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ABSTRACT

Introduction Colonoscopy is the reference method in screening and diagnosis of colorectal neoplasm, but its efficacy is closely related to the quality of bowel preparation. Poor patient compliance is a major risk factor for inadequate bowel preparation likely due to poor patient education. Such an education is usually provided via either oral or written instructions by clinicians. However, multiple education methods, like smartphone applications, have been proved useful in aiding patients through bowel preparation. Also, it was reported that a large proportion of patients feel anxious before colonoscopy. Virtual reality is a novel method to educate patients and provides them with an immersive experience. Theoretically, it can help patients better prepared for bowel preparation and colonoscopy. However, no prospective studies have assessed the role of this novel technology in patient education before colonoscopy. We hypothesize that VR videos can improve bowel preparation quality and reduce pre-procedure anxiety.

Methods/Design The trial is a prospective, randomized, single-blinded, single-center trial. Outpatients who were scheduled to undergo colonoscopy for screening or diagnostic purposes for the first time will be randomized to receive either conventional patient education or the conventional methods plus VR videos. 322 patients will be enrolled from the Peking Union Medical College Hospital. The primary endpoint is the quality of bowel preparation, measured by the Boston bowel preparation score. Secondary endpoints include polyp detection rate, adenoma detection rate, cecal intubation rate, patient compliance to complete bowel cleansing, withdrawal time, pre-procedure anxiety, overall satisfaction and willingness for the next colonoscopy.

Ethics and dissemination The study has been approved by the institutional review board of the Peking Union Medical College Hospital (No. ZS-1647). The results of this trial will be published in an open access way and disseminated among gastrointestinal physicians and endoscopists.

Trial registration This trial has been registered at the ClinicalTrials (NCT03667911)

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Strengths and limitations of this study

• This is a randomized controlled two-arm single-blinded trial providing evidence concerning the effectiveness of virtual reality education in improving the quality of bowel preparation and reducing pre-procedure anxiety.

•Patients will not bear additional risks in this trial but will possibly have better results of colonoscopy.

• This is a single-center trial.

Introduction

Colonoscopy is the reference method in screening and diagnosis of colorectal cancer, and its efficacy is closely related to the quality of bowel preparation, requiring consuming purgatives and restricting diet[4,5]. Optimal bowel preparation can lead to

a higher adenoma detection rate[6]. However, it has been reported that approximately 30% patients fail to achieve adequate bowel preparation in Asian patients[7]. Inadequate bowel preparation is mainly due to poor patient compliance[8], which closely relates to patient education[9].

In most occasions, such an education is offered only once through either oral or written instructions by clinicians during an initial appointment. Strong evidence has shown that extensive education methods, including booklet[10], telephone[11,12], message reminders[13,14], smartphone applications[15,16], social media[17], and online videos[18-21], have been used to aid patient education with variable effectiveness. These methods can increase patient motivation, which can improve the bowel preparation quality[22]. Also, it was reported that a large proportion of patients feel anxious before colonoscopy and pre-procedure information help reduce the anxiety[23]. Virtual reality (VR) is an interactive computer-generated experience taking place within a simulated environment. It will provide patients with an immersive experience, which is believed to be able to help patients better prepared for both bowel preparation and colonoscopy. However, to the best of our knowledge, no prospective studies have assessed the role of this novel technology in patient education before colonoscopy. We hypothesize that compared with conventional patient education methods, VR videos can improve the quality of bowel preparation thorugh enhancing patient motivation and compliance, reduce pre-procedure anxiety, and improve patient experience during conscious colonoscopy.

Methods

Design

The trial is a prospective, randomized, controlled, single-blinded, single-center trial. Outpatients who are arranged to undergo a conscious colonoscopy (i.e., without sedation) for screening or diagnostic purposes for the first time will be randomized to the control group or the VR intervention group. This study aims to explore whether VR videos can improve the bowel preparation quality, increase patient adherence and satisfaction, and reduce pre-procedure anxiety, compared with conventional patient education methods. Figure 1 summarises the design of the trial and each of the trials aspects is described in detail below.

Figure 1. Trial design.

Study Population

All patients who have the indications for colonoscopy screening presenting to Peking Union Medical College Hospital, a tertiary hospital in Beijing, China, will be assessed for eligibility during the appointment, starting from Sep 15th, 2018 and estimated to complete in April 2019.

