBQ was based on previous Dutch FOBT screening pilots and on studies investigating the acceptance of CT colonography and patient perception of diagnostic tests for fecal incontinence.\(^{18-21}\) With the EBQ we collected information on the expected embarrassment, pain and burden of the bowel preparation and the examination itself. All items were scored on a five-point Likert scale (1=not at all; 2=slightly; 3=somewhat; 4=rather; 5=extremely).\(^{22}\) Completed EBQs were scanned and responses were automatically transferred to a database. The questionnaire also collected information on background characteristics like educational and income levels.

**Perceived Burden Questionnaire (PBQ)**

Participants received a second questionnaire by postal mail 14 days after the examination. At that point, participants had already been informed about the final result of the screening procedure. This second questionnaire addressed the perceived burden of the screening procedure (PBQ). Similar to the EBQ, the PBQ was based on previous CRC screening pilots and had been validated in previous screening cohorts. The PBQ contained items on perceived embarrassment, pain and burden of the bowel preparation, the examination itself and on the overall burden of the screening procedure. In addition, the PBQ included specific items related to colonoscopy or CT colonography. All items were scored on a five-point Likert scale (1=not at all; 2=slightly; 3=somewhat; 4=rather; 5=extremely).\(^{22}\)

With the questionnaire we also collected information on previous experience with colonoscopy or CT colonography, the most burdensome part of the colonoscopy or CT colonography (preparation, examination, abdominal symptoms afterwards, waiting for the results or sedation in case of colonoscopy) and the willingness to return in future screening rounds.

Participants were asked to fill in the questionnaire directly after receiving it and to send it back by mail in a pre-paid envelop. If participants did not respond, they were not reminded. In case of a positive CT colonography test result, a subject was asked individually to complete the PBQ prior to follow-up colonoscopy. Completed PBQs were scanned and responses were automatically transferred to a database.

**Statistical analysis**

Expected burden was compared between colonoscopy and CT colonography invitees: those who had been invited, regardless participation. All EBQs completed after the screening procedure were excluded from the analysis. Perceived burden was compared between actual colonoscopy and CT colonography participants. Items allowing a comparison between expected and perceived burden were analyzed using the Mann-Whitney test or chi-square statistics.

In addition, items specific for colonoscopy or for CT colonography were analyzed separately. We performed additional analyses to investigate the influence of a delayed return of PBQ on the perceived burden. SPSS version 18.0 for Windows (SPSS, Chicago, Ill) was used to perform all statistical tests.
RESULTS

The EBQ was returned by 2,111 colonoscopy invitees (36%) and 1,199 CT colonography invitees (41%). Forty-four EBQs (27 in colonoscopy arm and 17 in CT colonography arm) of screening participants had to be excluded because participants had completed the EBQ after the screening procedure. As shown in Figure 1, 1,276 colonoscopy invitees participated (22%), compared to 982 CT colonography invitees (34%). The PBQ was returned by 1,009 colonoscopy participants (79%) and by 801 CT colonography participants (82%). Background characteristics are summarized in Table 1.

Figure 1: Overview of response to the expected and perceived burden questionnaire among invitees of a primary colonoscopy or CT colonography screening program. Forty-four EBQs (27 in colonoscopy arm and 17 in CT colonography arm) were excluded as they were completed after the procedure. EBQ = Expected Burden Questionnaire; PBQ = Perceived Burden Questionnaire.

Expected burden invitees

Figure 2 summarizes the results on expected burden, including (pooled) standard deviations. Twenty-seven percent of colonoscopy invitees expressed to be extremely reluctant to undergo screening compared to 6% of CT colonography invitees (overall mean score 3.3 versus 2.4; p<0.001).

Bowel preparation

A smaller proportion of responding colonoscopy invitees than CT colonography invitees expected to be not or only slightly embarrassed by drinking the bowel preparation (64% versus 77%; 2.2 versus 1.8; p<0.001). A majority of CT colonography invitees expected that drinking the bowel preparation would be not or only slightly painful, more than in colonoscopy invitees (79% versus 61%; 1.9 versus 2.4; p<0.001). Thirty-four percent of colonoscopy invitees expected
Table 1: Respondents’ baseline characteristics

<table>
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<th>Invitees</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Colonoscopy</td>
<td>CTC</td>
</tr>
<tr>
<td>Respondents (n)</td>
<td>N=5,924</td>
<td>N=2,920</td>
</tr>
<tr>
<td>Age in years (median, IQR)</td>
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<td>60 (55-66)</td>
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<tr>
<td>Gender (% male)</td>
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<td>1,015 (48%)</td>
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<td>Married/lived together (%)*</td>
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<td>990 (84%)</td>
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<td>3.1 (SD 1.4)</td>
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<td>Education*</td>
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<tr>
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<td>101 (5%)</td>
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<td>Tertiary and postgraduate (%)</td>
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</tr>
<tr>
<td>Prior endoscopy experience (%)*</td>
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<td>N/A</td>
</tr>
</tbody>
</table>

* As not all respondents completed the questions on their marital status, education and prior endoscopy experience, the percentages mentioned for these items are not based on the total number of respondents, but on the total number of invitees and participants who answered those questions.

