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The impact of low- versus standard-volume bowel preparation on participation in primary screening colonoscopy: a randomized health services study

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ABSTRACT

Background The aim of this study was to evaluate the impact of low-volume vs. standard-volume bowel preparation on participation in screening colonoscopy, bowel preparation quality, and lesion detection rates.

Methods This was a multicenter, randomized, health services study within the population-based primary colonoscopy screening program in Poland. Individuals aged 55 – 62 years were randomized in a 1:1 ratio to bowel preparation with a low-volume (0.3 L sodium picosulfate with magnesium citrate) or standard-volume (4 L polyethylene glycol) regimen and then invited to participate in screening colonoscopy. The primary outcome measure was the rate of participation in screening colonoscopy. Compliance with the assigned bowel preparation, bowel preparation quality, and lesion detection rates were also evaluated.

Results A total of 13 621 individuals were randomized and 13 497 were analyzed (6752 in the low-volume group and 6745 in the standard-volume group). The participation rate (16.6 % vs. 15.5 %; $P = 0.08$) and compliance rate (93.3 % vs. 94.1 %; $P = 0.39$) did not differ significantly between the groups. In the low-volume group, fewer participants had adequate bowel preparation compared with the standard-volume group (whole colon 79.0 % vs. 86.4 %, $P < 0.001$; proximal colon 80.1 % vs. 87.3 %, $P < 0.001$). Detection rates of advanced adenoma (AADR) and advanced serrated polyps (ASPDR) were lower in the low-volume group than in the standard-volume group (AADR in the proximal colon 2.6 % vs. 4.3 %, $P = 0.02$; ASPDR in the whole colon 2.0 % vs. 3.3 %, $P = 0.04$; ASPDR in the proximal colon 1.0 % vs. 1.9 %, $P = 0.048$).

Conclusion When compared with a standard-volume bowel preparation with polyethylene glycol, low-volume bowel preparation with sodium picosulfate/magnesium citrate did not improve participation rate or lesion detection rates, and negatively affected bowel preparation quality.

TRIAL REGISTRATION: multicenter, paralel group, health service randomized study RHS 005_2014_january at Finnish Cancer Registry

Introduction

Colorectal cancer (CRC) is the second leading cause of cancer-related death in Europe and the USA [1, 2]. Screening colonoscopy has been shown to decrease CRC incidence and mortality [3]; however, its effectiveness depends on many factors, including colonoscopy quality and participation of the target population [4]. Satisfactory participation rates of 60 % – 75 % have been reached in Scandinavian countries and the USA [5 – 7], but in most European countries rates remain much lower, ranging from 10 % to 34 % [7 – 12]. Bowel preparation, especially the large volume of the cleansing agent solution that needs to be ingested, is frequently indicated as one of the major reasons for nonparticipation in screening colonoscopy [13 – 15]. A low-volume preparation was shown to have similar effectiveness to standard 4-L regimens but was better tolerated by patients and was associated with higher patient satisfaction and increased willingness to repeat identical preparation in the future [16, 17]. Moreover, a low-volume preparation given in a split-dose regimen provided superior bowel cleansing and had a good safety profile compared with 4-L polyethylene glycol (PEG) administered the day before colonoscopy [18].

We hypothesized, therefore, that a low-volume regimen may increase participation in primary screening colonoscopy without compromising the quality of bowel preparation. The primary aim of this randomized health services study was to evaluate whether low-volume bowel preparation improves the participation in primary screening colonoscopy compared with the standard-volume preparation of 4 L PEG. Secondary aims were to compare compliance with the assigned bowel preparation, the quality of bowel preparation, and lesion detection rates in screening participants.

Methods

Study design and settings

This multicenter, parallel-group, randomized, health services study was conducted between March and December 2015, within the Polish Colonoscopy Screening Program (PCSP), an organized, population-based, primary colonoscopy screening program described elsewhere [19, 20]. The study was coordinated by the PCSP Main Office and involved six screening centers – two academic and four private – which were selected based on screening colonoscopy volume, quality indicators, and geographic location to include both urban and rural areas.

Participants and intervention

Study participants were randomly drawn from individuals eligible for PCSP in 2015, including men and women aged 55 – 62 years who were registered in the Polish Population Registry and living in the areas served by the six participating screening centers. The Polish National Cancer Registry and PCSP databases were searched to identify and exclude individuals with a previous CRC diagnosis and/or who had previously undergone screening colonoscopy. The remaining individuals were randomly assigned in a 1:1 ratio to bowel preparation for colonoscopy with a low-volume regimen (0.3 L of oral sodium picosulfate with magnesium citrate solution) or a standard-volume regimen (4 L of PEG solution). Randomized individuals were mailed a personalized letter inviting them to participate, free-of-charge, in colonoscopy screening with a proposed colonoscopy date in 6 weeks' time. The letter outlined the purpose of screening and advised the invitees to contact the local screening center in order to receive more information and schedule their pre-colonoscopy visit. If no response was received within 3 weeks, a reminder letter was sent.