Inclusion criteria

• Outpatients indicated for elective colonoscopy: 1) For screening purposes: asymptomatic patients with average or high risk for colorectal cancer[1]; 2) For diagnostic purposes: patients presented with abnormal imaging or lower gastrointestinal symptoms including bloody stool, chronic diarrhea and abdominal pain[2]
• No prior colonoscopy
• Age 18-75 years
• Written informed consent

Exclusion criteria
Patient who meet any of the following criteria will be excluded:
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• On constipation, laxatives, or anti-diarrheal medications
• Pregnant
• Severe constipation (<3 bowel movement/week)
• Inflammatory bowel disease (IBD)
• Unable to watch VR videos (e.g., blindness)

Randomization and Assignments
After the colonoscopy is scheduled and written informed consent is obtained, patients will be randomized with 1:1 ratio to the coventional education method or the conventional education plus VR video. A computerized random number table will be used in randomization. The randomization process is performed by a physician who will also provide education on bowel preparation and will not involved in performing procedures. All endoscopists in this trial will be unware of the allocation.

General bowel preparation requirement[24]
Diet restriction: Low-residue diet until the evening on the day before colonoscopy
Colon cleansing regimens:
The first dose: 2L laxatives (polyethyleneglycol) used on the evening of the day before colonoscopy (after dinner)
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The control group: conventional patient education methods
Patients in the control group will only receive routine patient education on bowel preparation of colonoscopy. A well-trained nurse or a doctor will provide oral instructions on bowel preparation (including definition, significance, correct steps as well as dietary limitations). Written instructions are also provided to patients to take away, which have the same contents as the oral instructions.

The intervention group: conventional methods plus VR videos

In addition to the routine patient education methods mentioned above, patients in the intervention group will watch a VR video for about 6 minutes. Videos will give instructions on bowel preparation step by step, emphasize on points for attention before and after the procedure, and give brief introductions to the procedures of colonoscopy and a to-do list after a therapeutic procedure (e.g., polypectomy).

Primary endpoint

The primary endpoint is the quality of bowel preparation measured by the Boston bowel preparation score (BBPS) evaluated during the procedure. In BBPS, 3 broad regions of colon right (including the cecum and ascending colon; transverse, including the hepatic and splenic flexures; and left, including the descending colon, sigmoid, and rectum) will be given a score from 0 to 3. 0 means unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared and 3 means Entire mucosa of colon segment seen well with no residual staining, small fragments of stool or opaque liquid. Endoscopists are blinded to the grouping of patients.

Secondary endpoints

We also hypothesize that VR videos can increase patient motivation and deepen their understanding of colonoscopy, which is likely to increase the detection rate of abnormity, reduce anxiety, and improve patient experiences. We set secondary endpoints as follows:

• Polyp detection rate (PDR).
• Adenoma detection rate (ADR).
• Cecal intubation rate.
• Patient compliance with bowel preparation (rate of complying with diet restriction and laxatives use).
• Withdrawal time.
• Pre-procedure anxiety (measured by self-rated sleep quality before the procedure).
• Overall satisfaction with bowel preparation.
• Willingness to take another colonoscopy if indicated.

Sample size calculation

The sample size estimation was based on the test of 2 independent proportions with a 2-sided α=0.05 and a power probability of 90% (β=0.1). The rate of adequate preparation (a score≥2 for all regions) in the control group is 70%[3], and we assumed an increase of 15% for the VR Group. We calculated that at least 161 evaluable patients would be required per group for the study to achieve this power.

Data collection

Data collection will be performed by using a standardized case report form during the appointment and on the day of colonoscopy.

Descriptive statistics

For categorical data, frequencies will be presented. Quantitative data will be presented as the mean and standard deviation or median and interquartile range. Baseline characteristics (all prior to randomization) are: age, sex, body mass index, education level, annual personal income, living habits (including smoking, drinking and exercise), dietary habit (vegetarianism/meatatarian/balanced diet), past medical history of comorbidity (hypertension, diabetes mellitus, bronchitis, asthma, congestive heart failure, chronic renal failure, coronary artery disease, IBD, malignancy), symptoms (chronic diarrhea, constipation, mucous stool or bloody stool), family history of colorectal cancer or specific inherited syndromes.

Analyses

All data will be analyzed according to the intention-to-treat approach in which all randomized patients are included. Occurrences of the primary and secondary endpoints are compared between the two groups. Results are presented as difference in two proportions. A two-tailed $P< 0.05$ is considered statistically significant.

Trial Mangement

A steering committee will manage the trial. Screening and recruitment will be reviewed at monthly meetings. An independent data and safety monitoring committee (DSMC) will meet regularly to ensure patient safety and data quality. DSMC will verify all primary and secondary endpoints as well as at least 10% of data in case report forms against on-site source data. Discrepancies detected by the committee will be resolved through a consensus by two investigators unaware of the study group assignment and not involved in patient care. Relevant clinical and radiological data submitted to the steering committee will facilitate duplicate blinded outcome adjudication.