** Socio-economic status was categorized as very low, low, medium, high and very high (1-5).

Figure 2: Reluctance to undergo screening and expected embarrassment, pain and burden of bowel prep and screening procedure. On top of the bars, mean scores, standard deviations (between parantheses), differences in mean scores and pooled standard deviations (pSD) are displayed. All items differed significantly between colonoscopy and CT colonography (p<0.001).
that drinking the bowel preparation would be rather or very burdensome compared to 10% of CT colonography invitees (3.0 versus 2.3; p<0.001).

**Examination itself**

A larger proportion of colonoscopy invitees expected to be somewhat, rather or extremely embarrassed by undergoing the screening procedure (44% versus 24%; 2.5 versus 1.9; p<0.001). Only 5% of colonoscopy invitees expected that the screening procedure would not be painful compared to 35% of CT colonography invitees (2.9 versus 1.9; p<0.001). Colonoscopy invitees expected the screening procedure to be more burdensome than CT colonography invitees (rather or extremely burdensome; 36% versus 9%, 3.1 versus 2.2; p<0.001).

**Perceived burden participants**

Figure 3 summarizes the findings with the perceived burden questionnaire, including (pooled) standard deviations.

**Bowel preparation**

Drinking the preparation was more often perceived as not or only slightly burdensome by CT colonography participants (39% versus 84%; overall mean score 3.0 versus 1.7; p<0.001), while colonoscopy participants perceived the related bowel movements more often as not

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**Figure 3: Perceived burden of colonoscopy and CT colonography.** On top of the bars, mean scores, standard deviations (between parantheses), differences in mean scores and pooled standard deviations (pSD) are displayed. All items differed significantly between colonoscopy and CT colonography (p<0.001), except for experienced pain caused by the bowel movements (related to the preparation), which was not significantly different between colonoscopy and CT colonography (p=0.06).
burdensome (36% versus 27%; 2.0 versus 2.2; p<0.001) and not embarrassing (72% versus 62%; 1.4 versus 1.6; p<0.001). The perceived pain of the related bowel movements was not significantly different (1.4 versus 1.5; p=0.06).

**Waiting for the results**
Colonoscopy participants perceived waiting for the results more often as not burdensome than CT colonography participants (78% versus 66%; 1.3 versus 1.5; p<0.001).

**Physical health around the examination**
On the day prior to the examination, 48% of colonoscopy participants and 37% of CT colonography participants were hindered in their normal activities (p<0.001), while CT colonography participants were hindered more often the day after the examination (15% versus 31%, p<0.001). Prior to the examination, colonoscopy participants more often experienced trouble sleeping (31% versus 24%, p=0.001), while CT colonography participants experienced this more often afterwards (6% versus 12%, p<0.001).

Abdominal complaints after the examination (more than normal) were experienced less often by colonoscopy participants (24% versus 48%, p<0.001), but if experienced, these abdominal complaints were perceived as more painful by colonoscopy participants (somewhat, rather or extremely painful: 40% versus 28%, p=0.01). The abdominal complaints were rated as not burdensome by 19% of colonoscopy participants versus 9% of CT colonography participants (p<0.05).

**Entire screening procedure**
Colonoscopy participants rated the entire screening procedure more often as not or only slightly embarrassing (95% versus 92%; overall mean score 1.4 versus 1.5; p<0.001), more often as not painful (53% versus 28%; 1.8 versus 2.1; p<0.001) and more often as not burdensome (48% versus 34%; 1.8 versus 2.0; p<0.001). The majority of colonoscopy participants (73%) scored the bowel preparation as most burdensome aspect of the overall screening procedure, while CT colonography participants scored the examination itself (37%) or the bowel preparation (32%) as most burdensome aspects.

The entire screening procedure turned out worse than expected by 12% of colonoscopy participants and by 21% of CT colonography participants, experienced as expected by 13% and 20%, and turned out better than expected by 75% and 59%, respectively (p mean score<0.001).