During the pre-colonoscopy visit, screening center personnel conducted the following activities: 1) reviewed the medical history of each individual to ensure that no contraindications to bowel preparation and/or screening colonoscopy were present; 2) provided detailed information about screening colonoscopy and the assigned bowel preparation; 3) dispensed the assigned preparation agent with written instructions on how to prepare for colonoscopy. Participants were not informed that they were participating in a study.

Study procedures

Bowel preparation for colonoscopy

Bowel preparation was in accordance with the European Society of Gastrointestinal Endoscopy recommendations [21]. On the day before colonoscopy, a low-residue breakfast and lunch (blended soup or broth) up to 15:00, followed by clear liquids in the afternoon, were recommended. On the day of colonoscopy, only clear liquids were allowed. Dietary restrictions were the same in both groups and did not differ depending on whether a split or nonsplit regimen was used. Preparation agents were used in standard doses in all individuals, irrespectively of their body mass. Day-before preparation was recommended for individuals who were scheduled for sedated morning colonoscopy in line with anesthesiologists' recommendations; a split-dose regimen was recommended for unsedated colonoscopy. The cleansing solution was prepared according to the manufacturer's instructions provided in the patient information leaflet and was self-administered by the patients.

Individuals in the low-volume group were prepared with oral sodium picosulfate/magnesium citrate solution (CitraFleet; Laboratories Casen-Fleet, Zaragoza, Spain) administered as an evening/morning split dose (2 × 0.15 L) or the day before colonoscopy (0.3 L). They were strongly advised to ingest an additional 4 L of water or clear liquids during preparation. Preparation in the standard-volume group consisted of oral PEG solution (Fortrans; IpsenPharma, Boulogne Billancourt, France) administered as an evening/morning split-dose (2 × 2 L) or the day before colonoscopy (4 L).

Screening colonoscopy

Colonoscopies were performed on an outpatient basis. Before colonoscopy, participants completed a simple questionnaire with questions on bowel preparation, the name of the agent used to cleanse the bowel, administration regimen, and whether or not the whole prescribed amount of cleansing solution and additional fluids were ingested. Sedation was not used routinely. Individuals with a history of abdominal/pelvic surgery

and/or unwillingness to undergo unsedated colonoscopy were offered sedation according to local center policy [22].

Standard or high resolution video colonoscopes were used. Polyps ≤ 10 mm diameter were removed immediately; polyps > 10 mm were removed either immediately or during a separate procedure on an inpatient basis. Other abnormalities were biopsied. All lesions removed or biopsied (including polyps > 10 mm removed during the separate inpatient procedure) were assessed histologically and included in the analysis. Categorization was performed according to the most advanced lesion [23].

Outcome measures

The primary outcome was the screening colonoscopy participation rate, defined as the proportion of individuals invited for screening who had colonoscopy performed within 90 days from the date proposed in the invitation letter.

Secondary outcomes included self-reported compliance, quality of bowel preparation, and lesion detection rates. Self-reported compliance with the assigned bowel preparation was defined as ingestion of the full dose of the assigned preparation agent, together with the recommended amount of water (clear liquids), as assessed by the questionnaire completed before screening colonoscopy. The quality of bowel preparation was assessed using the Boston Bowel Preparation Scale (BBPS) in the whole and proximal colon (cecum, ascending colon, and transverse colon including the splenic flexure). Adequate preparation was defined as BBPS score of ≥ 2 in each colon segment [24]. All participating endoscopists received training in BBPS use.

Lesion detection rates for the whole and proximal colon were defined as the proportion of individuals with at least one lesion of a given type detected on colonoscopy: 1) polyp detection rate (PDR; any polyp); 2) adenoma detection rate (ADR; any adenoma, traditional serrated adenoma or adenocarcinoma); 3) advanced adenoma detection rate (AADR; adenoma with any of the following characteristics: ≥ 10 mm, villous component, high grade dysplasia, adenocarcinoma, or traditional serrated adenoma ≥ 10 mm); 4) advanced serrated polyp detection rate (ASPDR; hyperplastic polyp ≥ 10 mm, sessile serrated polyp/adenoma, traditional serrated adenoma) [25].

Randomization and blinding

Randomization was performed by the study statistician and was stratified by study center, and by participant age and sex. Endoscopists and endoscopy nurses were blinded to participant allocation and the type of bowel preparation administered. They were instructed not to ask the participants about bowel preparation details.