Termination of the trial

An interim-analysis will be conducted on the primary endpoint when 25%, 50%, and 75% of patients have been enrolled. The interim-analysis is performed by an independent statistician, blinded for the treatment allocation. The statistician will report to the independent DSMC. The DSMC will have unrestricted access to all data and will discuss the results of the intention-to-treat analysis with the steering committee in a joint meeting. The steering committee decides on the continuation of the trial and will report to the central ethics committee. The Peto approach is used to terminate the trial when the intervention group has a significant benefit from the addition of VR to the patient education methods using symmetric stopping boundaries at $P<0.001$. The trial will not be stopped in case of futility unless the DSMC during safety monitoring advises otherwise. In this case, DSMC will discuss potential stopping for futility with the trial steering committee.

Safety

The DSMC will monitor the progress of the trial by examining safety variables quarterly. This evaluation is based on unblinded data, in the presence of the study

coordinator when DSMC requires details of the study. After the full explanation of the data is presented, the study coordinator is dismissed, and the DSMC discusses the consequences of the data presented. Adverse events are defined as "any undesirable experience occurring to a subject during a clinical trial, whether or not considered related to the intervention," such as a sense of dizziness after watching VR videos. All participating physicians will be asked to report any potential adverse events. These adverse events will be listed and discussed with the DSMC. The outcome of the meeting of the DSMC will be discussed with the trial steering committee. The outcome will also be sent to our hospital institutional review board (IRB). The DSMC will evaluate the data of the deceased patients for the cause of death, and possible trial related severe adverse events.

Discussions

The trial is aimed to explore whether VR videos can improve the bowel preparation quality through increasing patient adherence and experience, reduce pre-procedure anxiety, compared with the conventional patient education methods. To date, there have been several studies demonstrating that extensive patient education methods[10-21] are effective in enhancing the bowel preparation quality. However, there is a lack of evidence on the effect of VR videos , a novel technology which can provide patients with immersive experiences simulating the process of bowel preparation and colonoscopy that cannot be achieved by conventional education methods. It is likely that VRs will offer an effective means of educating patients before colonoscopy, leading to better results of the procedure.

Ethics and Dissemination

We will conduct the study following the declaration of Helsinki. The IRB of the Peking Union Medical College Hospital approved the protocol on the 24thof July 2018 (No. ZS-1647). We will obtain Informed consent from each participating patient in oral and written form before randomization. We will disseminate our results to the medical circle and will publish our results via open access.

Trial Status

We registered this trial in the ClinicalTrials on 20 August 2018 with identification number NCT03667911. The first patient was randomized on the 15th of September 2018. To date, 62 patients have been randomized, and enrollment is on schedule.

Reference

1. Wolf AM, Fontham ET, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society[J]. CA: A Cancer Journal for Clinicians, 2018, 68(4):250-281.

2. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy[J]. American Journal of Gastroenterology, 2015, 81(1):31-53.
3. Back SY, Kim HG, Ahn EM, et al. Impact of patient audio-visual re-education through a smartphone on quality of bowel preparation before colonoscopy; a single-blinded randomized study[J]. Gastrointestinal Endoscopy, 2017:S0016510717322691.
4. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. multi-society task force on colorectal cancer. Gastrointest Endosc 2014, 80:543.
5. ASGE Standards of Practice Committee, Saltzman JR, Cash BD, et al. Bowel preparation before colonoscopy. Gastrointest Endosc 2015, 81:781.
6. Pontone S, Hassan C, Maselli R, et al. Multiple, zonal and multi-zone adenoma detection rates according to quality of cleansing during colonoscopy. United European Gastroenterology Journal, 2016, 4(6):778–783.
7. Woo DH, Kim KO, Jeong DE, et al. Prospective analysis of factors associated with inadequate bowel preparation for colonoscopy in actual clinical practice. Intestinal Research, 2018, 16(2):293–298.
8. Nguyen DL, Wieland M. Risk factors predictive of poor quality preparation during average risk colonoscopy screening: the importance of health literacy. J Gastrointestin Liver Dis 2010; 19:369–72.
9. Rosenfeld G, Krygier D, Enns R, et al. The impact of patient education on the quality of inpatient bowel preparation for colonoscopy[J]. Canadian Journal of Gastroenterology & Hepatology, 2010, 24(9):543-546.
10. Spiegel BMR, Talley J, Shekelle P, et al. Development and validation of a novel patient educational booklet to enhance colonoscopy preparation. The American Journal of Gastroenterology, 2011,106(5):875–883.
11. Liu X, Luo H, Zhang L, et al. Telephone-based re-education on the day before colonoscopy improves the quality of bowel preparation and the polyp detection rate: a prospective, colonoscopist-blinded, randomised, controlled study. Gut, 2013, 63(1):125–130.
12. Sondhi AR, Kurlander JE, Waljee AK, Saini SD. A telephone-based education program improves bowel preparation quality in patients undergoing outpatient colonoscopy. Gastroenterology, 2015,148(3):657–658.
13. Park J, Kim TO, Lee NY, et al. The Effectiveness of Short Message Service to Assure the Preparation-to-Colonoscopy Interval before Bowel Preparation for Colonoscopy. Gastroenterology Research and Practice, 2015, 2015(7):628049–8.
14. Walter B, Klare P, Strehle K, et al. Improving the quality and acceptance of colonoscopy preparation by reinforced patient education with short message service: results from a randomized, multicenter study (PERICLES-II). Gastrointestinal Endoscopy, 2018.
15. Lorenzo-Zúñiga V, Moreno de Vega V, Marín I, Barberá M, Boix J. Improving the quality of colonoscopy bowel preparation using a smart phone application: a randomized trial. Digestive Endoscopy : Official Journal of the Japan Gastroenterological Endoscopy Society, 2015, 27(5):590–595.

