

Enhanced instructions improve the quality of bowel preparation for colonoscopy: a meta-analysis of randomized controlled trials



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Background and Aims: The success of a colonoscopy is highly dependent on the quality of bowel preparation (BP). Many patients have poor BP due to non-compliance with regular instructions. Reports concerning the effects of enhanced instructions on BP quality are inconsistent. The aim of this meta-analysis was to compare BP quality between patients receiving enhanced instructions in addition to regular instructions and those who received regular instructions only.

Methods: MEDLINE, EMBASE, Web of Science, and the Cochrane Library were searched to identify relevant studies published for August 2015. The quality of BP (adequate/inadequate), adenoma detection rate, polyp detection rate, willingness to repeat preparation, and adverse events were estimated by using odds ratios (OR) and 95% confidence intervals (CI) with random effects models.

Results: Eight randomized controlled trials (n = 3795) were included. Patients who received enhanced instructions showed significantly better BP quality than those receiving only regular instructions (OR, 2.35; 95% CI, 1.65-3.35; $P < .001$). Subgroup analysis showed that the beneficial effects of enhanced instructions on BP quality were consistent among patients receiving different purgative types, administration methods, or diet restriction (all $P < .05$). Patients in the enhanced instructions group showed more willingness to repeat the preparation (OR, 1.91; 95% CI, 1.20-3.04; $P = .006$).

Conclusions: Enhanced instructions significantly improved the quality of BP and willingness to repeat the preparation in patients undergoing colonoscopy. Factors related to patient instructions appear to be as important as the preparation method itself in improving BP quality. (Gastrointest Endosc 2017;85:90-7.)

INTRODUCTION

Colonoscopy is considered to be the standard method for the diagnosis, screening, and surveillance of colorectal lesions. Screening colonoscopies have been shown to

decrease colorectal cancer (CRC) incidence and mortality.^{1,2} The success of colonoscopy is highly dependent on the quality of bowel preparation (BP). However, previous studies have shown that 18% to 30.5% of patients had inadequate BP.³⁻⁵ Suboptimal BP can decrease the adenoma detection rate (ADR) and cecal intubation rate, reduce the time interval for surveillance, and prolong the procedural time.⁶⁻⁸

BP is a relatively complicated procedure, and many factors may influence the quality, including proper diet restriction, use of split-dose purgatives, and appropriate interval between the end of preparation and the start of colonoscopy. The adequacy of BP is also associated with patient-related factors, such as age, body mass index (BMI), comorbidities (eg, constipation and diabetes), and more importantly, patient compliance.⁹⁻¹¹ Although many intrinsic factors cannot be altered by interventions, patient compliance may be relatively easily improved by comprehensive communication. It has been found that nearly 20% of patients with poor BP had failed to follow

Abbreviations: ADR, adenoma detection rate; BBPS, Boston Bowel Preparation Scale; BMI, body mass index; BP, bowel preparation; CI, confidence interval; CRC, colorectal cancer; EI, enhanced instructions; HCS, Harefield Cleansing Scale; MD, mean difference; OBPS, Ottawa Bowel Preparation Scale; OR, odds ratio; PDR, polyp detection rate; PEG, polyethylene glycol; RCT, randomized controlled trial; RI, regular instructions; SMS, short message service; UPAS, Universal Preparation Assessment Scale.

DISCLOSURE: All authors disclosed no financial relationships relevant to this publication.

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0016-5107/\$36.00

<http://dx.doi.org/10.1016/j.gie.2016.05.012>

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preparation instructions.¹² Chan et al¹³ showed that non-compliance with instructions, lower education level, and longer waiting time were independent risk factors associated with poor BP, among which non-compliance had the highest odds ratio (OR) (4.76). Therefore, it is reasonable to hypothesize that improvement in compliance through enhanced instructions (EI) during the preparatory period might increase the adequacy of BP.

Usually, patients receive a written booklet and/or verbal instructions from medical practitioners weeks before colonoscopy for BP, which are defined as regular instructions (RI). However, RI were often found to be less effective in achieving adequate BP.⁵ Several tools have been developed to enhance RI, including cartoon pictures,¹⁴ phone calls,^{12,15} social media applications,⁵ and smart phone applications.¹⁶ The roles of these tools in improving BP quality have been investigated in some high-quality randomized controlled trials (RCTs). However, these studies have yielded conflicting results. Although BP quality was not improved in 2 studies in which patients received EI with additional explanation¹⁷ or visual aids,¹⁸ improvement was documented in many others.^{5,12,14-16,19} We performed a meta-analysis to evaluate the influence of different kinds of EIs on BP quality, ADR, polyp detection rate (PDR), and other outcomes.

METHODS

Search strategies

English studies were identified by a comprehensive search of MEDLINE, EMBASE, Web of Science, and the Cochrane Library for August 2015. Our key words and search strategies were as follows: 1, (“education” [All Fields] OR educate [All Fields]) AND (“colonoscopy” [All Fields] OR “colonoscopy” [MeSH Terms]); 2, (“instruction” [All Fields] OR “instruct” [All Fields]) AND (“colonoscopy” [All Fields] OR “colonoscopy” [MeSH Terms]); 3, (“education” [All Fields] OR “educate” [All Fields]) AND (“bowel preparation” [All Fields] OR “bowel preparation” [MeSH Terms] OR “bowel cleansing” [All Fields]); 4, (“instruction” [All Fields] OR “instruct” [All Fields]) AND (“bowel preparation” [All Fields] OR “bowel preparation” [MeSH Terms] OR “bowel cleansing” [All Fields]). Reference lists of primary study publications, reviews, editorials, and the proceedings of international congresses were searched manually. We did not consider abstracts or unpublished reports for inclusion.