Sample size and statistical methods

The expected participation rates in the standard-volume and low-volume groups were 21 % and 23 %, respectively, based on the current participation rate in the PCSP (unpublished data). In order to detect this 2 percentage point difference between two independent rates with 80 % power at a 5 % level of significance, 13 468 participants needed to be randomized in a 1:1 ratio and invited for screening colonoscopy.

The primary outcome was assessed by intention-to-treat analysis in all randomized individuals after excluding those who died or were diagnosed with CRC before the date of randomization, and those to whom the invitation letter could not be delivered (return of an unopened letter with post office annotation "addressee unknown").

Secondary outcomes were assessed in all individuals who had colonoscopy performed up to the end of 2015, including both those who did and did not reach the primary outcome.

Categorical variables were compared using chi-squared test or Fisher exact test. Univariable and multivariable logistic regression analyses were performed to identify factors that influenced participation rate in the study. Forward stepwise regression at a 0.1 significance level was used for variable selection. Study center, participant age, sex, and travel distance to the study center, and average per capita income in the area of residence were tested for inclusion in the multivariable model. Odds ratios (ORs) and 95 % confidence intervals (CIs) were reported. All tests were two sided. A P value of < 0.05 was considered to denote a statistically significant difference.

All analyses were performed using Stata software, version 13.1 (Stata Corp., College Station, Texas, USA). Figures were prepared using R statistical software, version 3.0.1 (R Development Core Team, Vienna, Austria).

Ethical issues

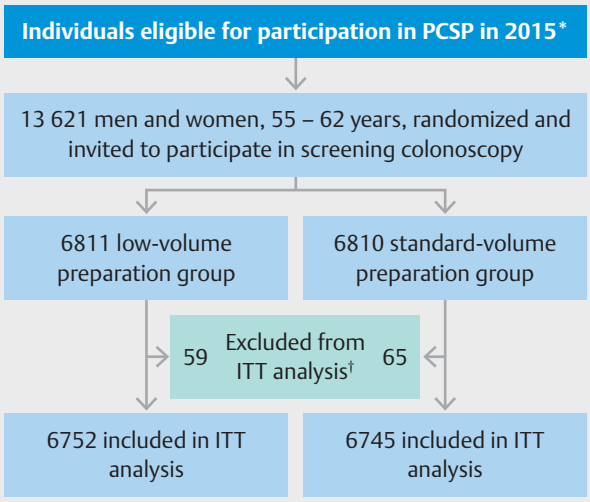
The research proposal was reviewed by the institutional review board at the authors' institutions and was judged to be exempt from oversight (5 March 2014). Participants signed an informed consent for screening colonoscopy within the PCSP in the routine way. Because this was a randomized health services study, no separate informed consent to participate in the study was obtained [19]. The study was registered at the Finnish Cancer Registry (No. RHS 005_2014_january).

Results

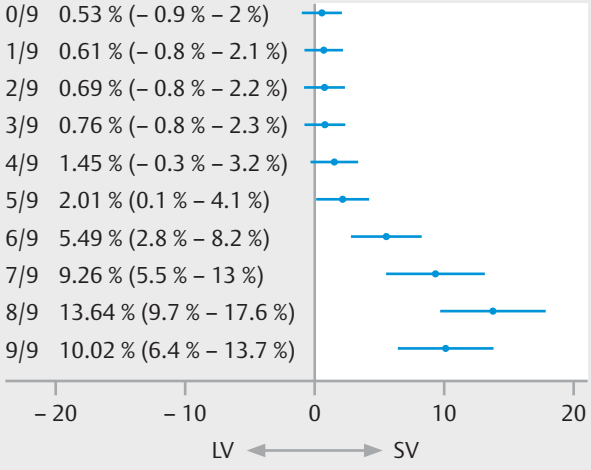
A total of 13 621 individuals aged 55 – 62 years were randomly assigned to the low-volume (n = 6811) or standard-volume (n = 6810) groups and invited to screening colonoscopy. After exclusion of 124 individuals who had died (n = 68) or were diagnosed with CRC before the randomization date (n = 3), or the invitation letter could not be delivered to them (n = 53), a total of 13 497 individuals (6752 and 6745 in the low-volume and standard-volume groups, respectively), were included in the intention-to-treat analysis (▶ **Fig. 1**). Baseline characteristics of the study groups are shown in ▶ **Table 1**.

Participation rate

A total of 1119 (16.6 %) and 1044 (15.5 %) individuals in the low-volume and standard-volume groups, respectively (P = 0.08), underwent screening colonoscopy within 90 days from the date proposed in the invitation letter and reached the primary outcome. Reasons for nonparticipation in screening are summarized in ▶ **Table 2**.