16. Cho J, Lee S, Shin JA, Kim JH, Lee HS. The Impact of Patient Education with a Smartphone Application on the Quality of Bowel Preparation for Screening Colonoscopy. Clinical Endoscopy, 2017, 50(5):479–485.
17. Wang SL, Wang Q, Yao J, et al. Effect of WeChat and short message service on bowel preparation: an endoscopist-blinded, randomized controlled trial. European Journal of Gastroenterology & Hepatology, 2018:1.
18. Garg S, Girotra M, Chandra L, et al. Improved Bowel Preparation with Multimedia Education in a Predominantly African-American Population: A Randomized Study. Diagnostic and Therapeutic Endoscopy, 2016, 2016(12):2072401–7.
19. Park JS, Kim MS, Kim H, et al. A randomized controlled trial of an educational video to improve quality of bowel preparation for colonoscopy. BMC Gastroenterology, 2016, 16(1):64.
20. Back SY, Kim HG, Ahn EM, et al. Impact of patient audiovisual re-education via a smartphone on the quality of bowel preparation before colonoscopy: a single-blinded randomized study. Gastrointestinal Endoscopy, 2018, 87(3):789–799.e4.
21. Pillai A, Menon R, Oustecky D, & Ahmad A. Educational Colonoscopy Video Enhances Bowel Preparation Quality and Comprehension in an Inner City Population. Journal of Clinical Gastroenterology, 2018, 52(6):515–518.
22. Serper M, Gawron AJ, Smith SG, et al. Patient Factors that Affect Quality of Colonoscopy Preparation[J]. Clinical Gastroenterology & Hepatology the Official Clinical Practice Journal of the American Gastroenterological Association, 2014, 12(3):451-457.
23. Yang C, Sriranjan V, Abou-Setta AM, Poluha W, Walker JR, & Singh H. Anxiety Associated with Colonoscopy and Flexible Sigmoidoscopy: A Systematic Review. The American Journal of Gastroenterology, 2018, 59(6 Pt 1):366.
24. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. Multi-Society Task Force on Colorectal Cancer[J]. Gastroenterology, 2014, 80(4):543-562.

