

# CLINICAL STUDY PROTOCOL



## Comparative Evaluation of Novel Strategies for Colorectal Cancer Screening in China: A Multicenter Randomized Controlled Trial (TARGET-C Study)

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## **1. Background**

Colorectal cancer (CRC) is the fifth most commonly diagnosed cancer and the fourth most common cause of cancer-related death in China. In the past decades, its incidence showed an increasing trend. The World Health Organization has pointed out that population-based screening is effective in reducing the burden of CRC through early diagnosis and treatment, that is, by detecting the malignancy and its precursor lesion at an early stage before symptom onset. Therefore, the key requirement currently is to establish a series of scientific, effective, and economically feasible CRC screening and intervention techniques and programs in the Chinese population.

Current guidelines have recommended various tests available for CRC screening, such as colonoscopy and the fecal occult blood test (FOBT). However, systematic evaluation on the effectiveness of these screening methods remains limited in China, especially on the basis of evidence from multicenter and large-scale randomized controlled trials. In addition, given the large population and unbalanced medical resource allocation in China, establishing a screening scheme, involving the identification of population at high-risk of CRC and further precise screening interventions for the risk-specific population, is highly needed, in order to improve the efficacy and effectiveness of CRC screening in China.

Therefore, a population-based randomized controlled trial is planned and organized to evaluate some relatively mature colorectal cancer screening techniques and programs in the Chinese population, and to explore and evaluate the effectiveness of new CRC biomarkers (including stool DNA, oral microbiota, fecal microbiota, and blood DNA methylation) based on a simultaneously established biobank. Moreover, a corresponding health economic evaluation will be conducted. We anticipate that our study will strongly support the identification and validation of novel biologically reasonable, economical, and effective CRC screening techniques and strategies tailored for the Chinese population, leading to higher detection rate of early-stage CRC and its precancerous lesions and lower mortality of CRC in China.

## 2. Objectives

- (1) To compare the effectiveness and cost-effectiveness of colonoscopy, fecal immunochemical test and risk-adapted screening in a large-scale, multicenter, population-based randomized controlled trial.
- (2) To establish a prospective population-based biobank and to explore and evaluate the application of blood, fecal, and salivary biomarkers for early detection of CRC.

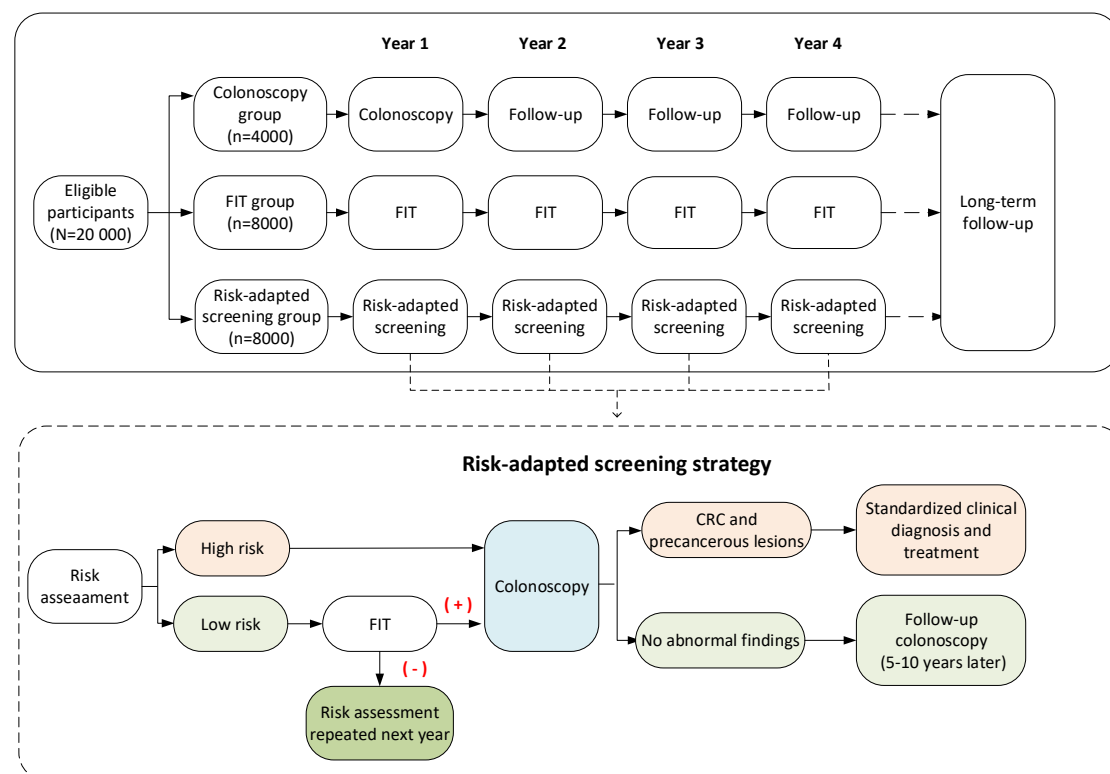
## 3. Study design

We aim to recruit 20,000 eligible participants at baseline in 6 study centers of five provinces (Zhejiang, Anhui, Jiangsu, Hunan, Yunnan) in China. The eligible participants will be randomly allocated into one of the three CRC screening groups in a 1:2:2 ratio:

- (1) One-time colonoscopy group (n=4000): participants are recommended to undergo a one-time screening colonoscopy at baseline. In the following years, all participants will be interviewed to complete the follow-up questionnaire annually.
- (2) Annual fecal immunochemical test (FIT) group (n=8000): FITs are offered to participants at baseline. Those with positive FIT results are further recommended to undergo diagnostic colonoscopies. During the subsequent annual follow-ups, participants who were not diagnosed with CRC will undergo FIT, and those with positive FIT results are recommended to undergo further colonoscopy.
- (3) Annual risk-adapted screening group (n=8000): CRC risk will be assessed at baseline. For participants at high risk of CRC, screening colonoscopy will be recommended, whereas for those at low risk of CRC, FITs will be recommended, and those with positive FIT results will be recommended to undergo further colonoscopy. Participants who have already undergone screening colonoscopy will complete a questionnaire annually during the subsequent study period. Meanwhile, the remaining participants will undergo another round of risk assessment and complete the corresponding screening interventions (colonoscopy or FIT)

according to the risk assessment results. See “Section 9, Follow-up” for more details.

4 rounds of screening will be plan, but the termination of the trial is subject to interim analysis regarding the primary outcome evaluation. Active- and passive- follow-up will also be conducted to trace the health status of the participants. For more details, see the figure below.



#### 4. Study population

The inclusion and exclusion criteria are as follows:

##### (1) Inclusion criteria:

- Registered permanent residents or people who have lived in the study region for  $\geq 3$  years
- Adults aged 50–74 years upon enrolment to the study
- Participants who are willing and able to sign informed consent

##### (2) Exclusion criteria:

Participants will be excluded if they meet any of the following criteria:

- Previous history of CRC
- Previous history of colonic resection
- Receipt of any kind of cancer-related therapy (except therapy for non-melanoma skin cancer)
- Previous colonic examination, including colonoscopy, flexible sigmoidoscopy, computed tomography (CT) colonography, and barium enema within 5 years
- Previous history of FOBT and fecal DNA test within 1 year
- Symptoms of lower gastrointestinal tract disease warranting colonoscopic evaluation such as:
  - More than one episode of rectal bleeding within the past 6 months
  - Documented iron deficiency anemia
  - Significant documented unintentional weight loss (>10% of baseline weight) over the past 6 months
  - Significant comorbidity that would preclude benefit from screening or pose a significant risk to the performance of colonoscopy (e.g., severe lung disease, end-stage renal disease, end-stage liver disease, severe heart failure, or recent diagnosis of cancer with the exception of non-melanoma skin cancer)

## **5. Technical route**

### **5.1 Recruitment**

Recruitment of potential participants aged 50–74 years from the selected communities and checking for eligibility will be conducted by trained study staff.

Recruited potential participants from selected communities or hospitals fill out the Qualification Checklist (Table A1), and whether they meet the requirements of our study is determined. Subjects who pass the eligibility assessment will be enrolled into the study.

Our study will be conducted on the basis of the Cancer Screening Program in Urban

China (CanSPUC), with reliance on its management system and medical resource platform. CanSPUC focuses on population aged 40–74 years, while the target population of this study is those aged 50–74 years. Community and hospital advertisements can be shared by two programs; however, the difference of the age range between the two target populations should be carefully considered.

To avoid uncertain impacts of the high-risk risk assessment system of CanSPUC, participants will be recruited and managed independent of CanSPUC. After checking for eligibility using the Qualification Checklist, signed written informed consent would be obtained from eligible participants. Subsequently, registration of participants in the Web-based data management system, unique study identification number assignment, and randomization will be carried out.

## **5.2 Informed consent**

Informed consent that includes the research authorization, purpose and contents of the research, confidentiality of personal information, inclusion criteria, time limit for record keeping, and cleaning will be prepared by the National Cancer Center, Cancer Hospital, the Chinese Academy of Medical Sciences, and Peking Union Medical College. Moreover, our study has been approved by the Ethics Committee of the National Cancer Center, Cancer Hospital, the Chinese Academy of Medical Sciences, and Peking Union Medical College. For colonoscopy screening, a higher incidence of complications has been observed for patients with organic heart and lung diseases, especially those aged 70–74 years. Although it does not strictly serve as an exclusion criterion, the number of such people should be minimized as far as possible when masses are detected.

## **5.3 Randomization scheme**

The randomization will be conducted in a centralized, controlled manner. Before recruitment, both the staff responsible for recruitment at each site and participants will be blinded to allocation results. The leading institute (Cancer Hospital, Chinese



Academy of Medical Sciences) is responsible for the generation of the randomization scheme, and selected communities and hospitals from each site are in charge of recruitment.

At first, the participant must complete a Qualification Checklist to confirm that he or she meets all inclusion criteria and has signed an informed consent form. Then, the study staff on site will enter the participant's name, sex, and ID number (each ID number can be entered only once) into the online random allocation system constructed by Cancer Hospital, Chinese Academy of Medical Sciences. The system will then automatically generate a unique study identification number for each participant, and allocation results will be revealed.

#### **5.4 Fecal immunochemical test (FIT)**

According to the study protocol, participants assigned to the FIT group and those at low risk of CRC in the risk assessment group should receive FITs (Pupu tube; New Horizon Health, Hangzhou, China). The FIT kit used in this study is a self-administered qualitative test device and will be concentratively purchased by our project team. The staff will distribute devices according to the research protocol and record the corresponding information as described in Table B3. Participants will collect their stool sample at home on the basis of operating instructions. Then, the sampler should be inserted back into the container. Keep shaking the sampling tube left and right for 10 seconds to mix the stool sample and diluent evenly. Then, press the tube cap down completely and keep it standing still for 5 min. By observing the color of stripes displayed and comparing it with the reference colors shown in the test result window, one can visually interpret the test results as positive, negative, or invalid according to the instruction. The test results are valid for 10 min. More details on the FIT operating procedure instructions can be found in Appendix VI.

Acquisition and feedback of FIT test results are as follows:

- (1) Participants scan the QR code in the FIT instructions using their mobile phones and

enter the name, study ID, tube number, sampling time, and test results (control line and test-line results) in the pop-up window. The system will automatically provide the outcomes and transmit them to the platform of our program. Study staff can obtain the test results reported by participants from the system.

- (2) Participants follow our Wechat official account. After logging in with the mobile number, one can enter the test results (upper and lower lines) and upload photos of the results window to the Wechat-official-account-based platform.
- (3) Study staff conduct active follow-up within 3 days after distributing the sampling tubes to obtain test results. Then, Table B3 is filled, and the information is entered into our Web-based platform.

Study staff can ask the participants to take photos of the FIT sampling tube results window or send the stool sample back to the communities or hospitals to verify the consideration of testing authenticity and validity.

### 5.5 Risk assessment for colorectal cancer (CRC)

For the risk assessment group, an established CRC risk scoring system, the Asia-Pacific Colorectal Screening (APCS) score, will be used for CRC risk assessment. The APCS score is derived from five common risk factors of CRC, including age, sex, family history of CRC in a first-degree relative, smoking, and body mass index (BMI). The five risk factors will be weighted differently, and the overall score is the sum of the five-item scores. On the basis of previous evidence, we define a score of  $\geq 4$  as indicating a high risk for CRC. The corresponding details of risk factors can be obtained from the Contact Information and Risk Factors Questionnaire (Table A2). After the information in Table A2 is entered into the Web-based platform, the system will automatically provide the CRC risk score as output.