▶ **Fig. 1** Participant flow chart. ITT, intention-to-treat; PCSP, Polish Colonoscopy Screening Program. *Men and women aged 55 – 64 years registered in the Polish Population Registry. †124 individuals who had been randomized and invited to screening colonoscopy were excluded: 68 had died and 3 had been diagnosed with colorectal cancer before the randomization date, and the invitation letter could not be delivered to 53 individuals.



▶ **Fig. 2** Forest plot of cumulative percentage (with 95 % confidence intervals) differences between groups in bowel preparation

The multivariate analysis model (▶ **Table 3**) showed that factors significantly affecting participation rate were participant sex (men vs. women OR 1.15, 95 %CI 1.05 – 1.26; P < 0.004), screening center (E vs. A OR 1.39, 95 %CI 1.20 – 1.62, P < 0.001; D vs. A OR 1.35, 95 %CI 1.13 – 1.62, P = 0.001; and C vs. A OR 1.23, 95 %CI 1.01 – 1.50, P = 0.04), and travel distance to the screening center (≥ 45 km vs. < 10 km OR 0.52, 95 %CI 0.44 – 0.63, P < 0.001; 25 – 44 km vs. < 10 km OR 0.84, 95 %CI 0.72 – 0.98, P = 0.02). Allocation to the low-volume or standard-volume group did not have a significant impact on the participation rate.

Secondary outcomes

Secondary outcomes (▶ **Table 4**) were assessed in 2456 individuals (1249 in the low-volume group and 1207 in the standard-volume group). This group included 2163 individuals who reached the primary outcome and 293 individuals who had colonoscopy performed later than 90 days from the date proposed in invitation letter (up to the end of 2015). Data on the use of split and nonsplit regimens and sedation for colonoscopy are presented in ▶ **Supplementary Table 5** (available online).

Compliance

The assigned bowel preparation agent was used by 1183 (94.7 %) and 1174 (97.3 %) participants in the low-volume and standard-volume groups, respectively (P = 0.001). A total of 1231 (98.6 %) and 1168 (96.8 %) participants, respectively, reported ingestion of the full recommended dose of liquids (P = 0.003). The proportion of individuals who met both conditions (1165 [93.3 %] and 1136 [94.1 %], respectively), did not differ significantly between groups (P = 0.39).

Bowel preparation quality

Adequate bowel preparation of the whole colon was achieved in 987 (79.0 %) and 1043 (86.4 %) participants in the low-volume and standard-volume groups, respectively (P < 0.001). Adequate preparation of the proximal colon was achieved in 1001 (80.1 %) and 1054 (87.3) participants, respectively (P < 0.001). The differences in favor of the standard-volume group became more pronounced when the more stringent criteria for preparation quality were applied (▶ **Fig. 2**).

Lesion detection rates

In the whole colon PDR, ADR, and AADR did not differ significantly between groups; ASPDR was significantly lower in the low-volume vs. standard-volume group (2.0 % vs. 3.3 %; P = 0.04). In the proximal colon PDRs and ADRs did not differ significantly between groups; AADR (2.6 % vs. 4.3 %; P = 0.02) and ASPDR (1.0 % vs. 1.9 %; P = 0.048) were significantly lower in the low-volume vs. standard-volume groups. When only individuals with adequate bowel preparation were considered, lesion detection rates did not differ significantly between groups except for ASPDR, which was lower in the low-volume vs. standard-volume group (whole colon 1.7 % vs. 3.6 %, P = 0.01; proximal colon 0.5 % vs. 2.0 %, P = 0.003).

Discussion

This is the first population-based, randomized study to investigate whether low-volume sodium picosulfate/magnesium citrate bowel preparation can improve participation in screening colonoscopy when compared with standard-volume PEG preparation. The answer to this research question is negative. Not only did the use of the low-volume preparation fail to improve the participation rate in screening colonoscopy, but it also failed to offer advantages in terms of better compliance, bowel

▶ **Table 1** Baseline characteristics of study groups.