Authors' contributions

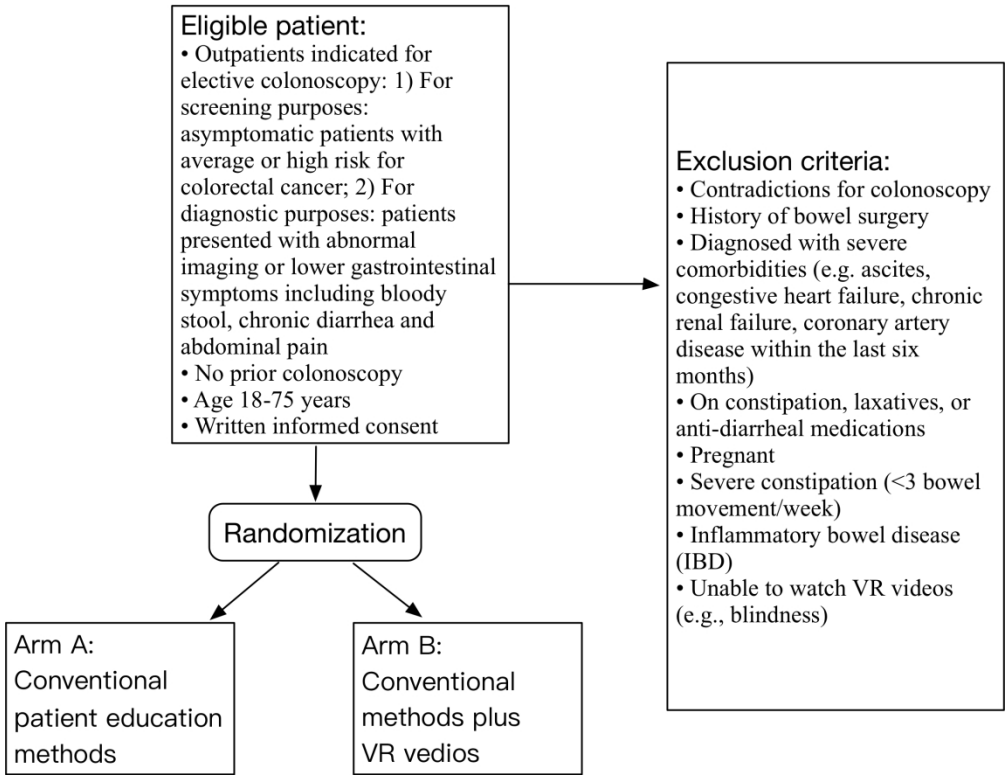
ZY is responsible for designing the trial, drafting the protocol, reviewing and final approval.
FX contributes to improving the methodology of this trial.
AY contributes to the design and managing this trial.
WD is the corresponding author, responsible for designing and managing the trial, drafting the protocol, reviewing and final approval.

Funding Statement

This research received no specific grant from any funding agency in public, commercial or not-for-profit sectors.

Competing interests statement

None.



Trial design.

207x159mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	3
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	4-5
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	5
	7b	When applicable, explanation of any interim analyses and stopping guidelines	6
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	4
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	4
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	4
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	4
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	4

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	N/A
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	N/A
	13b	For each group, losses and exclusions after randomisation, together with reasons	N/A
Recruitment	14a	Dates defining the periods of recruitment and follow-up	N/A
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	N/A
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	N/A
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	N/A
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	7
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	N/A
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	N/A
Other information			
Registration	23	Registration number and name of trial registry	7
Protocol	24	Where the full trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	9

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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Patients in the control group will only receive routine patient education on bowel preparation of colonoscopy. A well-trained nurse or a doctor will provide oral instructions on bowel preparation (including definition, significance, correct steps as well as dietary limitations). Written instructions are also provided to patients to take away, which have the same contents as the oral instructions.

The intervention group: conventional methods plus VR videos

In addition to the routine patient education methods mentioned above, patients in the intervention group will watch a VR video using a head-mounted 3D display (Figure 2) for about 6 minutes. Patients will be placed in the simulated settings of an operating room in the VR video. Four parts will be offered, including instructions on bowel preparation step by step, points for attention before and after the procedure, brief introductions to the specific procedures of colonoscopy and a to-do list after a therapeutic procedure (e.g., polypectomy). The device can track head movements and patients can familiarize themselves with the operating room and select the part they want to learn with head motion. Patients can only exit when they have finished all these four parts.

Figure 2. Head-mounted display for virtual reality videos.

Primary endpoint

The primary endpoint is the quality of bowel preparation measured by the Boston bowel preparation score (BBPS) evaluated during the procedure. In BBPS, 3 broad regions of colon right (including the cecum and ascending colon; transverse, including the hepatic and splenic flexures; and left, including the descending colon, sigmoid, and rectum) will be given a score from 0 to 3. 0 means unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared and 3 means Entire mucosa of colon segment seen well with no residual staining, small fragments of stool or opaque liquid. Endoscopists are blinded to the grouping of patients.

Secondary endpoints

We also hypothesize that VR videos can increase patient motivation and deepen their understanding of colonoscopy, which is likely to increase the detection rate of abnormity, reduce anxiety, and improve patient experiences. We set secondary endpoints as follows:

- Polyp detection rate (PDR).
- Adenoma detection rate (ADR).
- Cecal intubation rate.
- Patient compliance with bowel preparation (rate of complying with diet restriction and laxatives use).
- Withdrawal time.
- Pre-procedure anxiety (measured by self-rated sleep quality before the procedure).
- Overall satisfaction with bowel preparation.
- Willingness to take another colonoscopy if indicated.

Sample size calculation

The sample size estimation was based on the test of 2 independent proportions with a 2-sided α=0.05 and a power probability of 90% (β=0.1). The rate of adequate preparation (a score≥2 for all regions) in the control group is 70%[24], and we assumed an increase of 15% for the VR Group. We calculated that at least 161 evaluable patients would be required per group for the study to achieve this power.