Study selection

We included only RCTs comparing RI with EI. Study participants included patients more than 18 years old who underwent colonoscopy. Study interventions included EI plus RI versus RI only. The primary outcome was the rate of adequate BP. Four BP scales were used to assess BP quality: Boston Bowel Preparation Scale (BBPS), Ottawa Bowel

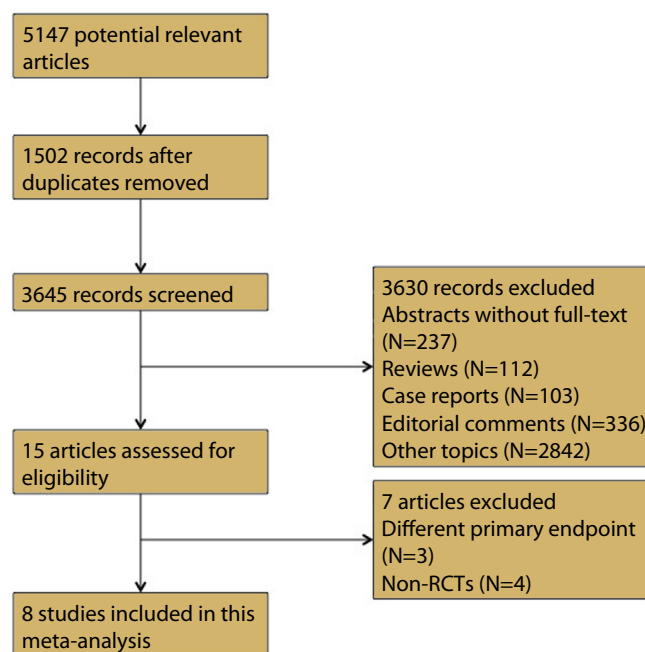


Figure 1. Search strategies. *RCT*, randomized controlled trial.

Preparation Scale (OBPS), Universal Preparation Assessment Scale (UPAS), and Harefield Cleansing Scale (HCS). The adequacy of BP was defined by a BBPS score ≥ 5 , an OBPS score < 6 , a UBPS score < 3 , or an HCS grade A or B.

Data extraction

Two investigators (X.Y.G. and S.G.Y.) extracted the data independently. Agreements and disagreements were resolved through discussion. The following data were extracted for each eligible study: author, year of publication, geographic location, study design, blinding, inclusion criteria, exclusion criteria, number of patients screened, number of patients allocated to each group, detailed information of interventions and controls, indications for colonoscopy, primary and secondary endpoints, BP scales, purgatives, diet restrictions, methods of administration, cecal intubation rates, insertion times, and withdrawal times.

Quality assessment

Two tools were used to evaluate study quality, including the Cochrane Risk Bias Tool ([Supplementary Fig. 1](#)) and Jadad score.²⁰ Only one study¹⁶ used a non-random component in the sequence generation process. Jadad scores were 2 in 2 studies and 3 in 6 studies (mean, 2.75; 95% confidence interval [CI], 2.36-3.14) ([Supplementary Table 1](#)). Because patients could not be blinded to instruction methods, all trials were only single blinded.

Statistical methods

All statistical analyses were performed using Review Manager (version 5.2) and Stata (version 12.0). Random

TABLE 1. Details of studies included in this meta-analysis

	Calderwood et al, 2011 ¹⁸	Kang et al, 2015 ⁵	Lee et al, 2015 ¹⁵	Liu et al, 2014 ¹²
Location	USA	China	Korea	China
Design	RCT	RCT	RCT	RCT
Blinding	Single	Single	Single	Single
Total number	969	770	386	605
EI	Visual aid	Social media app	Telephone, SMS	Telephone
RI	Written instructions	Verbal and written instructions	Verbal and written instructions	Verbal and written instructions
Indications	Screening	Mixed	Screening	Mixed
Primary endpoint	Rate of adequate BP	Rate of adequate BP	Rate of adequate BP	Rate of adequate BP
BP scale	BBPS	OBPS	BBPS	OBPS
Purgative	4 L of PEG or 4 L of PEG + bisacodyl	4 L of PEG-ELP	2 L of PEG + ascorbate solution	2 L of PEG-ELP or 1.5 L of sodium phosphate
Administration method	NR	Split dose	Split dose	Single dose
Diet restriction	NR	Clear liquid	Low-residue	Clear liquid
Timing of EI	NR	15 days before	2 days before	1 day before
Cecum intubation rate	NR	97.2% vs 93.2%	99.2% vs 98.5%	94.9% vs 85.4%
Insertion time (min), mean \pm SD	7.0 \pm 3.7 vs 7.0 \pm 3.7	7.2 \pm 4.6 vs 9.1 \pm 4.8	3.5 \pm 3.5 vs 3.4 \pm 3.1	7.7 \pm 5.1 vs 7.6 \pm 4.3
Withdrawal time (min), mean \pm SD	8.0 \pm 3.7 vs 7.0 \pm 3.0	7.2 \pm 2.2 vs 7.4 \pm 2.1	9.8 \pm 10.9 vs 9.1 \pm 7.6	6.2 \pm 2.3 vs 7.8 \pm 2.8
BP score, mean \pm SD	6.0 \pm 0.7 vs 6.0 \pm 0.7	3.6 \pm 1.7 vs 4.5 \pm 1.8	6.8 \pm 1.3 vs 6.3 \pm 1.4	3.0 \pm 2.3 vs 4.9 \pm 3.2

RCT, Randomized controlled trial; EI, enhanced instructions; SMS, short message service; RI, regular instructions; BP, bowel preparation; BBPS, Boston Bowel Preparation Scale; OBPS, Ottawa Bowel Preparation Scale; HCS, Harefield Cleansing Scale; UPAS, Universal Preparation Assessment Scale; PEG, polyethylene glycol; NR, not reported; SD, standard deviation.

effects models were used to combine the outcome effects of the difference between the experimental and control groups. Data were presented with 95% CIs using forest plots. A *P* value less than .05 was considered significant. Statistical heterogeneity was examined using the *Q* test (significant when *P* < .10) and the *I*² value (significant when *I*² > 50%).²¹