Scoring the risk factors mentioned above:

Risk factor	Criteria	Points
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	50-54	0
Age (years)	55-64	1
	65-74	2
Sex	Female	0
	Male	1
Family history of colorectal	Absent	0
cancer in a first-degree	Present	1
relative		
Smoking	No	0
	Current or past	1
BMI	<23	0
	≥23	1

## 5.6 Questionnaire survey

Eligible participants are required to fill out their Contact Information and the Risk Factors Questionnaire (Table A2). Information about CRC-related risk factors, including history of bowel disease and clinical examination, medication history, lifestyle and living habits, and disease history will be collected by well-trained staff and stored in a Web-based data management system. Information on epidemiological risk factors will be used to conduct the risk association analysis between these factors and CRC and to further optimize the CRC risk assessment system. Participants' contact information should also be provided to ensure that the study staff can keep in touch with the participants throughout the project.

## 5.7 Colonoscopy

### 1) Basic requirements

- During the colonoscopy, all polypoid lesions and ulcers found must be biopsied for exact pathological diagnosis.
- The colonoscopy up to the cecum must be completed.

- Participants with inadequate colonoscopy examination should undergo repeat colonoscopy once within 1 month after adequate bowel preparation.
- For participants who cannot tolerate conventional colonoscopy, colonoscopy under anesthesia can be considered.
- Descriptions of lesions found by the colonoscopy should follow the clinical routine.

## **2) Contraindications**

- Before colonoscopy, whether there is a contraindication for colonoscopy should be assessed.
- Severe purulent inflammation or painful lesions in the anus and rectum, such as perianal abscess and anal fissure.
- Acute enteritis, severe ischemic disease, and radiation colitis, such as the active phase of bacterial disease and acute stage of ulcerative colitis, especially the fulminant type.
- Colonoscopic indications should be carefully considered for pregnant women or individuals who have had pelvic surgery and pelvic inflammatory disease. Colonoscopic examination is not recommended for menstruating women.
- Peritonitis, intestinal perforation, extensive intraperitoneal adhesion, and intestinal lumen stenosis due to various causes.
- Cirrhosis ascites, mesenteric inflammation, abdominal large arterial aneurysm, highly abnormally curved intestine, and advanced cancer with extensive intra-abdominal metastasis.
- Be absolutely prudent when conducting colonoscopy in the elderly and in infirm patients, as well as in those with severe cardiovascular and cerebrovascular diseases.

## **3) Endoscopist qualification**

Endoscopists should be highly responsible and rich in clinical experience to handle various emergencies in colonoscopy. It is recommended that colonoscopies be

performed by experienced endoscopists such as an attending doctor or one with a higher qualification and with >5 years of experience in colonoscopic examination. After the examination, endoscopists should promptly propose treatment suggestions for suspicious cases and urge patients in need of therapy to enter the treatment procedure in time.

#### **4) Preparation**

Colonoscopies should be performed under the instructions of the local colonoscopy department. Standard clinical procedures for the screening colonoscopy should be followed, including appointment; obtaining informed consent; routine blood testing for hepatitis B virus and HIV infections if required; distribution of drugs for bowel preparation; diet control; bowel preparation; and colonoscopy examination accompanied by family members. The responsible institute for screening shall save the original or copy of the colonoscopy report.

Whether the preoperative preparation for colonoscopy is adequate or not is highly related to the success of the examination and the incidence of complications; therefore, preoperative bowel cleansing should be emphasized. Endoscopists should inquire about the disease history in detail beforehand and learn the patient's condition, especially the recent medication history. For participants who have undergone B-ultrasound, barium enema, etc., endoscopists should read the examination reports carefully to know the location of the lesion. Endoscopists should also carefully interpret the results to relieve the participant's concerns.

For 1–2 days, the participant is required to follow a no fiber or semi-liquid only diet. Examples are porridge and egg drop soup, among others. On the day of colonoscopy, the participant should fast. For those who cannot stand fasting, try to arrange the colonoscopy in the morning. If the participant feels hungry, he/she can have some syrup or slag-free sugar. Diabetic patients can drink a small amount of milk. The study staff should guide the participants in adequate diet control with a relatively detailed interpretation of the results. Cleanse the whole bowel the night before colonoscopy or

morning of the operation. Methods are as follows:

- i. Oral magnesium sulfate ionic laxative: on the morning of the day before the procedure, 50 g of magnesium sulfate powder should be poured into 1,000 ml of warm water, which should then be mixed. However, 600–1000 ml of 5% magnesium sulfate solution should be consumed first before continuing to consume the mixture (approx. 250 ml every 10–15 min) until defecation without feces (total amount not exceeding 3,000 ml).
- ii. Polyethylene glycol and electrolytes: Hygecon® polyethylene glycol and electrolyte powder, for example, should be consumed following the instructions. A packet of polyethylene glycol powder should be poured into 1,000 ml of water. Approximately 600–1,000 ml of the solution should be taken first, followed by approximately 250 ml every 10–15 min until defecation without feces (total amount not exceeding 3,000–4,000 ml).
- iii. Participants with heart, kidney, liver, and lung dysfunction; hypertension; coronary heart disease; intestinal obstruction; and intractable constipation should consult a specialist for their bowel preparation.

## **5) Principles on polyps during colonoscopy management**

Polyps found during colonoscopy will be carefully examined using standard clinical procedures, and tissue specimens will be collected for further biopsy and pathological diagnosis. Magnifying endoscopy and chromo-endoscopy observation should be performed to know the exact size, shape, pedicle condition, and number of polyps, if possible, with corresponding treatment plans determined on the basis of the results. Detailed management principles are shown in Appendix VI.

## **6) Endoscope equipment and types**

To meet the quality control requirements, this study protocol recommends the following colonoscopy equipment. LUCERA CV-260SL (OLYMPUS) and LUCERA CLV-260SL (OLYMPUS) are recommended for the endoscope mainframe and light source. H260AI, Q260AI, Q260JI, or Q240I is recommended for colonoscopy, which can be used in 260

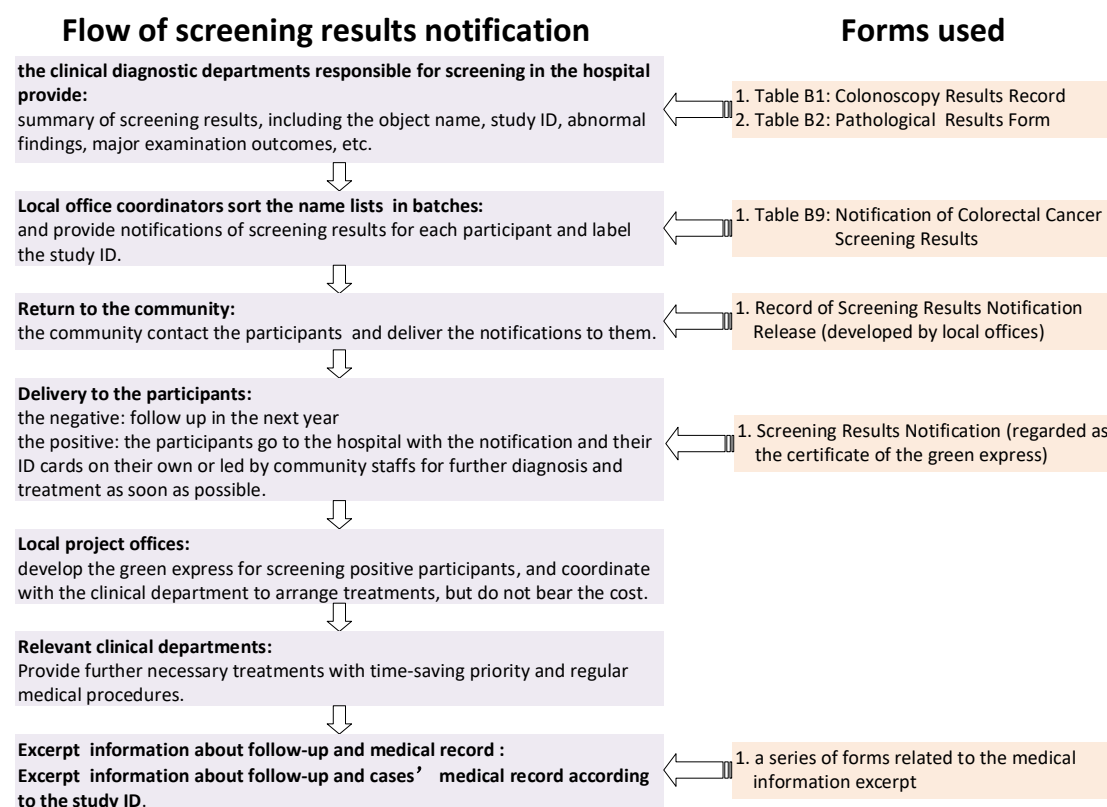
hosts.

### **7) Points for attention during colonoscopy**

Disinfection of the clinic and equipment should be strictly carried out, and separate cleaning and disinfection rooms and endoscopic treatment rooms should be set up. The cleaning and disinfection room should be well ventilated, and the colonoscopy clinic should be equipped with basic facilities such as treatment beds, aspirators, and treatment vehicles. For more details, refer to the 2017 edition of the “Operational Principles of Cleaning and Disinfection Techniques for Endoscopy.” If an accident occurs during colonoscopy, the emergency plan should be executed immediately.

### **5.8 Screening result notification**

Screening results are generated from the clinical departments of provincial cancer hospitals that conducted screening work and will be sent to the participants through the local project office. Detailed procedures are shown in the figure below. More details about follow-up and subsequent medical information collection protocols will be described later.



## 6. Biospecimen collection

In the era of precision medicine, exploring biomarkers for cancer screening and early diagnosis is an important research field with broad application prospects. Different types of biomarkers, including blood DNA methylation (methylated Septin9), fecal DNA methylation (KRAS,  $\beta$ -actin, etc.), fecal microbiota (fusobacterium nucleatum), and oral microbiota, have been associated with CRC and could be targets for screening and early diagnosis of CRC and CRC-related etiological studies. Prospective collection of biological samples in large cancer screening studies is currently an effective and cost-effective method. The obtained biological samples can be used for other related biomarker studies of cancer etiology and for early diagnosis.

Therefore, to establish a biobank that can be used for the exploration and evaluation of cancer-related biomarkers, some extra biological samples will be collected from participants who need to undergo colonoscopy before the examination, without affecting the implementation of existing randomized controlled trials. Biological



samples collected include stool, blood, and saliva samples.

## **1) Stool samples**

For all participants requiring colonoscopy, a stool sample collection device will be dispensed before the scheduled colonoscopy. More details about standard operating procedures (SOPs) for sample collection and separation can be found in Appendix II.

- Brief sampling procedures: The staff will distribute a set of stool sample collection devices (fecal sample collection box, ice pack, isothermal bag, gloves, toilet seat) to each participant, requiring them to collect feces within 24 h before colonoscopy (before taking the laxative). The stool sample box is placed in an isothermal bag equipped with frozen ice packs, and the isothermal bag containing the stool sample box will be sent to the hospital on the day of colonoscopy. The hospital staff record the corresponding information, label the samples, store them in a refrigerator at -80°C, and finally send them to the biobank of the Cancer Hospital, Chinese Academy of Medical Sciences, via cold-chain transportation.

## **2) Blood samples**

To meet future research requirements, we will collect blood samples to explore and evaluate blood protein, autoantibody, and other marker values for CRC screening and early diagnosis. Due to scientific research needs, participants will not receive feedbacks of test results. More details about SOPs for sample collection and separation can be found in Appendix III.

- Brief sampling procedures: For all participants requiring colonoscopy, approximately 10 mL of venous blood samples (including 5 mL anticoagulated blood and 5 mL non-anticoagulated blood) will be drawn by well-trained staff during their visit to the hospital before colonoscopy. According to the SOPs, blood samples are to be centrifuged; separated into plasma, serum, and leukocytes; and stored at -80°C, with the relevant information recorded. Finally, the samples will

be sent to the biobank of the Cancer Hospital, Chinese Academy of Medical Sciences, via cold-chain transportation for future use.

### **3) Saliva samples**

To meet future research requirements, we will collect saliva samples to explore and assess the association between saliva microbiota and intestinal microbiota and the relationship between saliva microbiota and the risk of CRC. Owing to scientific research needs, participants will not receive feedback on the test results. More details about the SOPs for sample collection and separation can be found in Appendix IV.

- Brief sampling procedures: For all participants requiring colonoscopy, they need to collect saliva samples using the saliva DNA collection tubes distributed according to the staff's instructions on the day of colonoscopy. Saliva samples are stored at the screening hospital at low temperature and transported at room temperature to the biobank of the Cancer Hospital, Chinese Academy of Medical Sciences, on a regular basis.

## **7. End-point events and outcome measures**

The main endpoints of our study are CRC and death.

Primary outcome is the detection rate of advanced neoplasm (CRC and advanced adenoma).