Groups	Low-volume group	Standard-volume group	*P* value
Total, n	6752	6745	
Sex, n (%)			0.98
▪ Men	3179 (47.1)	3174 (47.1)	
▪ Women	3573 (52.9)	3571 (52.9)	
Age, n (%)			0.06
▪ 55 – 59 years	5088 (75.4)	4986 (73.9)	
▪ 60 – 62 years	1664 (24.6)	1759 (26.1)	
Screening center, n (%)			0.50
▪ A	1164 (17.2)	1171 (17.4)	
▪ B	1778 (26.3)	1716 (25.4)	
▪ C	609 (9.0)	604 (9.0)	
▪ D	762 (11.3)	725 (10.7)	
▪ E	1552 (23.0)	1637 (24.3)	
▪ F	887 (13.1)	892 (13.2)	
Area of residence, n (%)			0.22
▪ Urban	4073 (60.3)	3999 (59.3)	
▪ Rural	2679 (39.7)	2746 (40.7)	
Travel distance to the screening center, n (%)			0.45
▪ < 45 km	4933 (73.1)	4889 (72.5)	
▪ ≥ 45 km	1819 (26.9)	1856 (27.5)	
Average income in the area of residence, n (%)			0.25
▪ ≤ country-wide average	4790 (70.9)	4724 (70.1)	
▪ > country-wide average	1962 (29.1)	2021 (29.9)	

▶ **Table 2** Reasons for nonparticipation in screening colonoscopy.

	Low-volume group	Standard-volume group	Total
Individuals in the ITT analysis, n	6752	6745	13 497
Did not respond to invitation/reminder letter, n (%)	4533 (67.1)	4616 (68.4)	9149 (67.8)
Responded to invitation but did not undergo screening colonoscopy, n (%)	970 (14.4)	922 (13.7)	1892 (14.0)
Colonoscopy within 2 years before invitation	171 (2.5)	137 (2.0)	308 (2.3)
Contraindications to bowel preparation or screening colonoscopy	21 (0.3)	10 (0.1)	31 (0.2)
Moved out of the area served by participating screening centers	65 (1.0)	54 (0.8)	119 (0.9)
Did not consent to participate in screening	691 (10.2)	699 (10.4)	1390 (10.3)
Withdraw consent after receiving bowel preparation instructions	22 (0.3)	22 (0.3)	44 (0.3)
Responded to invitation and underwent screening colonoscopy, n (%)	1249 (18.5)	1207 (17.9)	2456 (18.2)
Colonoscopy ≤ 90 days from the date proposed in the invitation letter	1119 (16.6)	1044 (15.5)	2163 (16.0)
Colonoscopy > 90 days from the date proposed in the invitation letter	130 (1.9)	163 (2.4)	293 (2.2)

ITT, intention-to-treat.

▶ **Table 3** Odds ratios of participation in screening colonoscopy.

Variables	Univariable analyses			Multivariable analyses*		
	OR	95%CI	*P*>z	OR	95%CI	*P*>z
Study group						
▪ Standard volume	Reference			Reference		
▪ Low volume	1.08	0.99 – 1.19	0.08	1.09	0.99 – 1.19	0.08
Sex						
▪ Women	Reference			Reference		
▪ Men	1.12	1.03 – 1.23	0.01	1.15	1.05 – 1.26	0.004
Age						
▪ 55 – 59 years	Reference					
▪ 60 – 62 years	1.32	1.19 – 1.46	<0.001			
Area of residence						
▪ Rural	Reference					
▪ Urban	0.98	0.89 – 1.07	0.62			
Travel distance to the screening centre						
▪ <10 km	Reference			Reference		
▪ 10 – 24 km	0.90	0.79 – 1.03	0.11	0.95	0.81 – 1.09	0.45
▪ 25 – 44 km	0.86	0.74 – 0.99	0.03	0.84	0.72 – 0.98	0.02
▪ ≥45 km	0.48	0.41 – 0.56	<0.001	0.52	0.44 – 0.63	<0.001
Average income in the area of residence						
▪ <country-wide average	Reference					
▪ ≥country-wide average	1.29	1.17 – 1.42	<0.001			
Screening center						
▪ A	Reference					
▪ B	0.77	0.66 – 090	0.001	1.01	0.85 – 1.19	0.92
▪ C	1.24	1.03 – 1.49	0.03	1.23	1.01 – 1.50	0.04
▪ D	1.40	1.18 – 1.66	<0.001	1.35	1.13 – 1.62	0.001
▪ E	1.37	1.18 – 1.58	<0.001	1.39	1.20 – 1.62	<0.001
▪ F	1.17	1.00 – 1.39	0.06	1.04	0.87 – 1.25	0.67

OR, odds ratio; CI, confidence interval.
* Only for variables found significant in stepwise regression.

preparation quality, and lesion detection rates. In fact, in this largest study to date, bowel preparation quality and some of the evaluated lesion detection rates (ASPDR) were significantly lower in participants prepared with the low-volume sodium picosulfate/magnesium citrate regimen (▶ **Fig. 3**). We believe, therefore, that sodium picosulfate/magnesium citrate-based low-volume bowel preparation should not be recommended for screening colonoscopy.