RESULTS

Study selection

According to our search strategy, 5147 articles were identified; 1502 records were removed because of duplication and 3630 articles were excluded after reading the abstract. Of the remaining 15 articles, 7 were excluded after reading the full text for the following reasons: primary outcome was not the rate of adequate BP (*n* = 3) or the study type was non-RCT (*n* = 4). Eight RCTs were included in the final analysis (Fig. 1).^{5,12,14-19}

Characteristics of the selected trials

The characteristics of the 8 RCTs are summarized in Table 1. The control treatment was verbal plus written instructions or written instructions only. Patients in the EI group were all supplied with additional tools or materials to enhance the instructions for BP. The primary

endpoint of the 8 trials was the rate of adequate BP; the secondary endpoints were different, and included PDR or ADR, cecal intubation rates, insertion times, withdrawal times, and patient's willingness to repeat BP.

The evaluation methods and the BP procedures in these studies were different. First, the quality of BP was evaluated by different scales: BBPS^{14,15,18} in 3 studies, OBPS^{5,12,19} in 3, UPAS¹⁷ in 1, and HCS in 1.¹⁶ Second, preparation methods, including the type, volume, and administration method of purgatives as well as diet restriction, were different.

Characteristics of the patients in the selected trials

The 4 screening studies enrolled patients more than 18,^{15,18} 20,¹⁴ or 40¹⁷ years old. The other 4 studies enrolled patients aged ≥ 18 years for indications other than screening.^{5,12,19,21} Furthermore, some studies had additional enrollment requirements. Two studies included patients who had smart phones¹⁶ or mobile phones.¹⁵ Another study requested that participants should have convenient access to a social media application (WeChat).⁵

Primary outcome

BP quality. The quality of BP was analyzed as the primary outcome in all studies (*n* = 3795) (Fig. 2 and

TABLE 1. Continued

Lorenzo-Zuniga et al, 2015 ¹⁶	Modi et al, 2009 ¹⁷	Spiegel et al, 2011 ¹⁹	Tae et al, 2012 ¹⁴
Spain	USA	USA	Korea
RCT	RCT	RCT	RCT
Single	Single	Single	Single
260	164	436	205
Smart phone app	Additional explanation	Newly designed booklet	Cartoon visual aids
Written instructions	Verbal and written instructions	Verbal and written instructions	Verbal and written instructions
Mixed	Screening	Mixed	Screening
Rate of adequate BP	Rate of adequate BP	Rate of adequate BP	Rate of adequate BP
HCS	UPAS	OBPS	BBPS
2 L of PEG + ascorbate solution	4 L of PEG + 3 bisacodyl tablets	2 L of PEG, sodium phosphate, or magnesium citrate	4 L of PEG
Split dose	NR	Single dose	Split dose
Low-fiber	Clear liquid	Clear liquid	NR
NR	21 days before	7 days before	NR
NR	NR	NR	NR
NR	20.1 ± 9.2 vs 25.8 ± 9.2	NR	7.7 ± 4.2 vs 7.1 ± 4.4
NR	11.0 ± 10.9 vs 13.2 ± 7.0	NR	9.0 ± 4.8 vs 11.1 ± 4.4
16.5 ± 3.1 vs 17.1 ± 3.2	NR	4.4 ± 2.3 vs 5.1 ± 2.9	7.4 ± 1.9 vs 6.1 ± 2.2

Supplementary Fig. 2). Adequate BP was achieved in 88.5% (1603/1812) of patients in the EI group and 78.4% (1367/1743) in the RI group (OR, 2.35; 95% CI, 1.65-3.35; $P < .001$).

Subgroup analysis. *BBPS versus OBPS.* Three studies^{14,15,18} used BBPS to evaluate BP quality. There was no significant difference between the 2 groups (770/830, 92.8% vs 636/725, 87.7%; OR, 2.34; 95% CI, 0.96-5.69; $P = .060$) (Supplementary Fig. 2). Three studies^{5,12,19} used OBPS. Compared with RI (539/786, 68.6%), the EI group (667/790, 84.4%) had a higher rate of adequate BP (OR, 2.64; 95% CI, 1.76-3.89; $P < .001$). Three studies reported the mean individual BBPS^{14,15,18} and OBPS,^{5,12,19} respectively. The mean individual BBPS in the EI and RI groups were 6.5 ± 1.2 and 6.1 ± 1.2 (mean difference [MD] -1.18 ; 95% CI, -1.88 to -0.47 ; $P < .001$). The mean individual OBPS scores were 3.5 ± 2.1 and 4.8 ± 2.6 , respectively (MD, 0.81; 95% CI, 0.42-1.19; $P < .001$). Both of these results indicate that patients receiving EI had better BP quality.

Polyethylene glycol (PEG, 4 L) versus PEG (2 L) plus ascorbate. Two studies^{5,14} chose 4 L of PEG as the purgative. Compared with RI, patients in the EI group had better BP quality (413/455, 90.8% vs 346/450, 76.9%; OR, 2.96; 95% CI, 2.01-4.35; $P < .001$). Another 2 studies^{15,16} used 2 L of PEG plus ascorbate solution as the purgative.

Patients in EI group also showed higher BP adequacy (351/359, 97.8% vs 264/287, 92.0%; OR, 4.67; 95% CI, 2.03-10.73; $P < .001$).

Split dose versus single dose. Split doses of purgatives were used in 4 studies^{5,14-16} and single doses were used in 2 studies.^{12,19} The studies using split doses (eg, 4 L of PEG) showed better BP quality in the EI group (764/814, 93.9% vs 610/737, 82.8%; OR, 3.21; 95% CI, 2.26-4.55; $P < .001$). Patients receiving single-dose purgatives in the EI group also had better BP quality (349/437, 79.9% vs 273/434, 62.9%; OR, 2.54; 95% CI, 1.33-4.85; $P = .005$).