**Perceived burden colonoscopy related items**
Of all colonoscopy participants 88% received sedation. Insertion of the endoscope into the rectum was perceived as not or slightly burdensome by 92% of colonoscopy participants, as not or slightly embarrassing by 93% and as not or only slightly painful by 89%. The rest of the examination, including cecal intubation and withdrawal of the colonoscope, was experienced as not or only slightly burdensome by 90%. It was scored as not or only slightly embarrassing by 98% and experienced as somewhat, rather or extremely painful by only 17%. Of those participants that received sedation, 98% scored recovering after colonoscopy as not or only slightly burdensome.
Perceived burden CT colonography related items
Of all CT colonography participants, 92% experienced diarrhea; in 37% of participants diarrhea had started after ingestion of 50mL of Telebrix, in 47% after 100mL and the remaining 16% of participants experienced it after ≥150mL. Insertion of the rectal catheter was experienced as not at all or slightly burdensome by 90% of participants. Insufflation of CO₂ was experienced as rather or extremely painful by 23% of participants and was rated as rather or extremely burdensome by 20% of participants. Changing positions during the procedure was scored as not or only slightly burdensome by 81% of participants.

Future screening rounds
Ninety-six percent of colonoscopy participants would recommend others to undergo screening compared to 95% of CT colonography participants. Ninety-six of colonoscopy and 93% of CT colonography participants would probably or definitely participate in a next screening round (p for mean score=0.99).

Influence of delayed return on perceived burden
The PBQ was returned within 4 weeks after the screening procedure by 45% of colonoscopy responders and by 67% of CT colonography responders, after 6 weeks these percentages were 72% and 82% respectively. CT colonography participants returned their PBQ more quickly, after a median of 22 days (IQR 18-31) versus 29 days in the colonoscopy group (IQR 20-42); p<0.001). In the analyses to investigate the influence of delayed return of PBQ, we found results comparable to those of the main analysis (data not shown).

DISCUSSION
In this study we compared the expected and perceived burden of primary colonoscopy and CT colonography screening in a randomized population-based screening program. The expected burden among responding colonoscopy invitees was significantly higher than in CT colonography invitees. In contrast, the perceived burden of the entire screening procedure was evaluated as significantly higher in CT colonography participants than in colonoscopy participants. Nevertheless, the level of intended participation in a next screening round was very much comparable in both groups.

Our study has several strengths. Subjects had been randomly invited for primary population-based CRC screening using either colonoscopy or CT colonography making a head-to-head comparison possible. Previous studies compared both screening methods in a tandem design, in which subjects underwent a colonoscopy after a CT colonography or vice versa. Invitees were not allowed to switch between both strategies, preventing the possibility of a selection bias. The information leaflets for colonoscopy and CT colonography invitees were identically designed, both written and reviewed by gastroenterologists, radiologists, nurses and experts from the comprehensive cancer centers, and aimed at providing decision relevant knowledge. Further, the invitation material was approved by the Dutch Health Council. All participants received a standardized prior consultation to inform them about the entire screening procedure, including the bowel preparation. Both questionnaires had been
validated in previous CRC screening pilots. Almost 80% of participants returned their PBQ, a very reassuring response rate.

A number of potential limitations should also be acknowledged. The lower participation rate in the colonoscopy screening group (22% versus 34%) should be kept in mind when interpreting the results. Participation can be expected to be influenced by the expected burden. A larger proportion of CT colonography participants than colonoscopy participants indicated that the screening procedure turned out worse than expected (21% versus 12%). This suggests that CT colonography invitees may have been more inclined towards participation, because they might have underestimated the burden of CT colonography.

Although all participants received the PBQ two weeks after the procedure, colonoscopy participants were more likely to return their questionnaire at a later stage compared to CT colonography participants. This difference may have affected the perceived burden scores, as perceived burden has been suggested to increase over time.(19,23) In our additional analyses however, which included the PBQs returned within 4 and within 6 weeks after the procedure, we observed comparable results, which suggest that our main findings were not affected by the delay in responding. As not all participants returned their PBQ, we must consider the possibility of a selective response but the number of participants who returned the PBQ was equally high in both arms, suggesting that comparisons are valid.

Although most of the differences between CT colonography and colonoscopy participants were statistically significant, the actual differences were sometimes small when evaluated relative to the variability within groups. In our study, for example, perceived burden scores of the entire screening procedure were 1.8 for colonoscopy and 2.0 for CT colonography. This difference of 0.2 on the five-point scale was highly significant (p<0.001) but the pooled standard deviation (SD) of the scores was 0.9, indicating a large within-group variability in scores. Norman et al. suggested to indicate clinically important differences as those above approximately half a standard deviation (SD).(24) This remark does not concern our results on expected burden as differences between mean scores were all larger than a half pooled SD.

We anticipated that a lower experienced burden would be associated with a higher willingness to participate in future screening rounds. This was not observed in our study, where the overwhelming majority of participants in both groups indicated they would participate in a next screening round and would recommend undergoing screening to others.