The total volume of fluid recommended to be ingested for preparation was nearly the same in both groups (4.3 L and 4.0 L in the low-volume and standard-volume groups, respectively); however, the amount of distasteful cleansing agent solution in the low-volume group was only 0.3 L, which is much lower than the 4.0 L of PEG solution required in the standard-volume regimen. Although we originally assumed that this difference might significantly affect participation in screening colonoscopy, our results showed the opposite. In fact, the vast majority of those who did not participate, either did not respond to the invitation at all or refused to participate before the preparation instructions were given to them. Therefore, in most cases, the knowledge of differences between low- and standard-volume preparations and their potential advantages or disadvantages could not affect individuals' decisions to participate in screening. The number of individuals who withdrew

▶ **Table 4** Secondary outcomes.

Groups	Low volume group	Standard volume group	*P* value	Total
Total, n	1249	1207		2456
Compliance, n (%)				
▪ Preparation agent as allocated	1183 (94.7)	1174 (97.3)	0.001	2357 (96.0)
▪ Consumed the total amount of liquid[1]	1231 (98.6)	1168 (96.8)	0.003	2399 (97.7)
▪ Both	1165 (93.3)	1136 (94.1)	0.39	2301 (93.7)
Quality of bowel preparation[2], n (%)				
▪ BBPS ≥ 2/2/2	987 (79.0)	1043 (86.4)	<0.001	2030 (82.7)
▪ BBPS cumulative values				
▪ ≥ 6/9	1047 (83.8)	1078 (89.3)	<0.001	2125 (86.5)
▪ ≥ 7/9	767 (61.4)	853(70.7)	<0.001	1620 (66.0)
▪ ≥ 8/9	553 (44.3)	699 (57.9)	<0.001	1252 (51.0)
▪ 9/9	326 (26.1)	436 (36.1)	<0.001	762 (31.0)
▪ BBPS ≥ 2 in the right colon	1019 (81.6)	1065 (88.2)	<0.001	2084 (84.9)
▪ BBPS ≥ 2 /2 in the proximal colon	1001 (80.1)	1054 (87.3)	<0.001	2055 (83.7)
Lesion detection rates overall, n (%)				
Whole colon				
▪ PDR	535 (42.8)	512 (42.4)	0.82	1047 (42.6)
▪ ADR	377 (30.2)	355 (29.4)	0.67	732 (29.8)
▪ AADR	97 (7.8)	104 (8.6)	0.45	201 (8.2)
▪ ASPDR	25 (2.0)	40 (3.3)	0.04	65 (2.6)
▪ Missing data	2 (<0.1)	1 (<0.1)		3 (<0.1)
Proximal colon				
▪ PDR	256 (20.5)	258 (21.4)	0.59	514 (20.9)
▪ ADR	194 (15.5)	195 (16.2)	0.67	389 (15.8)
▪ AADR	33 (2.6)	52 (4.3)	0.02	85 (3.5)
▪ ASPDR	12 (1.0)	23 (1.9)	0.048	35 (1.4)
▪ Missing data		1 (<0.1)		1 (<0.1)
Lesion detection rates in participants with BBPS ≥ 2 /2 /2, n (%)				
▪ Whole colon	n = 987	n = 1043		
▪ PDR	425 (43.1)	460 (44.1)	0.64	885 (43.6)
▪ ADR	308 (31.2)	316 (30.3)	0.66	624 (30.8)
▪ AADR	82 (8.3)	81 (7.8)	0.65	163 (8.0)
▪ ASPDR	17 (1.7)	37 (3.6)	0.01	54 (2.7)
▪ Missing data	1 (<0.1)	1 (<0.1)		2 (<0.1)
▪ Proximal colon	n = 987	n = 1043		
▪ PDR	203 (20.6)	238 (22.8)	0.22	441 (21.8)
▪ ADR	158 (16.0)	177 (17.0)	0.56	335 (16.5)

▶ **Table 4** (Continuation)

Groups	Low volume group	Standard volume group	*P* value	Total
▪ AADR	27 (2.7)	43 (4.1)	0.09	70 (3.5)
▪ ASPDR	5 (0.5)	21 (2.0)	0.003	26 (1.3)
▪ Missing data		1 (<0.1)		1 (<0.1)

BBPS, Boston Bowel Preparation Scale; PDR, polyp detection rate; ADR, adenoma detection rate; AADR, advanced adenoma detection rate; ASPDR, advanced serrated polyp detection rate.
[1] Low-volume group: 0.3 L of cleansing agent solution + 4 L of additional water/clear liquids; standard-volume group: 4 L polyethylene glycol solution.
[2] Data for the three colon sections.

their consent to screening after receiving bowel preparation instructions was negligibly low in both groups (0.3 %). This corroborates previous data indicating that the fear of preparation and colonoscopy in general, rather than details such as the volume and type of cleansing solution, is the most significant barrier to participation in CRC screening [13 – 15].