Screening colonoscopy versus diagnostic colonoscopy. Four studies^{14,15,17,18} enrolled only patients undergoing screening colonoscopy. The BP quality of screening patients was better in the EI group than in the RI group (828/914, 90.6% vs 682/805, 84.7%; OR, 2.05; 95% CI, 1.14-3.70; $P = .020$). Three studies^{5,12,15} enrolled patients with constipation. The BP quality of patients with constipation was better in the EI group than in the RI group (121/136, 89.0% vs 68/114, 59.6%; OR, 5.11; 95% CI, 2.62-9.96; $P < .001$).

Low-fiber/residual diet versus clear liquid diet. Two studies^{15,16} used a low-fiber/residual diet before colonoscopy. Patients in the EI group showed better BP quality

compared with the RI group (351/359, 97.8% vs 264/287, 92.0%; OR, 4.67; 95% CI, 2.03-10.73; $P < .001$). Four trials^{5,12,17,19} used a clear liquid diet. Patients in the EI group also showed better BP quality in comparison with patients in the RI group (725/874, 83.0% vs 585/866, 67.6%; OR, 2.42; 95% CI, 1.71-3.41; $P < .001$).

Long versus short time interval from EI to colonoscopy. The timing of EI was reported in 5 studies. Two studies reported a long time interval (>1 week) between EI and colonoscopy.^{5,17} Patients with a long time interval in the EI group had better BP quality compared with those in the RI group (376/437, 86.0% vs 312/432, 72.2%; OR, 2.32; 95% CI, 1.33-4.05; $P = .003$). Three studies^{12,15,18} reported a short interval time (≤ 1 week), in which patients also had better quality of BP after receiving EI (592/688, 86.0% vs 391/569, 68.7%; OR, 2.87; 95% CI, 1.66-4.95; $P < .001$).

Secondary outcome

Procedure-related parameters. Cecal intubation rate was reported in 3 studies.^{5,12,15} Compared with the RI group, the EI group showed a higher cecal intubation rate (853/879, 97.0% vs 819/886, 92.4%; OR, 2.77; 95% CI, 1.73-4.42; $P < .001$). The reasons for failed intubation were poor BP and technical difficulty or stricture (Supplementary Table 6). Failed intubations due to poor BP in the EI group were lower than in the RI group (8/882, 0.9% vs 45/762, 5.9%; OR, 0.15; 95% CI, 0.07-0.31; $P < .001$). The rates of failed intubation due to technical difficulty or stricture were similar between the 2 groups ($P = .340$).

Insertion and withdrawal times were presented in 6 studies.^{5,12,14,15,17,18} There was no difference between the 2 groups with regard to mean insertion time (7.3 ± 5.9 min vs 7.9 ± 6.8 min; MD, -0.57 ; 95% CI, -1.38 to 0.24 ; $P = .170$). However, patients in the EI group had a shorter withdrawal time (7.6 ± 5.3 min vs 8.5 ± 4.7 min; MD, -0.28 ; 95% CI, -0.49 to -0.06 ; $P = .010$).

PDR. PDR was reported in 5 studies.^{12,15-18} There was no significant difference in PDR between the EI and RI groups (448/1245, 36.0% vs 363/1179, 30.8%; OR, 1.25; 95% CI, 0.93-1.68; $P = .140$).

Adverse events. Four studies^{5,12,15,18} reported data on adverse events, including nausea/vomiting, abdominal pain, and distension. No significant differences were noted in overall adverse events (420/1359, 30.9% vs 398/1254, 31.7%; OR, 0.76; 95% CI, 0.54-1.07; $P = .120$) as well as nausea/vomiting (262/1359, 19.3% vs 260/1254, 20.7%; OR, 0.77; 95% CI, 0.60-0.99; $P = .050$), abdominal pain (OR, 0.99; 95% CI, 0.68-1.64; $P = .980$), and abdominal distention (OR, 0.86; 95% CI, 0.66-1.12; $P = .260$).

Willingness to repeat preparation. Three studies^{5,12,15} examined the willingness of patients to repeat BP. Patients in the EI group were more willing to repeat preparation (90.5% vs 83.1%; OR, 1.91; 95% CI, 1.20-3.04; $P = .006$) (Fig. 3).

Sensitivity analysis

By exclusion of each individual study one at a time, we found a significant change in the heterogeneity of the rate of BP quality (heterogeneity $P = .008$, $I^2 = 63\%$). If Calderwood's study¹⁸ was removed, there was no heterogeneity of BP quality (heterogeneity $P = .18$, $I^2 = 33\%$). Sensitivity analysis was also performed on other outcomes with ≥ 3 studies. Five outcomes had significant heterogeneity, including insertion time, withdrawal time, PDR, adverse events, and patient willingness to repeat BP. The studies associated with heterogeneity of each outcome are listed in Supplementary Table 2.

DISCUSSION

Publication bias

Begg's test indicated that there was no publication bias ($P = .95$) (Supplementary Figure 3).

Traditional instructions for BP before colonoscopy may not be effective enough to ensure high quality of BP.³ Many patients were not fully compliant with instructions, and up to a third of patients had inadequate BP.^{4,5} We conducted a meta-analysis demonstrating that EI can effectively improve the quality of BP. All of the patients in the EI group also received RI, so the effects of EI on BP quality are based on application of the RI. It is not known yet whether EI alone could achieve a similar effect on BP; this warrants further investigation.