Secondary outcome measures include:

- Screening participation rate
- Detection rate of any neoplasm
- Complication rate
- Rate of CRC mortality

CRC staging was classified according to the Union for International Cancer Control

tumor-node-metastasis stage classification (8<sup>th</sup> version). Final clinical diagnoses were classified according to the most advanced finding reported in the colonoscopy and/or histology report. Advanced adenoma was defined as high-grade dysplasia, villous or tubular-villous histologic features, measuring 1 cm or more in diameter, or intramucosal carcinoma. Regarding the location of the neoplasm, the proximal colon was considered to include the splenic flexure and all segments proximal to it, and the rest was considered distal colon/rectum.

## **8. Treatment for positive results**

All intestinal lesions found during screening should be actively treated or transferred. Abnormal findings during colonoscopy will be carefully examined based on standard clinical procedures, and tissue specimens will be collected for further pathological diagnosis. Detailed principles for the treatment of participants with positive results are shown in Appendix VII.

## **9. Follow-up**

We will recall all baseline (T0) enrolled participants in the second (T1), third (T2), and fourth years (T3) and provide them with the corresponding screening according to the protocol: participants in the colonoscopy group will undergo an annual follow-up questionnaire survey; participants in the FIT group who are not diagnosed with CRC will undergo FIT screening (FIT-positive participants undergoing colonoscopy); among risk-adapted screening group, those who are FIT-negative at baseline and those who do not receive colonoscopy according to the protocol will undergo risk assessment again.

Patients with confirmed or probable CRC who are identified through various means (mainly routine recalls or questionnaires) will undergo focus-on follow-up, and relevant information about the diagnosis, treatment, and death will be obtained.

Follow-up-related forms include: Table A3: Annual information update form; Table C1: Cancer report form; Table C2: Cancer diagnosis form; Table C3: Colorectal cancer

diagnostic information excerpt form; Table C4: Colorectal cancer therapeutic information excerpt form; and Table C5: Death certificate forms.

## **10. Data management and quality control**

### **10.1 Data management**

All data will be entered into the Web-based data management system of Cancer Hospital, Chinese Academy of Medical Sciences. Particular staff members are assigned to ensure timely entry of data in each participating institute. The Cancer Hospital will monitor the data to ensure the integrity of the data. The data management system will perform a preliminary logical check on the data as they are entered.

### **10.2 Data security**

All documents, reports, and information related to the participants must be kept strictly confidential. Reports to the Cancer Hospital, Chinese Academy of Medical Sciences, shall not contain identification information (such as name and ID number) of the participants. Each participant has a unique study ID number. Researchers who need to obtain identification information about the participant must obtain approval from the ethics committee first.

### **10.3 Staff qualification**

Endoscopists should be highly responsible and rich in clinical experience to handle various emergencies in colonoscopy. It is recommended that colonoscopies are performed by experienced endoscopists who are attending doctors or doctors with higher qualifications and with >5 years of experience in colonoscopy examination. After the examination, endoscopists should promptly propose treatment suggestions for suspicious cases and urge patients in need of therapy to undergo timely treatment-related procedures.

## 10.4 Operating rules

The implementation of this study needs to meet the following series of specific clinical trial management practices:

- Helsinki Declaration (2013) by the World Medical Association
- Relevant regulations of National Medical Products Administration
- Other applicable regulations

## 11. Complication management

Colonoscopy plays a great important role for CRC screening and early diagnosis. It can provide a visual diagnosis (e.g., colorectal cancer lesions, adenoma, polyps) and allows the opportunity for biopsy or removal of suspected lesions. However, perforation and bleeding are common complications during colonoscopy examination and treatment process, and improper handling can be life-threatening.

The lack of experience and rudeness are the main causes of intestinal perforation. Perforations during diagnostic colonoscopy are often due to imperfect bowel preparation, forceful insertion of an endoscope into the unidentified intestinal lumen, or extensive inflation of the intestinal lumen; perforations during therapeutic colonoscopy mainly result from improper use of electrocoagulation equipment or laser. Hemorrhages after adenoma and polyp removal are often caused by the scabs peeling off. For early diagnosis and better treatment of CRC and for prevention and timely treatment of complications such as perforation and hemorrhage, a series of preventive measures and operational regulations have been formulated. For details, see Appendix VII.

## 12. Reporting of adverse events

### (1) Definition of adverse events and serious adverse events

Adverse events:

Any inappropriate or unexpected indications, symptoms, signs, or illnesses that are

temporarily associated with healthcare or related medical operations, no matter whether or not considered to be related to healthcare or medical operations (including unrelated, possibly irrelevant, possibly relevant, probably relevant, or absolutely relevant).

Serious adverse events refer to any adverse events resulting in:

- Death
- Hospitalization (except for other exact reasons) or extended length of stay
- Loss of self-care ability of daily living or disability.

(2) Direct or indirect adverse events

- Direct adverse events are complications associated with primary operations.
- Indirect adverse events consist of the black mood and diagnostic operations caused by screening tests and complications associated with diagnostic operations.
- Primary operations refer to colonoscopy and blood sampling operations associated with biological specimen collection.
- In this study protocol, direct adverse events only associated with primary operations may be reported as adverse events, and indirect adverse events should be considered a type of end-point event and recorded in the case report form.

(3) Adverse event identification in the expert panel

The coordination center (Cancer Hospital, Chinese Academy of Medical Sciences) and five research sites jointly establish an expert panel to identify possible adverse events.

### **13. Research team composition**

Cancer Hospital, Chinese Academy of Medical Sciences takes the lead on the initiation and implementation of this program with screening sites dispersed in five cities, namely Zhejiang Cancer Hospital, Hunan Cancer Hospital, Anhui Provincial Cancer Hospital, Yunnan Cancer Hospital, and Xuzhou Cancer Hospital.

The Cancer Hospital of the Chinese Academy of Medical Sciences is in charge of study protocol development, technical training and supervision, data management and analysis, biological sample preservation, and laboratory testing, whereas the field implementation institutes are responsible for mobilization, recruitment, screening work,

data reporting, and biological sample collection.

#### **14. Contamination evaluation**

During the study period, the study team will contact the participants to evaluate the CRC status beyond the study protocol. Extra screening examinations attended by the participants during the study period are not allocated by randomization and therefore may introduce bias into the study results. To evaluate the contamination status of this study, all participants without abnormal findings and whose screening findings are negative will complete one round of questionnaire interview synchronized with the last round of interventions. A detailed plan will be developed 3 months before the contamination evaluation, including the questionnaire survey methods; the number of times that participants need to be contacted for this questionnaire survey; the reasons for not responding; and the tracking, reporting, and evaluation of the questionnaire collection. All data collected will be transmitted to the Cancer Hospital, Chinese Academy of Medical Sciences. The contamination evaluation process mainly refers to Table A4: Contamination Assessment Questionnaire. We anticipate controlling the contamination rate to <10%.

#### **15. Project management**

A person in charge or coordinator will be arranged to interact with the Cancer Hospital, the Chinese Academy of Medical Sciences, at each screening site.

(1) Duties include:

- Personnel and administration management of screening sites
- Timely distributions of unique ID numbers and forms after participants' randomization
- Filling and verification of all research forms required by the Chinese Academy, Medical Sciences Cancer Hospital
- Delivery of forms to the Cancer Hospital, Chinese Academy of Medical Sciences, as required

- Reporting and tracking of participants' health condition
- Reports of recruitment summary every week.

(2) Specific jobs include:

- Training and qualification of study staff
- Documenting non-response events, such as participants' withdrawal from research, migration, or death
- Recording errors during randomization
- Record information about unqualified participants (e.g., when, why, and how they were found to be unqualified)



## Supplementary Table Content

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Table B7	Stool Sample Collection and Processing Information Record Form
Table B8	Pass-on Sheet of Biospecimen
Table B9	Notification of Colorectal Cancer Screening Results
Table B10	Release Registration Form for Screening Results Notification
Table C1	Cancer Report Form
Table C2	Cancer Diagnosis Form
Table C3	Summary Form for Colorectal Cancer Diagnostic Information
Table C4	Summary Form for Colorectal Cancer Treatment Information
Table C5	Death Certificate Related Group Forms
Table D1	Screening Site Information Correction Record
Table D2	Record of Protocol Deviation Events
Table D3	Adverse Events Report Form
Table E1	Record of Contact with Screening Subject
Table E2	Subject's No-response Record

**TABLE A1: Participants Qualification Checklist**

[illegible]

Part II: Qualification examination	
1. Age (The current year minus the year of birth; if the current date—regardless of the year— is before the date of birth, then subtract 1 from the previous result.):  __ __  years old	
(If the actual age is <50 or >74, end the investigation; and stop the investigation as long as the exclusion criteria are met during the following section.)	
Other criteria	1=Yes; 2=No
2. Has a doctor ever told you that you are diagnosed with the colorectal cancer?	__
3. Have you ever had colonic resection?	__
4. Are you receiving any kind of cancer-related therapy (except for non-melanoma skin cancer)?	__
5. Have you ever had colonic examination, including colonoscopy, flexible sigmoidoscopy, CT colonography and barium enema in the past 5 years?	__
6. Have you ever had FOBT or faecal DNA test during the past 1 year?	__
7. Is there any of the following lower gastrointestinal diseases or symptoms warranting colonoscopic evaluation, including: 1) long-term bloody stools within the past 6 months; 2) documented iron deficiency anaemia; 3) significant documented unintentional weight loss (>10% of baseline weight) over the past 6 months?	__

8. Any other serious diseases, including severe lung disease, end-stage renal disease, end-stage liver disease, severe heart failure or recent diagnosis of cancer with the exception of non-melanoma skin cancer?	__
9. Whether he/she belongs to non-registered permanent residents or people who have lived in the study region for less than 3 years?	__
10. Whether he/she is unwilling or unable to sign informed consent?	__

### Part III: Randomization and recruitment

Only participants who meet the age requirement and answer “No” to Q2-Q10 concurrently could be recruited into our study.

<p>Assign the Study ID numbers and implement the random allocation based on the online system.</p> <p>Date of randomization/recruitment:</p> <p>  <u>2</u>   <u>0</u>   <u>1</u>   <u>8</u>   -   __   __   -   __   __  </p> <p>Study ID: TC   __   __   __   __   __  </p>	<p><b>Random allocation:</b>  __ </p> <p><b>1 = Colonoscopy group</b></p> <p><b>2 = FIT group</b></p> <p><b>3 = Risk-adapted screening group</b></p>
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For the study staffs	
<p>Date of interview: <u>2</u>   <u>0</u>   <u>1</u>   <u>8</u>   -   <u>  </u>   <u>  </u>   -   <u>  </u>   <u>  </u>  </p> <p>Screening site ID: <u>  </u>   <u>  </u>  </p> <p>Field staff code: <u>  </u>   <u>  </u>   <u>  </u>   <u>  </u>  </p>	<p>Signature of interviewer: _____</p> <p>Signature of examiner: _____</p> <div> <p>Study ID:</p> <p>TC   <u>  </u>   <u>  </u>   <u>  </u>   <u>  </u>   <u>  </u>  </p> </div>

## Part I General information

1.1 Height: |\_\_|\_\_|\_\_|cm

1.2 Weight: |\_\_|\_\_|\_\_|kg

1.3 Waist circumference: |\_\_|\_\_|\_\_|cm

1.4 What is the highest level of school education you ever completed?

- ☐ No formal education
 ☐ Graduate from elementary school  
☐ Graduate from middle school
 ☐ Graduate from high school/vocational school  
☐ Bachelor's degree/ Associate degree
 ☐ Master's degree and above

1.5 What is your current marital status?

- ☐ Never married
 ☐ unmarried but Living with a partner
 ☐ Married
 ☐ divorced  
☐ Widowed
 ☐ Others: \_\_\_\_\_

## Part II History of intestinal disease and bowel examination

2.1 Do you have symptoms of abdominal discomfort or other abnormalities in the bowel at present?

- ☐ No (skip to Q 2.2)  
☐ Yes (skip to Q 2.1.1)

***If the answer is Yes in Q2.1, skip to Q2.1.1:***

2.1.1 When does the intestinal discomfort or abnormal symptoms in the bowel appear?

|\_\_|\_\_|\_\_|\_\_|Year|\_\_|\_\_|Month|\_\_|\_\_|Day

2.1.2 What are the main symptoms?

- ☐ Abdominalgia  
☐ Abnormal defecation (diarrhea, constipation, shapeless stools, etc.)  
☐ Bloody stools (visible to the naked eyes)  
☐ Others (please specify them) \_\_\_\_\_

2.2 Have you ever taken drugs for intestinal diseases?

- ☐ No  
☐ Yes, the name of the drug is \_\_\_\_\_

2.3 Have you ever gone to the hospital for examination due to intestinal discomfort?

- ☐ No  
☐ Yes (skip to Q 2.3.1)

2.3.1 The examination item is \_\_\_\_\_,

2.3.2 Date of the last examination is |\_\_|\_\_|\_\_|\_\_|Year|\_\_|\_\_|Month|\_\_|\_\_|Day

2.4 Have you ever had a colonoscopy?

- ☐ No  
☐ Yes (skip to Q 2.4.1)

2.4.1 Date of the last colonoscopy examination is

|\_|\_|\_|Year|\_|\_|Month|\_|\_|Day

2.4.2 How many times have you undergone colonoscopy in total? |\_|\_|times

2.4.3 Whether colorectal polyps/adenomas are found during colonoscopy?

☐ No ☐ Yes ☐ Unknown

### Part III Medication history

**3.1 Analgesic or antirheumatic drugs:** Do you occasionally or regularly take analgesics or anti-rheumatic drugs (e.g. aspirin, acetaminophen/paracetamol, indomethacin, fustatin, ibuprofen, etc. ) ?