Men, people aged 60 – 62 years, those living closer to the screening center and in more affluent areas were more likely to participate in screening colonoscopy than women, people aged 55 – 59 years, and those living farther away from the screening center and in less affluent areas. Similar results were reported in previous studies [7, 10, 14]. In the multivariable model in the present study, only sex, travelling distance to the screening center, and the screening center itself were factors significantly associated with participation rate.

The compliance rates were similar in both groups and generally high; however, when the components of this composite outcome measure were analyzed separately, significant differences between the groups were observed. In the low-volume group, participants were less likely to prepare with the allocated regimen but more likely to ingest the whole recommended amount of liquid. The reason for using a preparation other than the one allocated was that some participants obtained the bowel cleansing agent from their general practitioner rather than from the screening center. Because 4 L PEG is by far the most popular cleansing agent in Poland, the general practitioner was more likely to recommend standard-volume rather than low-volume preparation.

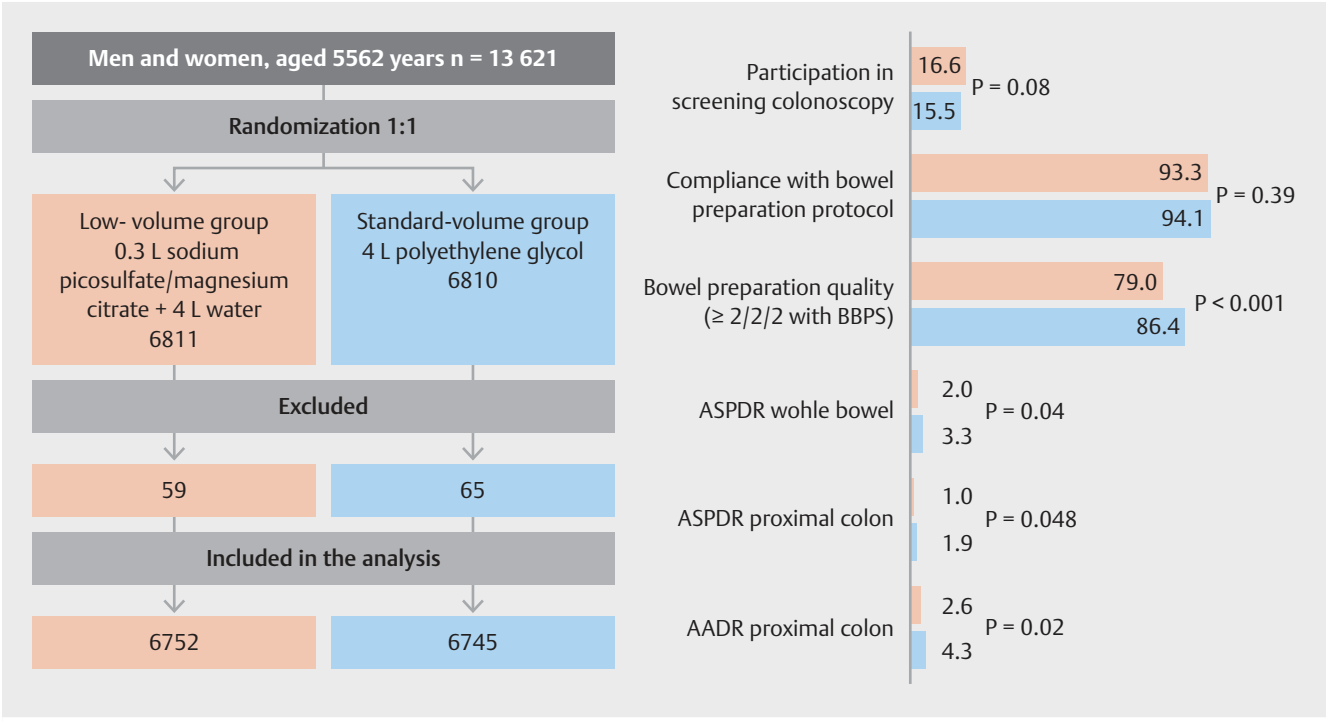
An interesting new finding is that although overall compliance rates did not differ between groups, and the individuals in the low-volume group were more likely to ingest the whole recommended amount of fluid, they were less likely to achieve adequate bowel preparation, both for the whole and the proximal colon. Moreover, the differences in preparation quality in favor of standard-volume preparation became more pronounced when more stringent criteria of preparation quality were applied. Compared with the low-volume group, the rates of individuals who achieved BBPS scores of ≥ 6/9, ≥ 7/9, ≥ 8/9, and 9/9 in the standard-volume group were higher by 5.5, 9.3, 13.6, and 10.0 percentage points, respectively. Previously, insignificant differences in bowel preparation quality and better tolerance of sodium picosulphate/magnesium citrate solution compared with PEG were reported [26 – 30]. Previous studies, however, were limited in size and demonstrated some methodological uncertainties leading to the conclusion that large, well-designed studies are warranted [26].