It remains unclear why EI can improve BP quality. Compared with RI, EI may provide more understandable materials for education, an easier method of accessing BP-related information, a more interactive routine for solving problems, or an additional method to avoid incorrect memory. The EI methods were quite diverse in the 8 RCTs, including additional explanation, visual aids, new booklet design, phone calls, short message service (SMS), social media applications, and smart phone applications. As shown in Supplementary Table 3, the characteristics and possible advantages of these EI methods were different. The common factor for patients receiving various EIs may be the better compliance with instructions, including correct diet restriction, appropriate methods of administration, and drinking enough volume of purgative. However, compliance was measured by patient interview in only 3 studies, which all showed an improvement.^{5,12,15} Newly designed booklets, visual aids, or cartoon visual aids, as a method of EI to facilitate understanding of the BP procedure in 3 RCTs, were found to be associated with better BP quality (88.2% vs 80.1%, $P < .001$). Phone calls or SMSs, with similar benefits of being more interactive and augmenting memory, were used in 2 studies and proven to be effective for BP quality improvement (88.5% vs 75.6%, $P < .001$). Smart phone applications or social media applications, with similar advantages of making instructions easily accessible, were

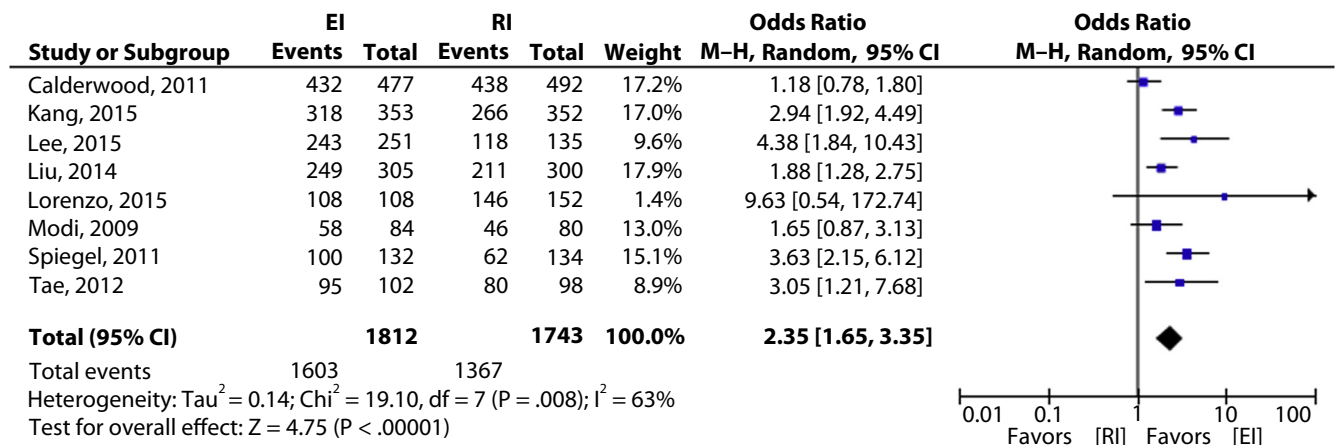


Figure 2. Forest plot comparing the bowel preparation quality between the enhanced instruction (EI) and regular instruction (RI) groups. *CI*, confidence interval.

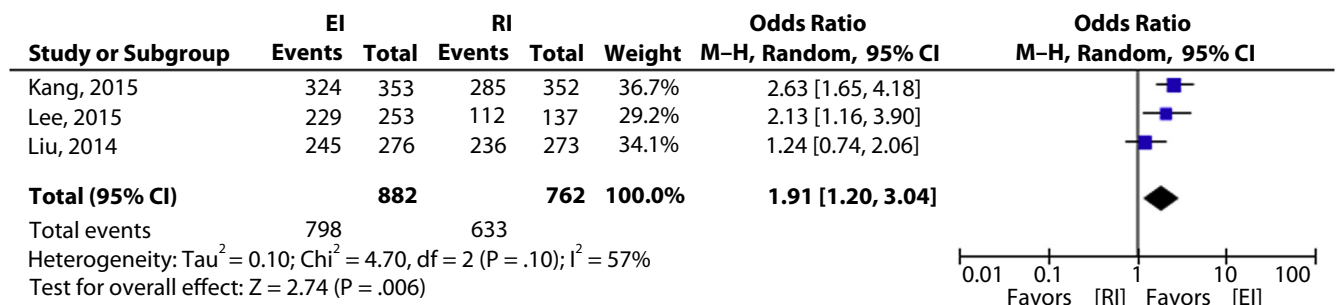


Figure 3. Forest plot comparing the willingness to repeat bowel preparation between the enhanced instruction (EI) and regular instruction (RI) groups. *CI*, confidence interval.

used in 2 studies and also proved to be more effective for BP quality (97.8% vs 92.0%, $P < .001$). However, because of the absence of head-to-head comparisons among different EI methods, it remains unknown which EI method or which combination of methods is the best for BP instruction.

As one of the quality indicators of colonoscopy, BP quality should be described in colonoscopy reports.²² However, no consensus method was available to measure bowel cleanliness and define the quality of BP. In the past few years, several rating scales were developed to evaluate the quality of BP, including BBPS,²³ OBPS,²⁴ Aronchick scale, and UPAS. Although BBPS is thought to be the best in clinical practice with high intra- and inter-observer reliability and good correlation with colonoscopic findings,²⁵ OBPS has also been widely used for many years. Both scales were used in 3 RCTs included in this meta-analysis. The subgroup analysis showed that patients in the EI group tended to have better BP quality no matter which methods of evaluation (BBPS or OBPS) were used, indicating that EIs have a substantial impact on the quality of BP.²⁶ Our study also showed that more patients evaluated by BBPS had adequate BP compared with those evaluated by OBPS (90.4% vs 76.5%, $P < .001$). Unlike the OBPS, BBPS is used during

the withdrawal phase with the requirement of bowel washing and fluid suctioning. The additional step of bowel cleansing improves the BP quality in patients evaluated by BBPS compared with OBPS, as revealed by the present study. The difference between the RI and EI groups was only 5% for trials using BBPS compared with 16% for trials using OBPS. The reasons for these differences are not clear. The method/scale used to rate the bowel preparation may somehow magnify differences.