To our knowledge, no previous randomized controlled trials have been published comparing the expected burden of colonoscopy and CT colonography. One small Australian (population-based) randomized screening study reported on perceived burden of six different screening strategies including colonoscopy and CT colonography. This study showed higher pain and embarrassment scores in the CT colonography group (n=38 participants) than in the colonoscopy group (n=63 participants).(25) As far as we know, other studies comparing the perceived burden of both techniques used non-randomized tandem designs and were therefore not comparable to our study.(7,8,26)

We observed that drinking the bowel preparation was experienced as more burdensome in the colonoscopy arm than in CT colonography participants. This can be attributed to the higher intake of fluid before colonoscopy, compared to the limited bowel preparation in CT
colonography. A high amount of fluid intake is a persistent burdensome aspect in colonoscopy. Switching to a more limited bowel preparation, such as sodium picosulfate, may reduce the burden in the future. However, additional intake of a substantial amount of clear fluid will still be necessary, comparable to polyethylene glycol, which was used in our study. In contrast, the related bowel movements were experienced as more burdensome in CT colonography. Possibly, these complaints were not anticipated by CT colonography participants.

In our study CT colonography participants reported more often abdominal complaints after the procedure, although colonoscopy participants experienced the associated pain as more burdensome. The larger proportion of CT colonography participants experiencing abdominal complaints could be explained by the lower expected burden or attributed to post-procedural diarrhea, caused by the tagging agent. Based on these findings, one may consider the use of non-ionic contrast agents in order to minimize the amount of related bowel movements, post-procedural diarrhea and other post-procedural abdominal complaints. However further studies are needed to evaluate whether non-ionic contrast agents will result in similar tagging quality for CT colonography, compared to ionic contrast agents. We aimed for homogeneous tagging and therefore did not choose barium only tagging. Bowel preparation with a combination of barium and iodine or lower doses of iodine has been proposed which may be a good compromise between homogeneous tagging and side effects.

Abdominal complaints were experienced as more painful by colonoscopy participants. This might be explained by the fact that colonic distention during CT colonography was achieved using CO₂, while colonic distention during colonoscopy was achieved using room air or CO₂. One previous randomized trial showed a reduction in patient discomfort using CO₂ for insufflation instead of room air during colonoscopy, as CO₂ is rapidly absorbed from the colon which probably results in fewer abdominal cramps. Using only CO₂ instead of using also room air may decrease the experienced post-procedural abdominal pain in colonoscopy screening.

To our surprise, CT colonography participants assigned higher burden scores to the entire examination than colonoscopy participants. It is likely that the higher perceived burden in CT colonography was also influenced by the relatively lower expected burden, as the examination turned out better than expected in 75% of the colonoscopy participants compared to 60% of CT colonography participants. An explanation for this difference might be that CT colonography invitees more often underestimated burdensome elements of CT colonography, such as the watery diarrhea caused by the intake of iodinated contrast agents, or the bowel cramps occurring after insufflations of 2.5 to 3.0 liters of CO₂ for achieving sufficient bowel distention. In addition, the use of sedation could be responsible for the lower experienced burden in colonoscopy, as this could lead to retrograde amnesia. Sedation is not common practice in CT colonography, as so far the advantages did not seem to outweigh the disadvantages, such as recovery time, restrictions on driving and additional costs.

Our information leaflets were identically designed and aimed at disseminating adequate decision-relevant information to all invitees. All participants received a standardized prior consultation to inform them about the entire screening procedure itself and the bowel preparation. Despite our efforts to inform all participants adequately, it is still possible that not
all had a similar understanding of the procedure. Future efforts could target improvements in information leaflets and the development of campaigns to increase appropriate awareness of all potentially burdensome aspects in CT colonography. The fact that colonoscopy participants were informed about the temporary result directly after the procedure, while CT colonography participants received their results after two weeks, may be a third explanation for the difference in perceived burden. We observed that waiting for the test results was perceived more burdensome by CT colonography participants, suggesting that providing a temporary CT colonography result on the day of the examination could contribute to a lower perceived burden of CT colonography.

A priori, based on studies in high-risk participants, we anticipated CT colonography to be less burdensome than colonoscopy, making CT colonography a good option for CRC screening. Our study, performed in an average risk population, showed that the entire screening procedure was experienced as more burdensome by CT colonography participants than by colonoscopy participants. This finding may attenuate some of the potential perceived advantages of CT colonography compared to colonoscopy in a screening setting. At the same time, it is reassuring that in both groups the majority of the patients experienced the screening procedure as not or only slightly burdensome and that there was no difference between the groups in intended participation in a next screening round.
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