The low-volume preparation did not offer any advantages over standard-volume preparation in terms of lesion detection rates. In fact, higher detection rates of advanced lesions (ASPDR in the whole and proximal colon, and AADR in the proximal colon) were observed in the standard-volume group. These findings, however, should be treated with caution, because they were not accompanied by higher detection rates of nonadvanced lesions (ADR and PDR).

The present study evaluated a large number of individuals drawn from a homogeneous, average CRC risk population, and was conducted within a well-established screening program as a randomized health services study. The participating screening centers were selected based on quality indicators. The participating endoscopists were trained in BBPS use and blinded to evaluated individuals' allocation.

We acknowledge the following limitations of the present study. Individuals aged 63 – 64 years, who are normally eligible for PCSP and demonstrate the highest compliance with screening, were not included in the present study because of administrative reasons (within each calendar year, the PSCP invites participants in descending order of age; individuals aged 63 – 64 years were invited in the first months of the year, before the study start). A total of 124 randomized individuals (0.9 %) were excluded from the ITT analysis because the invitation letter could not be delivered to them or, as it turned out, they had died or had been diagnosed with CRC before the randomization date. The number of individuals excluded for these reasons was similar in both groups. A further 308 individuals who responded to the invitation could not participate in screening because they had already undergone screening colonoscopy within the previous 2 years. Because this examination was done outside the PCSP, it was not recorded in the PCSP database and cross-checked before randomization and the sending of invitation letters.

The primary outcome measure – participation in screening colonoscopy – was arbitrarily defined as colonoscopy performed within 90 days from the date proposed in the invitation letter. This definition was chosen because it considers all possible factors affecting individuals' decisions to participate or not participate in screening that might be involved during the peri-



▶ **Fig. 3** Summary of study design and main results. BBPS, Boston Bowel Preparation Scale; AADR, advanced adenoma detection rate; ASPDR, advanced serrated polyp detection rate.

od between the invitation and screening colonoscopy. A sample size of 13 468 individuals was large enough to detect a small difference of 2 % in participation rates between groups. Randomization was done before invitation to screening in order to exclude the potential influence of the PCSP personnel, who provided the information about bowel preparation, on individuals' decision to participate or not participate. The proportion of individuals who did not respond to the invitation, did not attend the pre-colonoscopy visit, and hence did not receive any information on the assigned bowel preparation was similar in the two groups. With a time frame longer than 90 days, the participation rate would be higher. In fact, it increased by 2.2 % – from 16.0 % to 18.2 % – when all individuals who underwent colonoscopy up to the end of 2015 were analyzed, including both those who did and did not meet the 90-day limit. The increase was similar in both groups.

In 39 % of individuals, bowel preparation was administered as nonsplit, day-before dosing and this might have negatively affected the quality of bowel preparation. The proportion of individuals prepared in this way was similar in the low-volume and standard-volume groups, and therefore bias from this source is unlikely. In addition, the time between completion of the preparation and the start of colonoscopy – a factor known to influence the quality of bowel preparation – was not measured and cannot be compared between the groups. The cleansing agent was self-administered by the participants and data on compliance were self-reported.

Finally, data on tolerance, satisfaction, and adverse events related to preparation were not collected. Such data might be useful to evaluate individuals' decisions not to comply with recommended preparation, continue the preparation, or undergo screening colonoscopy; however, collecting such data would require modification of standard procedures of PCSP. Because the present study was designed and conducted as a pragmatic, randomized, health services study evaluating participation in PCPS under real life conditions, our aim was not to modify the standard procedures of PCSP. For the same reason, the information about bowel preparation was provided to screening participants in a standard way, without emphasizing potential advantages and disadvantages of low- or standard-volume regimens, and without informing the participants that they were taking part in a research study.

In conclusion, when compared with standard-volume PEG bowel preparation, low-volume sodium picosulfate/magnesium citrate bowel preparation did not improve participation or lesion detection rates, and negatively affected bowel preparation quality.

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Competing interests

Dr. Kaminski has taken part in advisory board meetings for Alfa Sigma and has received speaker fees from Norgine. Dr. Regula has taken part in advisory board meetings for IpsenPharma and Takeda.

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