Procedure-related factors were found to be changed after EI. Compared with the RI group, patients receiving EI had higher intubation success rates and shorter withdrawal times. Insertion times also tended to be shorter in the EI group. The influences of EI in these procedure-related factors may be associated with the improved BP quality in the EI group. It has been found that better BP quality is associated with increased cecal intubation rate and decreased total procedure time,⁶⁻⁸ which is consistent with the present study.

Both patient-related factors (eg, methods and the timing of instructions) and preparation-related factors (eg, types and drinking of purgatives, diet restrictions) influence BP quality. As shown in [Supplementary Table 4](#), patients receiving EI, the administration of split doses,

low-fiber or low-residual diet, or 2 L of PEG plus ascorbate solution all had better BP quality compared with the controls (all $P < .001$). Among the 3 preparation-related factors, the advantages of split doses have been widely accepted.^{25,27,28} Although our analyses also showed that a low-fiber or low-residual diet and 2 L of PEG plus ascorbate solution could improve BP quality compared with the controls, because of possible selection bias, these results needed to be confirmed in the further studies. Based on the data on absolute risk reduction, EI seems to have less or comparable influence on BP than preparation-related factors (10.0% vs 11.3%-19.9%). It remains unclear whether the effects of EI on BP quality are independent of the preparation-related factors. EI seems to have the complementary advantage of enhancing patient compliance with the preparation method.^{5,12} It is possible that patients receiving both EI and an appropriate preparation method could achieve optimal BP quality.

Although this meta-analysis confirms the effectiveness of EI in improving BP, several areas warrant further investigation. First, the preparation methods, including purgative types and volume, method of administration, and types of dietary regimens, were quite different among the 8 RCTs (Table 1). Furthermore, some studies used the same preparation in both arms but others used different preparations in the study arms although evenly balanced. The effects of different preparation methods on BP quality in patients receiving EI or RI needs to be further determined. Second, the interventions considered in the enhanced arm in this meta-analysis were very diverse (cartoons vs smartphone applications) (Supplementary Table 3). It is difficult to draw conclusions on a summary of them as a group when each individual intervention was different. Third, the indications for colonoscopy examinations may have the potential to affect the results of colonoscopies. Although EI was found to be effective for improving BP quality in screening patients and those with constipation, it remains unknown whether it had similar effects in patients for other indications. Fourth, most (7/8) of the studies were from East Asia or the USA. Although the benefits of EI were observed in patients in these 2 regions (Supplementary Table 5), the effects of EI on BP quality need to be further confirmed in patients in other countries. Fifth, all the EI methods produce a selection bias for a certain cohort of individuals (eg, the social media application method can only be used by individuals with convenient access to the Internet), which may not be representative of patients with other socioeconomic status.

In summary, the present study provides the evidence that EI significantly improves the quality of BP and willingness to repeat preparation in patients undergoing colonoscopy. Factors related to patient instructions appear to be as important as the preparation method itself in improving BP quality.

ACKNOWLEDGMENTS

This work was supported in part by the National Natural Science Foundation of China (81172288 and 81570482).

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Received November 23, 2015. Accepted May 4, 2016.

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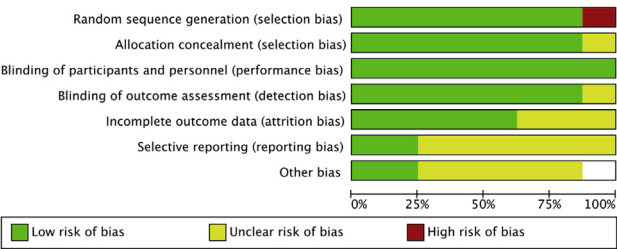
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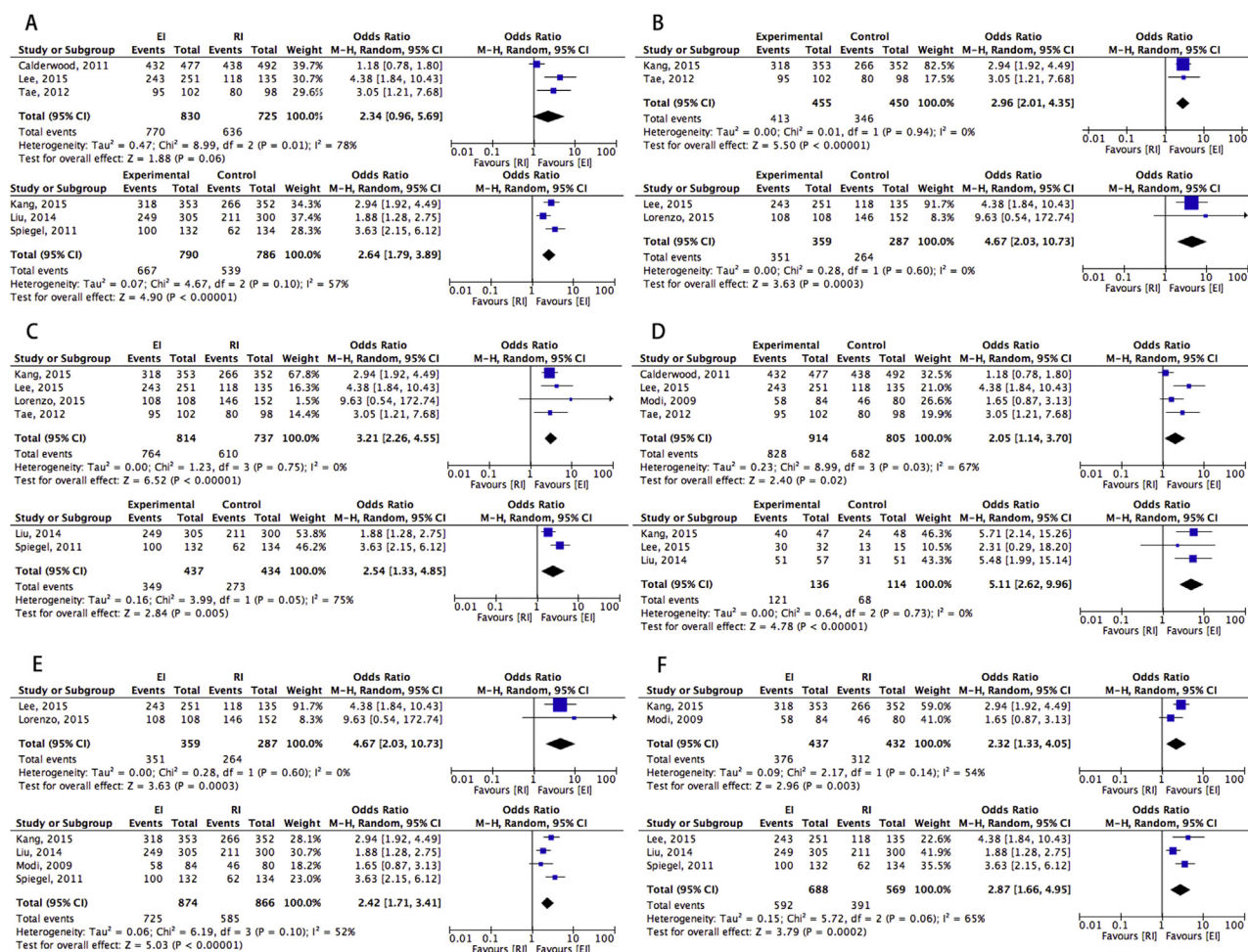
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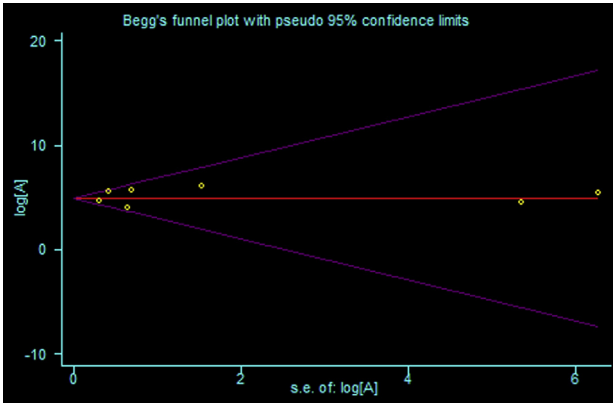
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Supplementary Figure 1. Evaluation of study quality by the Cochrane Risk Bias Tool.