Data collection

Data collection will be performed by using a standardized case report form during the appointment and on the day of colonoscopy.

Descriptive statistics

For categorical data, frequencies will be presented. Quantitative data will be presented as the mean and standard deviation or median and interquartile range. Baseline characteristics (all prior to randomization) are: age, sex, body mass index, education level, annual personal income, living habits (including smoking, drinking and exercise), dietary habit (vegetarianism/meatatarian/balanced diet), past medical history of comorbidity (hypertension, diabetes mellitus, bronchitis, asthma, congestive heart failure, chronic renal failure, coronary artery disease, IBD, malignancy), symptoms (chronic diarrhea, constipation, mucous stool or bloody stool), family history of colorectal cancer or specific inherited syndromes.

Analyses

All data will be analyzed according to the intention-to-treat approach in which all randomized patients are included. Occurrences of the primary and secondary endpoints are compared between the two groups. Results are presented as difference in two proportions. A two-tailed $P< 0.05$ is considered statistically significant.

Trial Mangement

A steering committee will manage the trial. Screening and recruitment will be reviewed at monthly meetings. An independent data and safety monitoring committee (DSMC) will meet regularly to ensure patient safety and data quality. DSMC will verify all primary and secondary endpoints as well as at least 10% of data in case report forms against on-site source data. Discrepancies detected by the committee will be resolved through a consensus by two investigators unaware of the study group assignment and not involved in patient care. Relevant clinical and radiological data submitted to the steering committee will facilitate duplicate blinded outcome adjudication.

Termination of the trial

An interim-analysis will be conducted on the primary endpoint when 25%, 50%, and 75% of patients have been enrolled. The interim-analysis is performed by an independent statistician, blinded for the treatment allocation. The statistician will report to the independent DSMC. The DSMC will have unrestricted access to all data and will discuss the results of the intention-to-treat analysis with the steering committee in a joint meeting. The steering committee decides on the continuation of the trial and will report to the central ethics committee. The Peto approach is used to terminate the trial when the intervention group has a significant benefit from the addition of VR to the patient education methods using symmetric stopping boundaries at $P<0.001$. The trial will not be stopped in case of futility unless the DSMC during

safety monitoring advises otherwise. In this case, DSMC will discuss potential stopping for futility with the trial steering committee.

Safety

The DSMC will monitor the progress of the trial by examining safety variables quarterly. This evaluation is based on unblinded data, in the presence of the study coordinator when DSMC requires details of the study. After the full explanation of the data is presented, the study coordinator is dismissed, and the DSMC discusses the consequences of the data presented. Adverse events are defined as "any undesirable experience occurring to a subject during a clinical trial, whether or not considered related to the intervention," such as a sense of dizziness after watching VR videos. All participating physicians will be asked to report any potential adverse events. These adverse events will be listed and discussed with the DSMC. The outcome of the meeting of the DSMC will be discussed with the trial steering committee. The outcome will also be sent to our hospital institutional review board (IRB). The DSMC will evaluate the data of the deceased patients for the cause of death, and possible trial related severe adverse events.

Patients and Public Involvement

Patients or public were not involved in the trial design.

Discussions

The trial is aimed to explore whether VR videos can improve the bowel preparation quality through increasing patient adherence and experience, reduce pre-procedure anxiety, compared with the conventional patient education methods. To date, there have been several studies demonstrating that extensive patient education methods [7-18] are effective in enhancing the bowel preparation quality. However, there is a lack of evidence on the effect of VR videos, a novel technology which can arouse patients' interests and motivation. Compared with conventional video, VR videos can provide patients with immersive experiences simulating the process of bowel preparation and colonoscopy. The sense of immersion provided by VR videos is believed to be able to reduce the attention distracted by surroundings, which is proved by the fact that VR is used in chronic pain control [25]. Thus, it is likely that VR videos can make patients more concentrated in the education and enhance the effect of patient education before colonoscopy, leading to better results of the procedure.

Ethics and Dissemination

We will conduct the study following the declaration of Helsinki. The IRB of the Peking Union Medical College Hospital approved the protocol on the 24thof July 2018 (No. ZS-1647). We will obtain Informed consent from each participating patient in oral and written form before randomization. We will disseminate our results to the medical circle and will publish our results via open access.

Trial Status

We registered this trial in the ClinicalTrials on 20 August 2018 with identification number NCT03667911. The first patient was randomized on the 15th of September 2018. To date, 62 patients have been randomized, and enrollment is on schedule.