☐ No

☐ Yes, occasionally

☐ Yes, regularly (more than 1 time per week)

**If yes, please answer the following questions in detail.**

3.1.1 How many years have you taken these drugs? |\_|\_|year(s)

3.1.2 Are you taking analgesics or anti-rheumatic drugs now?

☐ Yes, the current medication is: \_\_\_\_\_

☐ No, the last time I took the drug is: |\_|\_|\_|Year

**3.2 Anticoagulant drugs:** Do you occasionally or regularly take analgesics or anti-rheumatic drugs (e.g. warfarin, heparin, dabigatran, Tongxinluo, etc.)?

☐ No

☐ Yes, occasionally

☐ Yes, regularly (more than 1 time per week)

**If yes, please answer the following questions in detail.**

3.2.1 How many years have you taken these drugs? |\_|\_|year(s)

3.2.2 Are you taking anticoagulant drugs now?

☐ Yes, the current medication is: \_\_\_\_\_

☐ No, the last time I took the drug is: |\_|\_|\_|Year

**For women**

**3.3 Hormone replacement therapy (HRT):** Have you ever received or are currently receiving hormone replacement therapy? (**Estrogen or estrogen-progestin combination therapy**, the administration routes include oral, skin patches, creams or gels, vaginal creams, tablets, plugs, silicone rings, etc.)

☐ No

☐ Yes, how many years have you taken these drugs? |\_\_|\_\_|year(s)

**If yes, please answer the following questions in detail.**

3.3.1 Are you taking HRT now?

☐ Yes, the current medication is: \_\_\_\_\_

☐ No, the last time I took the drug is: |\_\_|\_\_|\_\_|\_\_|Year

## Part IV Lifestyle and living habits

### **A. Smoking and passive smoking**

4.1 Have you ever smoked?

☐ Never (skip to Q4.6)

☐ Yes

4.2 At about what age did you first start smoking on most days? |\_\_|\_\_| years old

4.3 How often do you smoke now?

☐ Almost every day

☐ Occasionally

☐ Quit smoking

**4.3.1 When was the last time you smoked?**

☐ 6 months ago

☐ 6 months to 4 years ago

☐ 4 to 10 years ago

☐ 10 to 15 years ago

☐ 15 years ago or more than 15years ago

4.4 How many years have you been smoking in total? |\_\_|\_\_| year(s)

4.5 How many cigarettes do you smoke per day when you smoke in the past or at present?

|\_\_|\_\_| cigarette(s)

4.6 Have you ever lived with smoker in the same house?

☐ No

☐ Yes

4.7 Have you been frequently exposed to other people's tobacco smoke in the indoor workplace?

☐ No

☐ Yes

4.8 What is the duration of your exposure to second-hand smoke? (The number of years in which the subjects live with the family members who smoke almost every day; if not, fill in 0)? |\_\_|\_\_| year(s)

### **B. Alcohol consumption**

4.9 How often did you drink any alcohol?

- ☐ Never or almost never      ☐ Once a month or less      ☐ 2 to 4 times a month  
☐ 2 to 3 times a week      ☐ 4 times a week or more

4.10 How many units of alcohol do you usually drink in a week? (1 unit of alcohol is approximately equal to: 350 ml of beer, or 150 ml of wine, or 50 ml of liqueur; alcohol consumption will be accumulated when drinking two or more types of the above)

- ☐ 1 unit or less      ☐ 2 to 3 units      ☐ 4 units  
☐ 5 to 7 units      ☐ 8 units or more

### **C. Diet**

4.11 During the past 12 months, about how often did you eat the following foods?

(Instructions: please tick the box that matches with your situation)

During the past 12 months	>once/ day	Once /day	>once /week	Once /week	≈once /month	Never /rarely
Meat (pork, beef, lamb, etc.)						
Fish/poultry (chicken, duck, goose, etc.)						
Eggs (hen's eggs, duck's eggs, etc.)						
Dairy products (milk, goat milk)						
Sausage						
Fine grains (rice, cooked wheaten food)						
Coarse grains (grain cereals, including millet, corn, sorghum, etc.)						
Fruits						
Fresh vegetables						

### **D. Exercise**

4.12 During the past 12 months, about how many hours per week did you spend on the following activities?

(Instructions: Please fill in the corresponding time you spent on the specific activity every week; less than 30 minutes— regarded as 0.5 hours, 30-59 minutes —regarded as 1 hour. Please fill in 0 if you didn't do the following activities.)



Type	hour(s)/week
Taking care of other adults	_ _  hour(s)
Taking care of babies/children	_ _  hour(s)
Moderate-intensity housework (including sweeping the floor, wiping the glass, washing clothes, cooking, tidying up the room, mopping the floor, etc.)	_ _  hour(s)
High-intensity housework (including handling heavy objects, chopping firewood, sweeping snow, etc.)	_ _  hour(s)
Ball games (including basketball, table tennis, badminton, etc.)	_ _  hour(s)
Walking or jogging	_ _  hour(s)
Riding a bicycle	_ _  hour(s)
High-intensity physical exercise (including swimming, mountain climbing, equipment exercise, etc.)	_ _  hour(s)
Low-intensity physical exercise (including Tai Chi, yoga, etc.)	_ _  hour(s)
Sedentary activities (including watching TV or listening to the radio, etc.)	_ _  hour(s)

## Part V Diseases history

5.1 Has the doctor ever diagnosed you with the following diseases? If so, when did you get diagnosed for the first time?

Diseases/Symptoms	Diagnosed disease? (1=Yes, 2=No)	Age at first diagnosis (years old)
Chronic diarrhea *	_	_ _
Chronic colitis	_	_ _
Chronic constipation **	_	_ _
Mucous and/or bloody stools	_	_ _
Intestinal polyps	_	_ _
Chronic appendicitis or history of appendectomy	_	_ _
Diabetes mellitus	_	_ _
Hypertension	_	_ _
Stroke	_	_ _
Heart disease or heart failure	_	_ _

\* Chronic diarrhea refers to diarrhea of which the cumulative duration are more than 3 months in the past 2 years, and each episode lasts for more than 1 week;

**\*\* Chronic constipation refers to constipation of which the cumulative duration are more than 2 months per year during the past 2 years.**

**5.2 Have you ever had any type of the following cancers?**

☐ No    ☐ Yes    **If yes, please fill out the form below:**

The type of cancer	Diagnosed cancer? (1=Yes; 2=No)	Age at first diagnosis	The type of cancer	Diagnosed cancer? (1=Yes; 2=No)	Age at first diagnosis
Bladder cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Lung cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Breast cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Oral Cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Cervical cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Nasal cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Colorectal cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Pancreatic cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Esophageal cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Gastric cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Kidney cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	Thyroid cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Laryngeal cancer	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>			

**6.3 Whether any of your immediate relatives has had colorectal cancer?**

☐ No    ☐ Unknown    ☐ Yes    **If yes, please fill out the form below:**

Immediate relatives	Diagnosed colorectal cancer? (1=Yes; 2=No)	Age at first diagnosis (years old)
Father	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Mother	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Brothers, including half-brothers	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>
Sisters, including half-sisters	<input type="checkbox"/>	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>

**Sincerely thank you for  
your participation!**

**TABLE A3: Annual Information Update Form**

For the study staffs	
Date of investigation:   2   0   1     -       -       Screening site ID:       Field staff code:           Year of investigation:   2   0       Name of the subject: _____	<div>Signature of interviewer: _____</div> <div>Signature of examiner: _____</div> <div>Study ID: TC          </div>

We need to know all the medical activities you have taken since you participated in this screening program for the first time (| | | | Year | | | Month | | | Day). Please try to answer the following questions. If you can't remember the exact date, the approximate one would be allowed.

1. Have you been diagnosed with cancer since you first participated in this screening program?

| |

1. Yes      2. No (skip to Q4)

2. What types of cancer have you been diagnosed with?

Order	The type or site of cancer	Date of cancer diagnosis	Cancer diagnosis hospital
A		-       -	
B		-       -	
C		-       -	

3. What is the name, phone number and address of the doctor who diagnosed you with cancer for the last time?

Name of hospital or doctor	
Address of the hospital	
Fixed-line phone number	-
Cellphone number	

4. In the event of death, the date of death is 20 | | | Year | | | Month | | | Day. (If still alive, skip to Q6.)

5. Source of death information: (multiple choices allowed)

- ☐ Family members of friends of the subject  
☐ Medical service staffs for the subject  
☐ Medical record or death certificate  
☐ Others: \_\_\_\_\_

6. Has the contact information of the subject changed since the last contact or follow-up survey? (only one choice allowed)

- ☐ No  
☐ Yes, the updated contact information is: \_\_\_\_\_  
☐ Unknown

7. Remarks:

**TABLE A4: Contamination Assessment Questionnaire**

For the study staffs	
Date of investigation:   2   0   1     -       -       Screening site ID:       Field staff code:           Year of sample investigation:   2   0         Name of the subject: _____	<div style="border: 1px solid black; padding: 5px; margin-bottom: 10px;"> Signature of interviewer: _____   Signature of examiner: _____ </div> <div style="border: 1px solid black; padding: 5px; text-align: center;"> Study ID:  <b>TC</b>          </div>
<b>Instruction:</b> Please answer the following questions and fill in the corresponding number in the      ; only one answer can be selected for each question.	
<b>Since 20      Year       Month, have you ever undergone any of the following physical examinations or medical examinations?</b>	
1. Have you ever had a blood pressure examination?       1. <input type="checkbox"/> Yes → 2. <input type="checkbox"/> No 3. <input type="checkbox"/> Unknown	1a. If yes, what is the main reason for your blood pressure examination?       1 <input type="checkbox"/> It is a certain disease's needs. 2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease. 3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *
2. Have you ever tested blood cholesterol levels?       1. <input type="checkbox"/> Yes → 2. <input type="checkbox"/> No 3. <input type="checkbox"/> Unknown	2a. If yes, what is the main reason for your blood cholesterol test?       1 <input type="checkbox"/> It is a certain disease's needs. 2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease. 3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *
3. Have you ever had examinations for glaucoma or cataract?       1. <input type="checkbox"/> Yes → 2. <input type="checkbox"/> No 3. <input type="checkbox"/> Unknown	3a. If yes, what is the main reason for your glaucoma or cataract examinations?       1 <input type="checkbox"/> It is a certain disease's needs. 2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease. 3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *
4. Have you ever had a colonoscopy?       1. <input type="checkbox"/> Yes → 2. <input type="checkbox"/> No 3. <input type="checkbox"/> Unknown	4a. If yes, what is the main reason for your colonoscopy examination?       1 <input type="checkbox"/> It is a certain disease's needs. 2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease. 3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *

**Instruction:** Please answer the following questions and fill in the corresponding number in the |\_\_|; only one answer can be selected for each question.

**Since 20| | |Year| | |Month, have you ever undergone any of the following physical examinations or medical examinations?**

<p>5. Have you ever had a sigmoidoscopy?  __ </p> <p>1. <input type="checkbox"/> Yes →</p> <p>2. <input type="checkbox"/> No</p> <p>3. <input type="checkbox"/> Unknown</p>	<p>5a. If yes, what is the main reason for your sigmoidoscopy examination?  __ </p> <p>1 <input type="checkbox"/> It is a certain disease's needs.</p> <p>2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease.</p> <p>3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *</p>
<p>6. Have you ever had a fecal occult blood test (FOBT)?  __ </p> <p>1. <input type="checkbox"/> Yes →</p> <p>2. <input type="checkbox"/> No</p> <p>3. <input type="checkbox"/> Unknown</p>	<p>6a. If yes, what is the main reason for your FOBT?  __ </p> <p>1 <input type="checkbox"/> It is a certain disease's needs.</p> <p>2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease.</p> <p>3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *</p>
<p>7. Have you ever had a stool DNA test?  __ </p> <p>1. <input type="checkbox"/> Yes →</p> <p>2. <input type="checkbox"/> No</p> <p>3. <input type="checkbox"/> Unknown</p>	<p>7a. If yes, what is the main reason for your stool DNA test?  __ </p> <p>1 <input type="checkbox"/> It is a certain disease's needs.</p> <p>2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease.</p> <p>3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *</p>
<p>8. Have you ever had a gas barium double contrast examination (DCBE)?  __ </p> <p>1. <input type="checkbox"/> Yes →</p> <p>2. <input type="checkbox"/> No</p> <p>3. <input type="checkbox"/> Unknown</p>	<p>8a. If yes, what is the main reason for your DCBE?  __ </p> <p>1 <input type="checkbox"/> It is a certain disease's needs.</p> <p>2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease.</p> <p>3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *</p>
<p>9. Have you ever had a CT bowel imaging examination?  __ </p> <p>1. <input type="checkbox"/> Yes →</p> <p>2. <input type="checkbox"/> No</p> <p>3. <input type="checkbox"/> Unknown</p>	<p>9a. If yes, what is the main reason for your CT bowel imaging examination?  __ </p> <p>1 <input type="checkbox"/> It is a certain disease's needs.</p> <p>2 <input type="checkbox"/> It is a reexamination for a certain diagnosed disease.</p> <p>3 <input type="checkbox"/> It is a part of the regular medical examination or is implemented as a screening item. *</p>


\* Screening is a kind of medical examination and regarded as the examination for diseases before any symptoms appear.