Supplementary Figure 2. Forest plots comparing the quality of bowel preparation in subgroups of patients. (A) BBPS versus OBPS; (B) 4 L of PEG versus 2 L of PEG + ascorbate; (C) split dose versus single dose; (D) screening colonoscopy versus diagnostic colonoscopy; (E) low-fiber/residual diet versus clear liquid diet; (F) long versus short time interval from EI to colonoscopy. *BBPS*, Boston Bowel Preparation Scale; *OBPS*, Ottawa Bowel Preparation Scale; *PEG*, polyethylene glycol; *EI*, enhanced instruction; *RI*, regular instruction.



Supplementary Figure 3. Begg's test indicating no significant publication bias.

SUPPLEMENTARY TABLE 1. Details of quality assessment using Jadad score

Study	Design	Randomization	Randomization method appropriate	Double blinded	Double blinding method appropriate	Description of withdrawals and dropouts	Total Jadad score
Calderwood et al, 2011 ¹⁸	RCT	1	1	0	0	0	2
Kang et al, 2015 ⁵	RCT	1	1	0	0	1	3
Lee et al, 2015 ¹⁵	RCT	1	1	0	0	1	3
Liu et al, 2014 ¹²	RCT	1	1	0	0	1	3
Lorenzo et al, 2015 ¹⁶	RCT	1	0	0	0	1	2
Modi et al, 2009 ¹⁷	RCT	1	1	0	0	1	3
Spiegel et al, 2011 ¹⁹	RCT	1	1	0	0	1	3
Tae et al, 2012 ¹⁴	RCT	1	1	0	0	1	3

RCT, Randomized controlled trial; 1, yes; 0, no.

SUPPLEMENTARY TABLE 2. Sensitivity analysis

BP	Number of trials	Patients	OR/MD (95% CI)	P value (Q test)	I ² (%)	Study associated with heterogeneity
Primary outcome						
Rate of BP quality	8	3795	2.35 (1.65-3.35)	.008	63	Calderwood et al, 2011 ¹⁸ (I ² = 33%)*
Secondary outcome						
Intubation rate	3	1765	2.27 (1.73-4.42)	.68	0	–
Insertion time	6	2921	-0.65 (-1.64-0.33)	<.01	92	Kang et al, 2015 ⁵ and Modi et al, 2009 ¹⁷ (I ² = 0%)†
Withdrawal time	6	2921	-1.02 (-1.69-[-0.35])	<.01	81	Kang et al, 2015 ⁵ and Calderwood et al, 2011 ¹⁸ (I ² = 28%)†
PDR	5	2424	1.25 (0.93-1.68)	.05	59	Liu et al, 2014 ¹² (I ² = 0%)*; Calderwood et al, 2011 ¹⁸ (I ² = 38%)*
Adverse events	4	2613	0.76 (0.54-1.07)	.02	71	Calderwood et al, 2011 ¹⁸ (I ² = 49%)*
Willingness to repeat BP	3	1644	1.91 (1.20-3.04)	.10	57	Liu et al, 2014 ¹² (I ² = 0%)*; Kang et al, 2015 ⁵ (I ² = 45%)*

OR, Odds ratio; MD, mean difference; CI, confidence interval; BP, bowel preparation; PDR, polyp detection rate.