Reference

1. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. multi-society task force on colorectal cancer. Gastrointest Endosc 2014, 80:543.
2. ASGE Standards of Practice Committee, Saltzman JR, Cash BD, et al. Bowel preparation before colonoscopy. Gastrointest Endosc 2015, 81:781.
3. Pontone S, Hassan C, Maselli R, et al. Multiple, zonal and multi-zone adenoma detection rates according to quality of cleansing during colonoscopy. United European Gastroenterology Journal, 2016, 4(6):778–783.
4. Woo DH, Kim KO, Jeong DE, et al. Prospective analysis of factors associated with inadequate bowel preparation for colonoscopy in actual clinical practice. Intestinal Research, 2018, 16(2):293–298.
5. Nguyen DL, Wieland M. Risk factors predictive of poor quality preparation during average risk colonoscopy screening: the importance of health literacy. J Gastrointestin Liver Dis 2010; 19:369–72.
6. Rosenfeld G, Krygier D, Enns R, et al. The impact of patient education on the quality of inpatient bowel preparation for colonoscopy[J]. Canadian Journal of Gastroenterology & Hepatology, 2010, 24(9):543-546.
7. Spiegel BMR, Talley J, Shekelle P, et al. Development and validation of a novel patient educational booklet to enhance colonoscopy preparation. The American Journal of Gastroenterology, 2011,106(5):875–883.
8. Liu X, Luo H, Zhang L, et al. Telephone-based re-education on the day before colonoscopy improves the quality of bowel preparation and the polyp detection rate: a prospective, colonoscopist-blinded, randomised, controlled study. Gut, 2013, 63(1):125–130.
9. Sondhi AR, Kurlander JE, Waljee AK, Saini SD. A telephone-based education program improves bowel preparation quality in patients undergoing outpatient colonoscopy. Gastroenterology, 2015,148(3):657–658.
10. Park J, Kim TO, Lee NY, et al. The Effectiveness of Short Message Service to Assure the Preparation-to-Colonoscopy Interval before Bowel Preparation for Colonoscopy. Gastroenterology Research and Practice, 2015, 2015(7):628049–8.
11. Walter B, Klare P, Strehle K, et al. Improving the quality and acceptance of colonoscopy preparation by reinforced patient education with short message service: results from a randomized, multicenter study (PERICLES-II). Gastrointestinal Endoscopy, 2018.

12. Lorenzo-Zúñiga V, Moreno de Vega V, Marín I, Barberá M, Boix J. Improving the quality of colonoscopy bowel preparation using a smart phone application: a randomized trial. Digestive Endoscopy : Official Journal of the Japan Gastroenterological Endoscopy Society, 2015, 27(5):590–595.
13. Cho J, Lee S, Shin JA, Kim JH, Lee HS. The Impact of Patient Education with a Smartphone Application on the Quality of Bowel Preparation for Screening Colonoscopy. Clinical Endoscopy, 2017, 50(5):479–485.
14. Wang SL, Wang Q, Yao J, et al. Effect of WeChat and short message service on bowel preparation: an endoscopist-blinded, randomized controlled trial. European Journal of Gastroenterology & Hepatology, 2018:1.
15. Garg S, Girotra M, Chandra L, et al. Improved Bowel Preparation with Multimedia Education in a Predominantly African-American Population: A Randomized Study. Diagnostic and Therapeutic Endoscopy, 2016, 2016(12):2072401–7.
16. Park JS, Kim MS, Kim H, et al. A randomized controlled trial of an educational video to improve quality of bowel preparation for colonoscopy. BMC Gastroenterology, 2016, 16(1):64.
17. Back SY, Kim HG, Ahn EM, et al. Impact of patient audiovisual re-education via a smartphone on the quality of bowel preparation before colonoscopy: a single-blinded randomized study. Gastrointestinal Endoscopy, 2018, 87(3):789–799.e4.
18. Pillai A, Menon R, Oustecky D, & Ahmad A. Educational Colonoscopy Video Enhances Bowel Preparation Quality and Comprehension in an Inner City Population. Journal of Clinical Gastroenterology, 2018, 52(6):515–518.
19. Serper M, Gawron AJ, Smith SG, et al. Patient Factors that Affect Quality of Colonoscopy Preparation[J]. Clinical Gastroenterology & Hepatology the Official Clinical Practice Journal of the American Gastroenterological Association, 2014, 12(3):451-457.
20. Yang C, Sriranjan V, Abou-Setta AM, Poluha W, Walker JR, & Singh H. Anxiety Associated with Colonoscopy and Flexible Sigmoidoscopy: A Systematic Review. The American Journal of Gastroenterology, 2018, 59(6 Pt 1):366.
21. Wolf AM, Fontham ET, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society[J]. CA: A Cancer Journal for Clinicians, 2018, 68(4):250-281.
22. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy[J]. American Journal of Gastroenterology, 2015, 81(1):31-53.
23. Johnson DA, Barkun AN, Cohen LB, et al. Optimizing adequacy of bowel cleansing for colonoscopy: recommendations from the U.S. Multi-Society Task Force on Colorectal Cancer[J]. Gastroenterology, 2014, 80(4):543-562.
24. Back SY, Kim HG, Ahn EM, et al. Impact of patient audio-visual re-education through a smartphone on quality of bowel preparation before colonoscopy; a single-blinded randomized study[J]. Gastrointestinal Endoscopy, 2017:S0016510717322691.