### TABLE B1: Colonoscopy Result Record Form

## Part I Basic information

[illegible]

## Part II Digital rectal examination (DRE)

Whether the participant (who cannot tolerate the colonoscopy) has a digital rectal examination?		
<input type="checkbox"/> Yes <input type="checkbox"/> No <u>If yes, please answer the following questions.</u>	<div> <div>With or without lumps?</div> <div> <input type="checkbox"/> Yes    <input type="checkbox"/> No </div> </div> <div> The lump is at a distance of ____cm from the anus and located in the ____ o' clock direction of the anus, occupying ____ / ____ (fraction) of the intestine. </div>	
Did the participant complete the colonoscopy? <input type="checkbox"/> Yes <input type="checkbox"/> No		
If the colonoscopy is completed, please continue; if not, the form is finished here.		

### Part III Colonoscopy result

<b>Operating mode</b>	<input type="checkbox"/> Single <input type="checkbox"/> Double <input type="checkbox"/> Single/double	<b>Anesthesia used</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<b>Depth of insertion</b>	<input type="checkbox"/> Terminal ileum <input type="checkbox"/> Cecum <input type="checkbox"/> Ascending colon <input type="checkbox"/> Hepatic flexure <input type="checkbox"/> Transverse colon <input type="checkbox"/> Splenic flexure <input type="checkbox"/> Descending colon <input type="checkbox"/> Sigmoid colon <input type="checkbox"/> Rectum		
<b>Bowel preparation</b>	<input type="checkbox"/> Level I (excellent) <input type="checkbox"/> Level II (good) <input type="checkbox"/> Level III (poor)		
<b>Withdrawal time from caecal entry</b>	_____minutes		
<b>Adverse events (multiple choices allowed)</b>	<input type="checkbox"/> None <input type="checkbox"/> Intestinal perforation <input type="checkbox"/> Bleeding (degree:_____; handling situation_____) <input type="checkbox"/> Other_____		
<b>Polyps detected</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No    If yes, the number of polyps detected is _____.		
<b>Other lesions</b>	<input type="checkbox"/> Yes <input type="checkbox"/> No	<b>If yes, please illustrate</b> _____.	

(except for polyps)

**Part IV Colonoscopic lesions****Lesion 1**

Site: <input type="checkbox"/> Terminal ileum <input type="checkbox"/> Ileocaecal valve <input type="checkbox"/> Ascending colon <input type="checkbox"/> Hepatic flexure <input type="checkbox"/> Transverse colon <input type="checkbox"/> Splenic flexure <input type="checkbox"/> Descending colon <input type="checkbox"/> Junction of descending colon and sigmoid colon <input type="checkbox"/> Sigmoid colon <input type="checkbox"/> Junction of sigmoid colon and rectum <input type="checkbox"/> Rectum	At a distance of ____ cm from the anus
Type of lesions under colonoscopy: _____	Specimen accession number: _____
Maximum diameter:  __ __ .  __  cm	Appearance: <input type="checkbox"/> Elevated <input type="checkbox"/> Flat <input type="checkbox"/> Depressed
Pedunculated: <input type="checkbox"/> Yes <input type="checkbox"/> No	Shape of pedicle: <input type="checkbox"/> Broad-pedunculated <input type="checkbox"/> Semipedunculated
Color: <input type="checkbox"/> Red <input type="checkbox"/> Offwhite <input type="checkbox"/> Other	Bleeding: <input type="checkbox"/> Yes <input type="checkbox"/> No

**Lesion 2**

Site: <input type="checkbox"/> Terminal ileum <input type="checkbox"/> Ileocaecal valve <input type="checkbox"/> Ascending colon <input type="checkbox"/> Hepatic flexure <input type="checkbox"/> Transverse colon <input type="checkbox"/> Splenic flexure <input type="checkbox"/> Descending colon <input type="checkbox"/> Junction of descending colon and sigmoid colon <input type="checkbox"/> Sigmoid colon <input type="checkbox"/> Junction of sigmoid colon and rectum <input type="checkbox"/> Rectum	At a distance of ____ cm from the anus
Type of lesions under colonoscopy: _____	Specimen accession number: _____
Maximum diameter:  __ __ .  __  cm	Appearance: <input type="checkbox"/> Elevated <input type="checkbox"/> Flat <input type="checkbox"/> Depressed
Pedunculated: <input type="checkbox"/> Yes <input type="checkbox"/> No	Shape of pedicle: <input type="checkbox"/> Broad-pedunculated <input type="checkbox"/> Semipedunculated
Color: <input type="checkbox"/> Red <input type="checkbox"/> Offwhite <input type="checkbox"/> Other	Bleeding: <input type="checkbox"/> Yes <input type="checkbox"/> No

**Lesion 3**

Site: <input type="checkbox"/> Terminal ileum <input type="checkbox"/> Ileocaecal valve <input type="checkbox"/> Ascending colon <input type="checkbox"/> Hepatic flexure <input type="checkbox"/> Transverse colon <input type="checkbox"/> Splenic flexure <input type="checkbox"/> Descending colon <input type="checkbox"/> Junction of descending colon and sigmoid colon <input type="checkbox"/> Sigmoid colon <input type="checkbox"/> Junction of sigmoid colon and rectum <input type="checkbox"/> Rectum	At a distance of ____ cm from the anus
Type of lesions under colonoscopy: _____	Specimen accession number: _____



Maximum diameter:  __ __ .  __ cm	Appearance: <input type="checkbox"/> Elevated <input type="checkbox"/> Flat <input type="checkbox"/> Depressed
Pedunculated: <input type="checkbox"/> Yes <input type="checkbox"/> No	Shape of pedicle: <input type="checkbox"/> Broad-pedunculated <input type="checkbox"/> Semipedunculated
Color: <input type="checkbox"/> Red <input type="checkbox"/> Offwhite <input type="checkbox"/> Other	Bleeding: <input type="checkbox"/> Yes <input type="checkbox"/> No

**Lesion 4**

Site: <input type="checkbox"/> Terminal ileum <input type="checkbox"/> Ileocaecal valve <input type="checkbox"/> Ascending colon <input type="checkbox"/> Hepatic flexure <input type="checkbox"/> Transverse colon <input type="checkbox"/> Splenic flexure <input type="checkbox"/> Descending colon <input type="checkbox"/> Junction of descending colon and sigmoid colon <input type="checkbox"/> Sigmoid colon <input type="checkbox"/> Junction of sigmoid colon and rectum <input type="checkbox"/> Rectum	At a distance of ____ cm from the anus
Type of lesions under colonoscopy: _____	Specimen accession number: _____
Maximum diameter:  __ __ .  __ cm	Appearance: <input type="checkbox"/> Elevated <input type="checkbox"/> Flat <input type="checkbox"/> Depressed
Pedunculated: <input type="checkbox"/> Yes <input type="checkbox"/> No	Shape of pedicle: <input type="checkbox"/> Broad-pedunculated <input type="checkbox"/> Semipedunculated
Color: <input type="checkbox"/> Red <input type="checkbox"/> Offwhite <input type="checkbox"/> Other	Bleeding: <input type="checkbox"/> Yes <input type="checkbox"/> No

Other lesions:	
Diagnosis at colonoscopy:	
Doctor's name:	

(Added tables allowed)

**Instructions:**

1. Bowel preparation: Level I (excellent): no feces or slag in the intestine, no retention of liquid feces, clear intestinal juice, smooth operation, clear observation; Level II (good): no feces or slag in the intestine, dirty liquid feces in the intestine, relatively smooth operation, basically clear observation; Level III (poor): fecal residue or fecal mass in the intestine, unsmooth operation, even forced to stop due to insufficient bowel preparation.
2. The location is the distance of \*\*cm away from the anus (subject to the length of colonoscopy withdrawal); and regarding the center of anterior intestinal paries as 12 o'clock direction and the center of posterior intestinal paries as 6 o'clock direction, the position of the lesion in the intestinal lumen is described in a clockwise direction.
3. Every lesion's information needs to be filled in completely.

### TABLE B2: Pathology Result Record Form

## Part I Basic information

<b>Study ID:</b> TC _ _ _ _ _					
<b>National ID number:</b>  _					
<b>Name:</b> _____			<b>Sex:</b> <input type="checkbox"/> Male <input type="checkbox"/> Female		
<b>Age:</b> _____ years			<b>Date of procedure:</b> _____ Year ____ Month ____ Day		

## Part II Pathological diagnosis

**Need for consultation (review) from National Cancer Center? (☐ No/☐ Yes)**

1. Specimen accession number	2. Specimen site	3. Specimen location (distance from the anus)	4. Pathological diagnosis (code)	5. Percentage of high-grade intraepithelial neoplasia (%)	6. Structural proportion of adenomatous polyps (%)		7. Remarks
					Tubular	Villous	
		_ _ cm	_ _   _ _   _ _   _ _				
		_ _ cm	_ _   _ _   _ _   _ _				
		_ _ cm	_ _   _ _   _ _   _ _				
		_ _ cm	_ _   _ _   _ _   _ _				



### Instructions for coding in TABLE B2: Pathology Results Form

- 1. Specimen accession number** is in accordance with the number in TABLE B1: Colonoscopy Result Record Form.
- 2. Specimen site** is in accordance with the lesion's site in TABLE B1: Colonoscopy Result Record Form.
- 3. Specimen location** is in accordance with the record of the lesion's location in TABLE B1: Colonoscopy Result Record Form.

#### 4. Pathological diagnostic code:

- |  |  |
|--|--|
| 01. Normal/ generally normal colorectal mucosa | 12. Tubulovillous adenoma  |
| 02. Chronic colitis/ proctitis                 | 13. Low-grade intraepithelial neoplasia of glandular epithelium (dysplasia)                    |
| 03. Chronic active colitis/ proctitis          | 14. High-grade intraepithelial neoplasia of glandular epithelium (dysplasia)                   |
| 04. Chronic granulomatous colitis/proctitis    | 15. High-grade intraepithelial neoplasia of glandular epithelium (intramucosal adenocarcinoma) |
| 05. Non-adenomatous polyp                      | 16. Intraepithelial neoplasia of glandular epithelium that cannot be graded                    |
| 06. Hyperplastic polyp                         | 17. Invasive adenocarcinoma  |
| 07. Sessile serrated adenoma                   | 18. Cancer that cannot be classified   |
| 08. Traditional serrated adenoma               | 19. Malignant tumors that cannot be classified   |
| 09. Serrated polyps that cannot be classified  | 20. Others   |
| 10. Tubular adenoma                            | 99. Weak evidence for diagnosis  |
| 11. Villus adenoma                             |  |

#### 5. Percentage of high-grade intraepithelial neoplasia (%):

Record the proportion of high-grade intraepithelial neoplasia in intraepithelial neoplasia.

#### 6. Structural proportion of adenomatous polyps (%):

Record the proportion of the tubular structure and the villus structure respectively, expressed as percentages.

#### 7. Remarks:

Any questions uncovered by the above content that need to be explained.