*If the study is excluded, the value of I² changes to ≤50%.

†If the 2 studies are excluded, the value of I² changes to ≤50%.

SUPPLEMENTARY TABLE 3. Different characteristics of the EI methods in the 8 RCTs

EI method	Description	Possible advantages compared with RI			
		More understandable	More easily accessible	More interactive	Augmenting memory
Additional explanation ¹⁷	Reviewing the questionnaire completed by the patients, providing additional explanation for the identified incorrect knowledge associated with the BP procedure	✓		✓	
Visual aid ¹⁸	Providing patients with endoscopic images of poorly prepared and well-prepared colons as well as some polyps	✓			
Cartoon visual aids ¹⁴	Including cartoons designed for easy understanding, providing pictures of good and bad BP and pictures of foods to avoid before colonoscopy, etc.	✓			
Newly designed booklet ¹⁹	Including an overview emphasizing the importance of patient participation, steps of daily BP instructions before colonoscopy, pictures of allowable and prohibited foods, and a visual color scale for interpreting the grade of effluent	✓			
Phone call ^{12,15}	Calling patients to emphasize the importance of BP, the methods using purgatives, proper food choices, and the possible adverse effects, etc., and encouraging patients to ask questions			✓	✓
Smart phone app ¹⁶	Using a smartphone app to introduce the whole procedure, tips, and examples of a low-fiber diet, pictures of preparation quality, and an educational video explaining how to prepare the purgative	✓	✓		
SMS ¹⁵	Sending an SMS to patients to inform the schedule time of colonoscopy, proper diet restriction, the instructions on drinking purgatives, and answering the questions			✓	✓
Social media app ⁵	Using social media app to provide BP-related information, including proper use of purgatives, appropriate diet, management of adverse events, and answering questions		✓	✓	

EI, Enhanced instruction; RCT, randomized controlled trial; RI, regular instruction; BP, bowel preparation; SMS, short message service.

SUPPLEMENTARY TABLE 4. Patient-related and preparation-related factors associated with BP quality

Interventions	Controls	No. of study	No. of patients	Percentage	OR (95% CI)	ARR (95% CI)	P value
Patient-related factors							
EI	RI	8:8	3795 (1812:1743)	88.5% vs 78.4%	2.35 (1.65-3.35)	10.1% (7.6%-12.5%)	<.001
Timing of EI >1 week	Timing of EI ≤1 week	2:3	2126 (869:1257)	79.2% vs 78.2%	1.06 (0.86-1.31)	1.0% (−2.5% to 4.5%)	.590
Preparation-related factors							
Split dose	Single dose	4:2	2442 (1551:871)	88.6% vs 71.4%	3.11 (2.51-3.85)	17.2% (13.8%-20.6%)	<.001
2 L of PEG+ ascorbate	4 L of PEG	2:2	1551 (646:905)	95.2% vs 83.9%	3.82 (2.55-5.70)	11.3% (8.4%-14.2%)	<.001
Low-fiber or low-residual	Clear liquid	2:4	2386 (646:1740)	95.2% vs 75.3%	6.51 (4.47-9.49)	19.9% (17.3%-22.5%)	<.001

BP, Bowel preparation; OR, odds ratio; CI, confidence interval; ARR, absolute risk reduction; EI, enhanced instruction; RI, regular instruction; PEG, polyethylene glycol.

SUPPLEMENTARY TABLE 5. Subgroup analysis of patients in different geographic locations

	East Asia (n = 4)			USA (n = 3)		
	EI vs RI	OR (95% CI)	P value	EI vs RI	OR (95% CI)	P value
Rate of adequate BP	86.6% vs 73.7%	2.20 (1.66-2.91)	<.001	82.0% vs 73.9%	1.71 (1.04-2.81)	.030
ADR	20.8% vs 14.4%	1.49 (1.09-2.04)	.010	NR	NR	NR
Adverse events	39.9% vs 41.1%	0.67 (0.49-0.91)	.010	18.9% vs 17.3%	1.11 (0.80-1.55)	.520
Cecal intubation rate	97.0% vs 92.4%	2.77 (1.73-4.42)	<.001	NR	NR	NR

EI, Enhanced instruction; RI, regular instruction; OR, odds ratio; CI, confidence interval; BP, bowel preparation; ADR, adenoma detection rate; NR, not reported.

SUPPLEMENTARY TABLE 6. Reasons for failed intubation

	EI vs RI			Overall OR/MD (95% CI)	P value
	Kang et al, 2015 ⁵	Liu et al, 2014 ¹²	Lee et al, 2015 ¹⁵		
Failed intubation	2.8% vs 6.8%	5.1% vs 14.7%	0.8% vs 1.5%	2.77 (1.73-4.42)	<.001
Poor BP	0.8% vs 4.3%	1.8% vs 10.6%	0% vs 0.7%	0.15 (0.07-0.31)	<.001
Technical difficulty or stricture	2.0% vs 2.6%	3.3% vs 4.0%	0.8% vs 0.7%	0.74 (0.39-1.39)	.340
BP score	OBPS	OBPS	BBPS		
Individual BP score	3.6 ± 1.7 vs 4.5 ± 1.8	3.0 ± 2.3 vs 4.9 ± 3.2	6.8 ± 1.3 vs 6.3 ± 1.4	−1.38 (−2.36 to −0.40)*	.006*
BP score in the right side of the colon	1.3 ± 0.8 vs 1.5 ± 0.7	1.0 ± 0.9 vs 1.5 ± 1.0	2.2 ± 0.5 vs 2.0 ± 0.6	−0.35 (−0.64 to −0.05)*	.020*

EI, Enhanced instruction; RI, regular instruction; OR, odds ratio; MD, mean difference; CI, confidence interval; BP, bowel preparation; OBPS, Ottawa Bowel Preparation Scale; BBPS, Boston Bowel Preparation Scale.

*Calculated by the OBPS scores.