25. Gupta A, Scott K, Dukewich M, et al. Innovative Technology Using Virtual Reality in the Treatment of Pain: Does It Reduce Pain via Distraction, or Is There More to It?[J]. Pain Medicine, 2018, 19(1): 151-159.

Authors' contributions

ZY is responsible for designing the trial, drafting the protocol, reviewing and final approval.
XF contributes to improving the methodology of this trial.
BX contributes to the design and reviewing the protocol.
YA contributes to the design and managing this trial.
WD is the corresponding author, responsible for designing and managing the trial, drafting the protocol, reviewing and final approval.

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Competing interests statement

None.

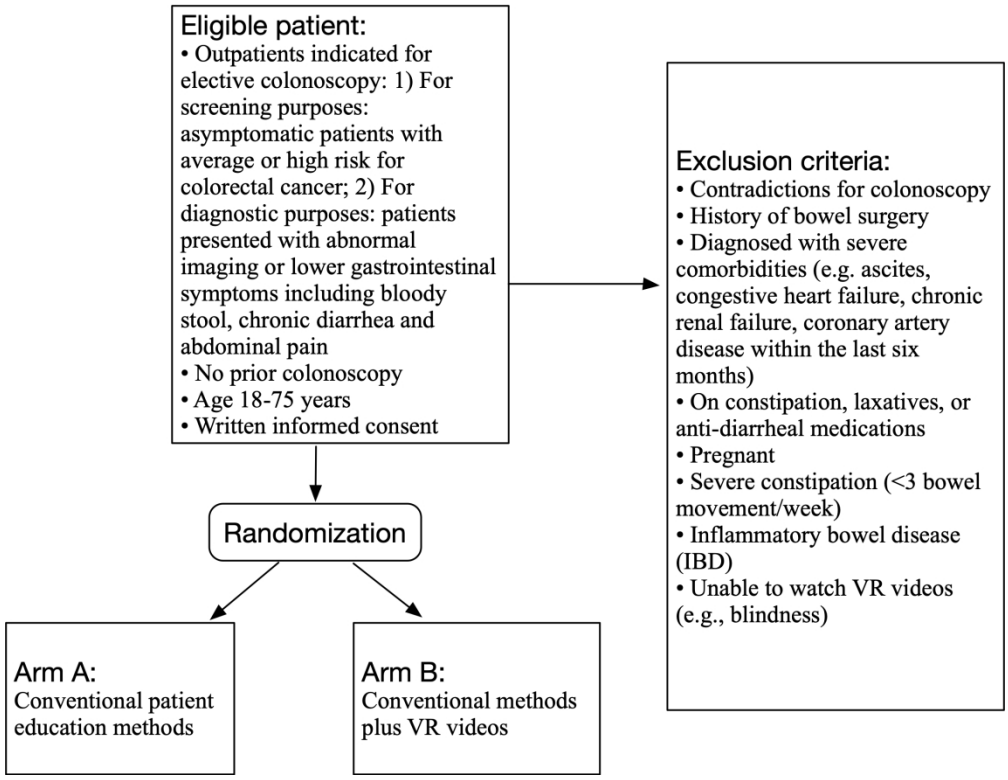

Figure 1. Trial design.

207x159mm (300 x 300 DPI)

Figure 2. Head-mounted display for virtual reality videos.

199x90mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	3
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	4-5
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	5
	7b	When applicable, explanation of any interim analyses and stopping guidelines	6
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	4
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	4
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	4
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	4
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	4

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	N/A
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	N/A
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	N/A
	13b	For each group, losses and exclusions after randomisation, together with reasons	N/A
Recruitment	14a	Dates defining the periods of recruitment and follow-up	N/A
	14b	Why the trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	N/A
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	N/A
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	N/A
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	N/A
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	7
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	N/A
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	N/A
Other information			
Registration	23	Registration number and name of trial registry	8
Protocol	24	Where the full trial protocol can be accessed, if available	N/A
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	10

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.