**TABLE B3: Distribution Record of FOBT Devices (Pupu tube) and Test Result Form**

Page \_\_\_\_\_

<b>Consumables distribution</b>						<b>Results feedback record</b>			
Distributing site: _____									
Referring staff's work number: _____ Signature: _____									
Record number	Name	Study ID (handwritten)	Screening group*	Date of distribution	ID of the 'puff-puff tube'	Date of result-receipt	Test results ( <u>value of the control-line</u> )	Test results ( <u>value of the test-line</u> )	Remarks

\* 1= Colonoscopy group; 2=FIT group; 3= Risk-adapted screening group

Page\_\_\_\_\_

[illegible]

\* 1= Colonoscopy group; 2=FIT group; 3= Risk-adapted screening group

**TABLE B5: Blood Sample Collection and Processing Information Record Form**

Page \_\_\_\_\_

Name	Study ID	Sample ID (top 7)	Date	Serum						Plasma						Leukocytes		Remarks (e.g. <u>hemolysis</u> <u>etc.</u> )
				Box number	Location					Box number	Location					Box number	Location	

**TABLE B6: Saliva Sample Collection and Processing Information Record Form**

Page \_\_\_\_\_

Name	Study ID	Sample ID (top 7)	Date of sample collection	Saliva sample		Remarks
				Box number	Location	



**TABLE B7: Stool Sample Collection and Processing Information Record Form**

Page\_\_\_\_\_

Name	Study ID	Sample ID (top 7)	Date of sample collection	Stool sample		Remarks
				Box number	Location	

**TABLE B8: Pass-on Sheet of Biospecimen****Pass-on Sheet of Biospecimen (the first pair part)**Screening site \_\_\_\_\_ Date of issue: 2 | 0 | 1 | \_\_\_\_ | - | \_\_\_\_ | \_\_\_\_ | - | \_\_\_\_ | \_\_\_\_ |

Name of stuffing operator: \_\_\_\_\_

Name of deliveryman (/company in-charge and waybill number):\_

Number of frozen storage box	Type of biospecimen	Remarks

**Pass-on Sheet of Biospecimen (the second pair part)**Screening site: \_\_\_\_\_ Date of arrival: 2 | 0 | 1 | \_\_\_\_ | - | \_\_\_\_ | \_\_\_\_ | - | \_\_\_\_ | \_\_\_\_ |

Signature of recipient: \_\_\_\_\_

Number of frozen storage box	Type of biospecimen	Remarks

**TABLE B9: Notification of Colorectal Cancer Screening Results**

Dear \_\_\_\_\_: the results of the colorectal cancer screening organized by \_\_\_\_\_, which you participated in recently, and further treatment suggestions are as follows.

Examinations	Results	Further treatment suggestions
<input type="checkbox"/> <b>1. Findings at colonoscopy</b>	<div style="display: flex; flex-wrap: wrap;"> <div style="width: 50%;"> <input type="checkbox"/> 1= Normal  <input type="checkbox"/> 2= Polyp(s)  <input type="checkbox"/> 3= Rectal cancer  <input type="checkbox"/> 4= Suspected rectal cancer  <input type="checkbox"/> 5= Colon cancer  <input type="checkbox"/> 6= Suspected colon cancer  <input type="checkbox"/> 7= Crohn Disease  <input type="checkbox"/> 8= Ulcerative Colitis </div> <div style="width: 50%;"> <input type="checkbox"/> 9= Atypical colitis  <input type="checkbox"/> 10= Vascular malformation  <input type="checkbox"/> 11= Diverticulum  <input type="checkbox"/> 12= Anal fissure  <input type="checkbox"/> 13= Hemorrhoid(s)  <input type="checkbox"/> 14= Rectal prolapse  <input type="checkbox"/> 15= Other: _____ </div> </div>	<input type="checkbox"/> Waiting for pathological diagnosis <input type="checkbox"/> Conservative treatment <input type="checkbox"/> Therapeutic endoscopy <input type="checkbox"/> Surgical treatment <input type="checkbox"/> Other: _____
<input type="checkbox"/> <b>2. FIT for fecal occult blood test</b>	<input type="checkbox"/> 1= Negative <input type="checkbox"/> 2= Positive <input type="checkbox"/> 3= Invalid	<input type="checkbox"/> Re-visit in next year <input type="checkbox"/> Comprehensive enteroscopy as soon as possible <input type="checkbox"/> Collect stool sample anew
<input type="checkbox"/> <b>3. Pathological diagnosis at colonoscopy</b>	<div style="display: flex;"> <div style="flex: 1;"> <input type="checkbox"/> <u>Type of lesions</u>  <input type="checkbox"/> Benign tumor  <input type="checkbox"/> Tubular adenoma  <input type="checkbox"/> Tubulovillous adenoma  <input type="checkbox"/> Villous adenoma  <input type="checkbox"/> Flat adenoma (tubular)  <input type="checkbox"/> Flat adenoma (tubulovillous)  <input type="checkbox"/> Flat adenoma (villous)  <input type="checkbox"/> Mixed adenoma  <input type="checkbox"/> Other: _____ </div> <div style="flex: 1;"> <input type="checkbox"/> <u>Other benign lesions</u>  <input type="checkbox"/> Hyperplastic polyps  <input type="checkbox"/> Granulomatous polyps  <input type="checkbox"/> Inflammatory polyps  <input type="checkbox"/> Other: _____   <input type="checkbox"/> <u>Atypical hyperplasia (intraepithelial neoplasia) / degree of differentiation</u>  <input type="checkbox"/> Low-grade intraepithelial neoplasia  <input type="checkbox"/> High-grade intraepithelial neoplasia  <input type="checkbox"/> Well-differentiated adenocarcinoma  <input type="checkbox"/> Moderately differentiated adenocarcinoma  <input type="checkbox"/> Low-differentiated adenocarcinoma  <input type="checkbox"/> Other: _____ </div> </div>	<input type="checkbox"/> Close observation <input type="checkbox"/> Conservative treatment <input type="checkbox"/> Therapeutic endoscopy <input type="checkbox"/> Surgical treatment <input type="checkbox"/> Other: _____

Our program only covers the cost of colorectal cancer screening, and if necessary, we recommend you to choose a local cancer hospital for further examination/treatment. Cancer Hospital/ Chinese Academy of Medical Sciences can also provide you with a green channel, but the cost should be covered by yourself. This screening is not and cannot replace the comprehensive medical examination in the hospital. If you have any questions about the screening results or this screening program, please call the local coordinator directly: \_\_\_\_\_ (name of the screening site coordinator), and his/her phone number is: \_\_\_\_\_. We extend our sincerest thanks for your participation.

\_\_\_\_\_ Cancer Hospital

Date: \_\_\_\_\_

**TABLE B10: Release Registration Form for Screening Results Notification**

Releasing site (community) \_\_\_\_\_; ID of quality controller: |\_|\_|\_|\_|;

Signature of quality controller \_\_\_\_\_;

Page \_\_\_\_\_

Record number	Name	Study ID (handwritten)	Screening group*	Notification of CRC screening results			Signature of receiver	Work number and signature of releasing staff referred	Remarks
				Released**	Type of releasing site#	Date of release			
		_ _ _ _				20 _ _ - _ _ - _ _		_ _ _ _	
		_ _ _ _				20 _ _ - _ _ - _ _		_ _ _ _	
		_ _ _ _				20 _ _ - _ _ - _ _		_ _ _ _	
		_ _ _ _				20 _ _ - _ _ - _ _		_ _ _ _	
		_ _ _ _				20 _ _ - _ _ - _ _		_ _ _ _	

\* \* 1= Colonoscopy group; 2=FIT group; 3= Risk-adapted screening group

\*\* 1=Yes; 2=No

# 1=taken by the participants or their family members from the community center; 2=delivered to their home by the community staffs; 3=taken by the neighbors by the way from the community center; 4= taken by the participants or their family members from the hospital; 5= Other: \_\_\_\_\_.

**TABLE C1: Cancer Report Form**

General Information		
Screening site ID:  __	Signature of preparer: _____	
Field staff code:  __ __ __ __	Signature of quality controller: _____	Study ID: TC __ __ __ __
Year of investigation:  __ __ __ __		
Cancer information		
1. Type/site of cancer (can be any type of cancer)	2. Date of report	3. Diagnostic material source *
A. _____	A.  2 0 __ __ _ - __ __ _ - __ __	A.  __ , more details: _____
B. _____	B.  2 0 __ __ _ - __ __ _ - __ __	B.  __ , more details: _____
C. _____	C.  2 0 __ __ _ - __ __ _ - __ __	C.  __ , more details: _____
D. _____	D.  2 0 __ __ _ - __ __ _ - __ __	D.  __ , more details: _____
E. _____	E.  2 0 __ __ _ - __ __ _ - __ __	E.  __ , more details: _____
	F.  2 0 __ __ _ - __ __ _ - __ __	F.  __ , more details: _____
Code of diagnostic material source		
* 1. The participant himself/herself; 4. Medical record;	2. Relatives, spouse or friends of the participant; 5. Death certificate;	3. Health center; 6. Other: _____

**TABLE C2: Cancer Diagnosis Form**

General information	
Date of filling:   2   0       -       -       Report date of suspected cancer:   2   0       -       -       Screening site ID:       Field staff code:           Year of investigation:	<div style="display: flex; justify-content: space-between;"> <div style="width: 60%;">           Signature of preparer:            _____             Signature of quality controller:            _____         </div> <div style="width: 35%; border: 1px solid black; padding: 10px; text-align: center;">           Study ID:  <b>TC</b>                      </div> </div>
A. Information of cancer case reported	
1. Cancer diagnosed: _____	
2. Information completion forms for suspected cancer: <input type="checkbox"/> Annual Information Update Form; <input type="checkbox"/> Cancer Report Form	
3. Diagnosed cancer (only one choice allowed)	
<input type="checkbox"/> The primary focus is in the colorectum. (Must complete <u>the Diagnostic Information of Colorectal Cancer Summary Form</u> ) <input type="checkbox"/> The primary focus is outside the colorectum. <input type="checkbox"/> There is a clear primary malignant tumor outside the colorectal and it metastasizes to the colorectum. <input type="checkbox"/> Malignant tumor of unknown origin metastasizes to the colorectum	<input type="checkbox"/> The primary focus is in the colorectum and it metastasizes to other sites. (Must complete <u>the Diagnostic Information of Colorectal Cancer Summary Form</u> ) <input type="checkbox"/> Diagnosed cancer before randomization (Violator of random grouping conditions must complete the <u>Violation of the Protocol Event Record Form</u> ) <input type="checkbox"/> Improper diagnosis of cancer (skip to Section C) <input type="checkbox"/> Non-colorectal primary focus metastasizes to other sites.

3a. Have you ever been diagnosed with this type of cancer before?

- ☐ Yes (skip to Section C)
- ☐ No (For non-colorectal primary malignant tumor, skip to Section B; for colorectal primary malignant tumor, skip to Section C.)

### B. Diagnostic information of non-colorectal primary malignant tumor

4. Date of diagnosis of the primary tumor: | 2 | 0 | | | - | | | - | | |

5. Primary malignant tumor classification (ICD-O-3):

C: |\_| |\_| |\_|    |\_| |\_| |\_| |\_|    |\_|    |\_|  
Topography      Morphology   Invasiveness   Grade

**ID of staff involved in information excerpt:** |\_\_|\_\_|\_\_|\_\_|

### C. Remarks

[illegible]

- ☐ Additional pages allowed



**TABLE C3: Summary Form for Colorectal Cancer Diagnostic Information**

General information				
<input type="checkbox"/> Tick here if the object has filled out another sheet of this form Date of excerpt:   2   0       -       -       ID of excerpt staff:           Screening site ID:       Year of investigation:            Objectives: <input type="checkbox"/> First excerpt <input type="checkbox"/> Second excerpt for quality assurance			Signature of preparer: _____  Signature of quality controller: _____  <div style="border: 1px solid black; padding: 5px; text-align: center;">             Study ID:  <b>TC</b>                    </div>	
Section A: Diagnostic evaluation and staging				
1. Whether the subject has entered the diagnostic procedure? <input type="checkbox"/> Yes <input type="checkbox"/> No, reported by the doctor <input type="checkbox"/> No, reported by the subject		2. Reasons for first visit (multiple choices allowed): <input type="checkbox"/> Appearance of symptoms <input type="checkbox"/> Follow-up of the positive ones in the screening program <input type="checkbox"/> Other: _____		
3. Comprehensive enteroscopy (No need to record the results)				
Date of procedure	Ileum level reached	Bowel preparation	Hyperplastic polyp(s)	
2   0       -       -	<input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Unknown	<input type="checkbox"/> Excellent <input type="checkbox"/> Poor <input type="checkbox"/> Unknown	<input type="checkbox"/> None <input type="checkbox"/> 1 polyp detected <input type="checkbox"/> >1 polyps detected	
4. Assessment of adenoma at comprehensive enteroscopy				
Site	Size	Type of histology	Intraepithelial neoplasia	High-risk adenoma
a <input type="checkbox"/> Ileum <input type="checkbox"/> Ascending colon <input type="checkbox"/> Hepatic flexure of colon <input type="checkbox"/> Transverse colon <input type="checkbox"/> Splenic flexure of colon <input type="checkbox"/> Descending colon <input type="checkbox"/> Sigmoid colon <input type="checkbox"/> Rectum <input type="checkbox"/> Vermiform appendix	Maximum diameter _____cm <input type="checkbox"/> Unknown	<input type="checkbox"/> Tubular adenoma <input type="checkbox"/> Tubulovillous adenoma <input type="checkbox"/> Villous adenoma <input type="checkbox"/> Adenoma (unknown)	<input type="checkbox"/> None <input type="checkbox"/> Low-grade <input type="checkbox"/> High-grade <input type="checkbox"/> Unknown	Definition: (At least one of the following must be met to define a high-risk adenoma: ① ≥1cm; ② Villous adenoma; ③ High-grade

b Distance from anal edge ____cm <input type="checkbox"/> Unknown				intraepithelial neoplasia) Amount:
5. Assessment of diagnosis (No need to record the results, and for CEA, record the value.)				
Procedure	Date		Diagnostic methods (For code, see the table below.)	
1	2   0   1     -       -			
2	2   0   1     -       -			
3	2   0   1     -       -			
4	2   0   1     -       -			
5	2   0   1     -       -			
6	2   0   1     -       -			
7	2   0   1     -       -			
8	2   0   1     -       -			
9	2   0   1     -       -			
10	2   0   1     -       -			
11	2   0   1     -       -			
12	2   0   1     -       -			
<b>Diagnostic method code</b>				
01= Abdominal plain X-rays 02= Barium enema radiography 03= Biopsy (please clearly illustrate) 04=Chest X-rays 05= Clinical assessment 06= Abdominal/ hepatic CT 07= CT of other sites(please clearly illustrate) 08= Pelvic CT 09= Cystoscopy 10= Digital rectal examination 11=IVP or VCUG 12= Abdominal/ hepatic MRI 13= MRI of other sites(please clearly illustrate) 14= Pelvic MRI 15= Preoperative CEA (please record the value)		16=FOBT 17=Record 18= Resection (please clearly illustrate) 19= Abdominal ultrasound 20= Abdominal pelvic CT 21= Partial colectomy 22= Laparoscopy 23= Exploratory laparotomy 24= Lymph node biopsy 25= X-ray examination of other sites (please clearly illustrate) 26= Ultrasonography (please clearly illustrate) 27= Upper gastrointestinal assessment— endoscopy or contrast-enhanced upper gastrointestinal imaging 88= Others (please clearly illustrate)		
<b>Complication code</b>				
1=Infection (please record the value)		30= Hypotension		
2=Fever (antibiotics needed)		31= Congestive heart-failure (CHF)		
3= Perforation		32= Wound dehiscence		
4= Hemorrhage		33= Hypokalemia		
6= Respiratory arrest		300= Diarrhea		

20= Cardiac Arrest	301= Small-bowel obstruction
22= Hospitalization	302= Ileus
23= Pulmonary embolism	306= Rectal injury
24= Myocardial infarction	307= Hematochezia
25= Arrhythmia	
26= Cerebral vascular accident (CAV)/Stroke	
27= Blood loss (blood transfusion needed)	
28= Deep venous thrombosis	

6. Are there complications due to examinations for diagnosis and staging?  
☐ No      ☐ Yes (fill out the following table)      ☐ Unknown

Date of implications occurrence (yyyy-mm-dd)	Medical complications (See the previous table for code; multiple choices allowed)
2   0   1       -       -	
2   0   1       -       -	
2   0   1       -       -	
2   0   1       -       -	
2   0   1       -       -	

7. Colorectal cancer diagnostic assessment results:  
☐ Non-malignant, confirmed by histology or cytology (skip to Section D)  
☐ Non-malignant, only based on clinical evaluation and without pathological evidence (skip to Section C)  
☐ Primary colorectal malignancy, confirmed by histology (skip to Section C)  
☐ Other malignant tumors, confirmed by histology or cytology (skip to Section B)  
☐ Primary colorectal malignancy, confirmed by cytology (skip to Section C)  
☐ None results (skip to Section D)

**Section B: Information of other diagnoses except for colorectal cancer**

8a. Non-tumor diagnoses      ☐ Yes      ☐ None  
Classification based on ICD-10: | | | | | . | | | | |

8b. Date of diagnosis: | 2 | 0 | | | - | | | - | | |  
ID of disease classification information provider: | | | | |

8c. Diagnosis of tumor in other sites (non-primary invasive colorectal cancer)      ☐ Yes      ☐ No  
Classification based on ICD-O-3: | C | | | | | - | | | | | - | | | - | | |  
Topography      Morphology      Invasiveness      Grade

8d. Date of diagnosis: | 2 | 0 | | | - | | | - | | |  
ID of certified tumor register (CTR): | | | | |

8e. Whether the cancer is transferred to the large intestine?      ☐ Yes      ☐ No

**Section C: Information of primary colorectal cancer**

9. Date of primary colorectal cancer diagnosis: | 2 | 0 | | | - | | | - | | |

10. Diagnosis report of primary colorectal cancer (single choice):  
☐ No report/clinical examinations  
☐ Histological / histopathological (copy attached)  
☐ Cytological / cytopathological (copy attached)

<input type="checkbox"/> Reported but not available					
11. Repeat the primary colorectal cancer diagnosis in medical records:					
12. Classification based on ICD-O-3 (filled in by CTR or equal-qualified staffs):					
C _ _ _ _ - _ _ _ _ - _ _ - _ _			CTR ID:  _ _ _ _ _		
Topography Morphology Invasiveness Grade					
13. Primary cancer's location (multiple choices allowed):					
<input type="checkbox"/> Ileum <input type="checkbox"/> Ascending colon <input type="checkbox"/> Hepatic flexure of colon <input type="checkbox"/> Transverse colon <input type="checkbox"/> Splenic flexure of colon <input type="checkbox"/> Descending colon <input type="checkbox"/> Sigmoid colon <input type="checkbox"/> Rectum <input type="checkbox"/> Vermiform appendix <input type="checkbox"/> Unknown					
Distance from anal edge: _____ cm					
14. Pathological type of primary colorectal cancer (filled in by CTR or equal-qualified staffs):					
<input type="checkbox"/> Adenocarcinoma <input type="checkbox"/> Undifferentiated carcinoma <input type="checkbox"/> Mucinous adenocarcinoma <input type="checkbox"/> Carcinoma <input type="checkbox"/> Signet-ring cell carcinoma <input type="checkbox"/> Other (please clearly illustrate) <input type="checkbox"/> Squamous cell carcinoma <input type="checkbox"/> Unknown <input type="checkbox"/> Adenosquamous carcinoma					
15. Differentiation degree of primary colorectal cancer (filled in by CTR or equal-qualified staffs):					
<input type="checkbox"/> Unable to evaluate (GX) <input type="checkbox"/> Well differentiated (G1) <input type="checkbox"/> Moderately differentiated (G2) <input type="checkbox"/> Poorly differentiated (G3) <input type="checkbox"/> Undifferentiated (G4) <input type="checkbox"/> Not described in the report <input type="checkbox"/> Unknown--- pathological report lost					
16. TNM staging of primary colorectal cancer (filled in by CTR or equal-qualified staffs):					
16a. TNM clinical staging: (下表单选)			16b. TNM pathological staging: (下表单选)		
<input type="checkbox"/> Yes <input type="checkbox"/> No			<input type="checkbox"/> Yes <input type="checkbox"/> No		
			Whether new adjuvant therapy has been performed before the staging result is known?		
			<input type="checkbox"/> Yes <input type="checkbox"/> No		
Single choice					
Size of Primary tumor (T):	lymph node metastasis (N):	Distant metastasis (M):	Size of Primary tumor (T):	lymph node metastasis (N):	Distant metastasis (M):
<input type="checkbox"/> T <sub>x</sub>	<input type="checkbox"/> N <sub>x</sub>	<input type="checkbox"/> M <sub>x</sub>	<input type="checkbox"/> T <sub>x</sub>	<input type="checkbox"/> N <sub>x</sub>	<input type="checkbox"/> M <sub>x</sub>
<input type="checkbox"/> T <sub>0</sub>	<input type="checkbox"/> N <sub>0</sub>	<input type="checkbox"/> M <sub>0</sub>	<input type="checkbox"/> T <sub>0</sub>	<input type="checkbox"/> N <sub>0</sub>	<input type="checkbox"/> M <sub>0</sub>
<input type="checkbox"/> T <sub>1</sub>	<input type="checkbox"/> N <sub>1</sub>	<input type="checkbox"/> M <sub>1</sub>	<input type="checkbox"/> T <sub>1</sub>	<input type="checkbox"/> N <sub>1</sub>	<input type="checkbox"/> M <sub>1</sub>
<input type="checkbox"/> T <sub>2</sub>	<input type="checkbox"/> N <sub>2</sub>	<input type="checkbox"/> Unknown	<input type="checkbox"/> T <sub>2</sub>	<input type="checkbox"/> N <sub>2</sub>	<input type="checkbox"/> Unknown
<input type="checkbox"/> T <sub>3</sub>	<input type="checkbox"/> N <sub>3</sub>		<input type="checkbox"/> T <sub>3</sub>	<input type="checkbox"/> N <sub>3</sub>	
<input type="checkbox"/> T <sub>4</sub>			<input type="checkbox"/> T <sub>4</sub>		
<input type="checkbox"/> Unknown	<input type="checkbox"/> Unknown		<input type="checkbox"/> Unknown	<input type="checkbox"/> Unknown	

17. Record staging: only if there are unknown items in the TNM staging (filled in by CTR or equal-qualified staffs)

### Staging

11

11

□ III

□ IV

☐ Unknown

DUKES

☐ A☐ B

☐ C

☐ Unknown

### Brief staging

☐ Local/non-diffusion☐ Partially invasion☐ Distant metastasis☐ Unknown

## Section D: Remarks

18. Remarks: ☐ No ☐ Yes (please clearly illustrate)

[illegible]

**TABLE C4: Summary Form for Colorectal Cancer Treatment Information**

General information													
Date of filling:   2   0       -       -       Screening site ID:       ID of excerpt staff:           Year of investigation:            Objectives: <input type="checkbox"/> First excerpt <input type="checkbox"/> Second excerpt for quality assurance	Signature of preparer:  Signature of quality controller:  <div style="border: 1px solid black; padding: 5px; margin-top: 10px; text-align: center;">             Study ID:  <b>TC</b>                     </div>												
Section A: Initial treatment for primary colorectal cancer													
<div style="text-align: right; margin-bottom: 5px;"><input type="checkbox"/> No</div> 1. Surgical treatment of primary colorectal cancer: <input type="checkbox"/> Yes (Complete the table below using the surgical procedure codes listed) <div style="text-align: right; margin-bottom: 5px;"><input type="checkbox"/> Unknown</div>													
<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr style="background-color: #cccccc;"> <th style="width: 40%; padding: 5px;">Surgical procedure code</th> <th style="width: 60%; padding: 5px;">Date of procedure</th> </tr> </thead> <tbody> <tr><td style="padding: 5px;">         </td><td style="padding: 5px;">  2   0       -       -      </td></tr> <tr><td style="padding: 5px;">         </td><td style="padding: 5px;">  2   0       -       -      </td></tr> <tr><td style="padding: 5px;">         </td><td style="padding: 5px;">  2   0       -       -      </td></tr> <tr><td style="padding: 5px;">         </td><td style="padding: 5px;">  2   0       -       -      </td></tr> <tr><td style="padding: 5px;">         </td><td style="padding: 5px;">  2   0       -       -      </td></tr> </tbody> </table>		Surgical procedure code	Date of procedure		2   0       -       -		2   0       -       -		2   0       -       -		2   0       -       -		2   0       -       -
Surgical procedure code	Date of procedure												
	2   0       -       -												
	2   0       -       -												
	2   0       -       -												
	2   0       -       -												
	2   0       -       -												
<b>Surgical procedure codes</b>													
<table style="width: 100%;"> <tr> <td style="width: 50%; vertical-align: top;">           01 = Local excision (including transanal local excision)            03 = Surgical resection and anastomosis            04 = Surgical resection and ostomy            06 = By-pass operation or palliative resection            07 = Cryotherapy         </td> <td style="width: 50%; vertical-align: top;">           08 = Lymphadenectomy /lymph node sampling            09 = Appendectomy (only for primary appendix tumor)            10 = Ablation            88 = Other: _____         </td> </tr> </table>		01 = Local excision (including transanal local excision) 03 = Surgical resection and anastomosis 04 = Surgical resection and ostomy 06 = By-pass operation or palliative resection 07 = Cryotherapy	08 = Lymphadenectomy /lymph node sampling 09 = Appendectomy (only for primary appendix tumor) 10 = Ablation 88 = Other: _____										
01 = Local excision (including transanal local excision) 03 = Surgical resection and anastomosis 04 = Surgical resection and ostomy 06 = By-pass operation or palliative resection 07 = Cryotherapy	08 = Lymphadenectomy /lymph node sampling 09 = Appendectomy (only for primary appendix tumor) 10 = Ablation 88 = Other: _____												
2. Postoperative residual tumor tissues (filled in by CTR staffs): <div style="float: right; margin-top: 10px;"> <input type="checkbox"/> No  <input type="checkbox"/> Yes—Residual under colonoscopy  <input type="checkbox"/> Yes—Residual visible to the naked eyes  <input type="checkbox"/> Unknown           </div>													
CTR ID: #													

3. Radiotherapy for primary colorectal cancer: Radiotherapy start date:   2   0           -           -	<input type="checkbox"/> No <input type="checkbox"/> Yes (fill in the start date of radiotherapy ) <input type="checkbox"/> Unknown
4. Systemic chemotherapy for primary colorectal cancer: Chemotherapy start date:   2   0           -           -	<input type="checkbox"/> No <input type="checkbox"/> Yes (fill in the start date of chemotherapy ) <input type="checkbox"/> Unknown
5. Other treatments for primary colorectal cancer: Start date:   2   0           -           -	<input type="checkbox"/> No <input type="checkbox"/> Yes (fill in the start date ) <input type="checkbox"/> Unknown
<b>Section B: Assessments/Remarks</b>	
6. Assessments: <input type="checkbox"/> No <input type="checkbox"/> Yes, please clearly illustrate in the table below	
Content	Assessments/Remarks
<b>Section C: Information of doctors and medical institutions</b>	
1. Name of doctor: _____ Name of medical institution: _____ Address: _____ Province _____ City _____ District/County _____ Street/Village No. _____ Postcode: _____ Fax number: _____ Phone number 1: _____ Phone number 2: _____ Medical record number: _____	
2. Name of doctor: _____ Name of medical institution: _____ Address: _____ Province _____ City _____ District/County _____ Street/Village No. _____ Postcode: _____ Fax number: _____ Phone number 1: _____ Phone number 2: _____ Medical record number: _____	

**TABLE C5: Death Certificate Related Group Forms**

### 1. Death certificate tracking record

Study ID: TC _ _ _ _ _ _ _	Signature of investigator:  Signature of quality controller:
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[illegible]



**2. Death certificate materials checklist**

Screening site ID: |\_\_|

Date of subject's death:

| 2 | 0 | | | - | | | - | | |

Signature of preparer:

Signature of quality controller:

Study ID label

**Section A: Cancer confirmation****Please confirm each of the following:**

- ☐ All the Annual Information Update Forms have been received;  
☐ All externally reported cancer cases have been recorded in the Cancer Report Form;  
☐ All suspected cancer cases have been confirmed in the Cancer Diagnosis Form;  
☐ Follow-up information of all screening positive ones has been recorded in the Summary Form for Colorectal Cancer Diagnostic Information;  
☐ All confirmed patients with colorectal cancer have been recorded in the Summary Form for Colorectal Cancer Diagnostic Information.

**Whether this case was selected as an audit case?**☐ Yes (Please complete Section B and Section C)☐ No (Over)**Section B: Medical record certificate****Complete the following table based on the type of tumor diagnosis record**

File type (Please attach the following documents attainable.)	Receipt (√)	Unapplicable (√)	Remarks
Endpoint events			
History of hospitalization/ physical examination			
Surgical report			
Pathological report			
Chemotherapy record			
Radiotherapy record			
Management of multiple tumors			
Abstract of disease history as of discharge			
Summary of disease history as of discharge			
Diagnostic report			
Imageological diagnostic report			
Outpatient record			
Autopsy report			
Clinical trial data			
Advisory report			
Medical record on emergency			
Other diagnostic record			

**Detailed****Illustration:** \_\_\_\_\_

Other treatment record

**Detailed****illustration:** \_\_\_\_\_

**Section C: Edit and mail relevant documents for cancer case confirmation**

Please verify each of the following and fill in the verification record:

- ☐ Subject's identity information has been removed
- ☐ Tumor examination method information has been deleted or not applicable
- ☐ The content related to this study has been deleted or not applicable
- ☐ Group information related to subjects has been deleted or not applicable
- ☐ Study ID code labels have been pasted to each page

Is the medical record complete? ☐ Yes ☐ No

Mailed materials:

- ☐ Folder copy of tumor validation procedure
- ☐ Copy of death certificate
- ☐ Copy of medical history questionnaire
- ☐ Multiple Study ID labels
- ☐ Files have been settled in good order
- ☐ Materials of tumor validation procedure have been turned in

Date of mailing to the Coordination Center: | 2 | 0 | | | - | | | - | | |

Remarks:

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[illegible]

**TABLE D1: Screening Site Information Correction Record**

<div style="border: 1px solid black; padding: 5px;"> <p>Date of filling in:   2   0   _   _   -   _   _   -   _   _  </p> <p>Screening site ID:   _  </p> <p>ID of study staff:   _   _   _   _  </p> </div>			<p>Signature of preparer: _____</p> <p>Signature of quality controller: _____</p> <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> <p style="text-align: center;">Study ID</p> <p>TC   _   _   _   _   _  </p> </div>		
<b>Instructions:</b> Please fill in the form name, program number and correct data for update					
Form name	Program Number	Correction description (please list the correct data)			

Please send the electronic scan version to the Coordination Center, and keep the original one on site.

**TABLE D2: Record of Protocol Deviation Events**

<b>Date of filling in:</b>   2   0   1   _   -   _   _   -   _   _   <b>Screening site ID:</b>   _   <b>ID of study staff:</b>   _   _   _   _   <b>Year of inspection:</b>   _   _   _   _	<b>Signature of preparer:</b> _____ <b>Signature of quality controller:</b> _____ <div style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <b>Study ID:</b>  TC   _   _   _   _   _   </div>
<b>Instructions: Please tick the protocol deviations below and complete the required information in the form based on the deviation type. (Added pages allowed)</b>	

1. Please tick the type of protocol deviation.

- ☐ 01= Invalid random allocation of screening subjects; (skip to Q3a.)
- ☐ 02= More than one random allocation of the screening subjects (**Initial ID:** | \_ | \_ | \_ | \_ | );
- ☐ 03= No completed informed consent from the screening subject before study;
- ☐ 04= Reported or diagnosed cancer of the screening subject before screening;
- ☐ 05= Interference from other screening interventions to the randomized grouped subjects, and please illustrate in details: \_\_\_\_\_
- ☐ 06= Incorrect results reported to the screening subject;
- ☐ 07= Repeated screening;
- ☐ 08= Leakage of protected medical information;
- ☐ 09= Withdrawal from the trial after proceeding to a certain extent due to subjective reasons (detailed description: \_\_\_\_\_) after random allocation and the ID number assignment; (scheduled or completed examinations: \_\_\_\_\_)
- ☐ 10= Others, detailed description (please illustrate any deviations not covered above): \_\_\_\_\_

2a. Detection date of protocol deviation: | 2 | 0 | \_ | \_ | - | \_ | \_ | - | \_ | \_ |

2b. Occurrence date of protocol deviation: | 2 | 0 | \_ | \_ | - | \_ | \_ | - | \_ | \_ |

## 3a. Reasons for invalidation: (please tick all applicable choices)

- ☐ 01= Less than 50 or more than 74 years old;
- ☐ 02= Previous diagnosis of colorectal cancer, if so, then  
Date of colorectal cancer confirmation: | 2 | 0 | | | | - | | | | - | | | |  
☐ Estimated date
- ☐ 03= History of colorectal resection;
- ☐ 04= Any ongoing cancer-related treatments (except for non-melanoma skin cancer)
- ☐ 05= Prior colorectal cancer screening, including colonoscopy, flexible sigmoidoscopy, CT colonography and barium enema within 5 years;
- ☐ 06= Prior history of FOBT and faecal DNA test within 1 year
- ☐ 07= Symptoms of lower gastrointestinal tract disease warranting colonoscopic evaluation, including: 1) more than one episode of rectal bleeding within the past 6 months; 2) documented iron deficiency anaemia; 3) significant documented unintentional weight loss (>10% of baseline weight) over the past 6 months;
- ☐ 08= Other serious diseases (severe lung disease, end-stage renal disease, end-stage liver disease, severe heart failure or recent diagnosis of cancer with the exception of non-melanoma skin cancer);
- ☐ 09= Unsigned informed consent;
- ☐ 10= Withdrawal from the trial before receiving any screening interventions due to subjective reasons (detailed description: \_\_\_\_\_) after random allocation and the ID number assignment.

## 4. Detailed description of protocol deviations:

Please describe the deviations based on the following points: How was the deviation discovered? How did it happen? What was the impact on the subject? What was the handling of this deviation (including contacting with the screening subject, changing the system or process, filling out the form, etc.)? What measures have been taken to prevent the recurrence of such incidents?

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(Added pages allowed)

**TABLE D3: Adverse Events Report Form**

<b>Adverse event related screening date :</b>   2   0       -       -       <b>Date of adverse event occurrence:</b>   2   0       -       -       <b>Screening site ID:</b>       <b>ID of screening staff:</b>           <b>Year of investigation:</b>           <b>Number of visits:</b>	<b>Signature of preparer:</b> _____ <b>Signature of quality controller:</b> _____ <div style="border: 1px solid black; padding: 5px; margin-top: 10px;"> Study ID:  TC           </div>
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- Type of event (please tick all applicable options):
  - ☐ 01=Death;
  - ☐ 02= Life-threatening event;
  - ☐ 03=Hospitalization;
  - ☐ 04= Sustained or apparent disability or loss of ability;
  - ☐ 05= Medical or surgical intervention to prevent the above events;
  - ☐ 06=Other: \_\_\_\_\_
- Please describe the screening subject in adverse events, such as gender, age, etc.  
(Do not involve any identification information):  
\_\_\_\_\_  
\_\_\_\_\_
- Please describe the adverse event briefly:  
\_\_\_\_\_  
\_\_\_\_\_
- Please describe the outcome of the event:  
\_\_\_\_\_  
\_\_\_\_\_
- According to your judgment, is this adverse event related to the study program?
  - ☐ 01=Related;
  - ☐ 02=Possibly related;
  - ☐ 03=Unrelated;
  - ☐ 04=Unknown.
- Do you think it is necessary to amend the informed consent form?
  - ☐ 01=Yes, it is;
  - ☐ 02=Possibly necessary;
  - ☐ 03=Unnecessary;
  - ☐ 04=Unknown

Signature of investigator and date: \_\_\_\_\_.

\* Please attach any forms or documents related to the adverse events.

**TABLE E1: Record of Contact with Screening Subject**

Name of screening subject: _____		Sex: _____		<b>Study ID:</b> TC _ _ _ _ _ _ _
Phone number: _____ / _____				
Address: _____				
The ___ contact Contact date:   2   0       -       -       Communication time (in 24-hour time system):     :	Communication results: <input type="checkbox"/> Unanswered <input type="checkbox"/> Busy <input type="checkbox"/> Callback <input type="checkbox"/> Message <input type="checkbox"/> Completed form <input type="checkbox"/> Rejection <input type="checkbox"/> Other: _____	Reasons for rejection: <input type="checkbox"/> Being busy <input type="checkbox"/> No interest <input type="checkbox"/> Other: _____ _____ _____	Degree of rejection: <input type="checkbox"/> Gentle <input type="checkbox"/> Resolute <input type="checkbox"/> Ill-mannered	Remarks: _____ _____ _____ _____ _____
The ___ contact Contact date:   2   0       -       -       Communication time (in 24-hour time system):     :	Communication results: <input type="checkbox"/> Unanswered <input type="checkbox"/> Busy <input type="checkbox"/> Callback <input type="checkbox"/> Message <input type="checkbox"/> Completed form <input type="checkbox"/> Rejection <input type="checkbox"/> Other: _____	Reasons for rejection: <input type="checkbox"/> Being busy <input type="checkbox"/> No interest <input type="checkbox"/> Other: _____ _____ _____	Degree of rejection: <input type="checkbox"/> Gentle <input type="checkbox"/> Resolute <input type="checkbox"/> Ill-mannered	Remarks: _____ _____ _____ _____ _____

(Added tables allowed)



**TABLE E2: Subject's No-response Record**

For administrative staff		
Date of filling in:   2   0       -       -       Screening site ID:       ID of study staff:           Year of inspection:           Date of last contact:   2   0       -       -	Signature of investigator:  Signature of quality cotroller: <div style="border: 1px solid black; padding: 5px; display: inline-block; margin-left: 20px;"> <b>Study ID:</b>              TC                     </div>	
Status of screening subject	Please tick one answer	Remarks
<b>Out of contact</b> Unable to contact the screening subject.	<input type="checkbox"/>	
<b>Rejection</b> The screening subject refuses to continue to participate in the study, or completely withdraws from the study.	<input type="checkbox"/> <input type="checkbox"/>	
<b>Medical reasons</b> Physiological diseases or cognitive disorder.	<input type="checkbox"/>	
<b>Death</b> Date of death:   2   0       -       -	<input type="checkbox"/>	
<b>Return to the study program</b>	<input type="checkbox"/>	