BMJ Open

Protocol of a randomised controlled trial to assess medical staff's inhalation exposure to infectious particles exhaled by patients during oesophagogastroduodenoscopy and the efficacy of surgical masks in this context

Shengyu Zhang,[1,2] Zhiyu Yan ,[1,2,3] Yuheng Zhang,[1,2] Xi Wu,[1,2] Li Liu,[4,5] Aiming Yang,[1,2] Mengjie Duan [4,5,6]

To cite: Zhang S, Yan Z, Zhang Y, *et al*. Protocol of a randomised controlled trial to assess medical staff's inhalation exposure to infectious particles exhaled by patients during oesophagogastroduodenoscopy and the efficacy of surgical masks in this context. *BMJ Open* 2023;**13**:e068291. doi:10.1136/bmjopen-2022-068291

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-068291).

SZ and ZY contributed equally.

SZ and ZY are joint first authors. AY and MD are joint senior authors.

Received 13 September 2022
Accepted 16 February 2023

For numbered affiliations see end of article.

Correspondence to
Dr Mengjie Duan; mengjie_archi@tsinghua.edu.cn and
Professor Aiming Yang; yangam2020@126.com

ABSTRACT

Background Aerosol-generating procedures such as oesophagogastroduodenoscopy (OGD) result in infectious particles being exhaled by patients. This substantially increases the medical staff's risk of occupational exposure to pathogenic particles via airway inhalation and facial mucosal deposition. Infectious particles are regarded as a key route of transmission of SARS-CoV-2 and, thus, represents a major risk factor for medical staff during the ongoing COVID-19 pandemic. There is a need for quantitative evidence on medical staff's risk of multiroute exposure to infectious particles exhaled by patients during OGD to enable the development of practical, feasible and economical methods of risk-reduction for use in OGD and related procedures. This randomised controlled trial (RCT)—Personal protective EquiPment intervention Trial for oesophagogastroDuodEnoscopy (PEPTIDE)—aims to establish a state-of-the-art protocol for quantifying the multiroute exposure of medical staff to infectious particles exhaled by patients during real OGD procedures.

Method and analysis PEPTIDE will be a prospective, two-arm, RCT using quantitative methods and will be conducted at a tertiary hospital in China. It will enrol 130 participants (65 per group) aged over 18. The intervention will be an anthropomorphic model with realistic respiratory-related morphology and respiratory function that simulates a medical staff member. This model will be used either without or with a surgical mask, depending on the group allocation of a participant, and will be placed beside the participants as they undergo an OGD procedure. The primary outcome will be the anthropomorphic model's airway dosage of the participants' exhaled infectious particles with or without a surgical mask, and the secondary outcome will be the anthropomorphic model's non-surgical mask-covered facial mucosa dosage of the participants' exhaled infectious particles. Analyses will be performed in accordance with the type of data collected (categorical or quantitative data) using SPSS (V.26.0) and RStudio (V.1.3.959).

Ethics and dissemination Ethical approval for this RCT was obtained from the Ethics Committee of Peking Union Medical College Hospital (ZS-3377). All of the potential participants who agree to participate will provide their written informed consent before they are enrolled. The results will be disseminated through presentations at national and international conferences and publications in peer-reviewed journals.

Trial registration number NCT05321056.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This randomised controlled trial study reveals actual occupational exposure during procedures with 130 patients with oesophagogastroduodenoscopy (OGD) general anaesthesia.
⇒ An anthropomorphic model is developed to quantify the airway and facial mucosa exposure of medical staff to patients' exhaled infectious particles.
⇒ A non-toxic fluorescent vitamin, vitamin B_2, will be used to label patients' exhaled infectious particles and their dispersion.
⇒ Efficacy of wearing surgical masks during OGD procedures will be quantitively evaluated.
⇒ Exposure assessment based on such surrogates does not reveal the overall infection risk due to unrealistic aerosolisation and inoculation mechanisms.

INTRODUCTION

Infectious particles are the main vectors for the transmission via air of respiratory viruses via air, which can result in disease outbreaks, epidemics or pandemics.[1–3] SARS-CoV-2, which causes COVID-19, is transmitted via infectious particles exhaled by an infected person being inhaled by another person into the respiratory tract or depositing on another person's eyes, nose or mouth and subsequently entering the body.[4 5] The risks of transmission of SARS-CoV-2 are particularly high in confined spaces,[6] especially in medical

facilities, as these may house patients with COVID-19 or who are asymptomatic carriers of SARS-CoV-2.[7 8]

Oesophagogastroduodenoscopy (OGD) procedures are regarded as aerosol-generating procedures, as they involve instrumental probing of the alimentary tract that typically causes patients to cough, belch, vomit or perform other bodily movements involving the airway.[9–11] Consequently, as viruses or other pathogenic organisms are commonly shed from the airway, infectious particles exhaled by infected patients may have a high microbial load, even if the patients are no longer ill.[12–14] Additionally, patients and medical staff are in very close proximity during OGD procedures, which means there is a high risk of transmission of microbes via air from patients to medical staff during OGD procedures. Furthermore, there is also a high risk of nosocomial transmission of microbes from medical staff to uninfected patients.[15]

Given the above-mentioned risks, various professional gastroenterological organisations, represented by the Asian Pacific Society for Digestive Endoscopy and American Society for Gastrointestinal Endoscopy (ASGE),[16–19] have strongly recommended that medical staff using proper personal protective equipment (PPE), especially surgical mask/N95 respirators or equivalent during OGD procedures. Many regional surveys and the experience of medical centres and specialists have demonstrated that there is widespread support for these recommendations.[9 20–23] In addition, wearing PPE does not affect the objective physiological state of medical staff during OGD procedures or the success of such procedures.[24 25] A few gastroenterologists have reported subjective adverse effects (eg, frustration and fatigue) from the use of PPE during OGD procedures, but these reports were not statistically significant.[26] Many clinicians have also designed various disposable mask sets for patients to prevent the dispersion of their infectious particles during OGD procedures, which further reduces the risk of transmission of microbes via air.[27–31]

However, although the efficacy of surgical mask/N95 respirators or equivalent has been proven based on clinical observations and metrics such as infection rate,[32–34] there are still several medical staff who do not wear a PPE in a real-world endoscopic clinic working scenario. Additionally, objective evidence based on direct indicators and the potential sites of exposure in humans are lacking at this stage, such as the airway and mucous membranes. Notably, although the physical properties, distribution and dispersion processes of infectious particles have been examined,[35–39] the actual exposure of medical staff to infectious particles exhaled by patients during OGD procedures has not been examined, especially for the exposure baseline. Moreover, there is limited knowledge of how effectively PPE protect medical staff from exposure to such infectious particles during OGD procedures.

The development of efficacious and cost-effective methods, such as surgical masks or N95 respirators, to reduce medical staff's risk of occupational exposure to infectious particles exhaled by patients during OGD procedures requires actual exposure baseline to these infectious particles during such procedures. In addition, quantitative data will aid the optimisation of environmental control strategies in clinical settings, and a quantitative investigation will provide practical experience that will be useful in future outbreaks and public health settings.

Objective

The objective of this randomised controlled trial (RCT), denoted Personal protective EquiPment intervention TrIal for oesophagogastroDuodEnoscopy (PEPTIDE), is to quantify the inhalation exposure of medical staff to infectious particles exhaled by participants during OGD procedures and to determine the efficacy of surgical masks in protecting against such exposure.

METHODS AND ANALYSIS

The Standard Protocol Items: Recommendations for Interventional Trials reporting guidelines were used in the development of the protocol for PEPTIDE (online supplemental additional file 1).[40]

Trial design and setting

PEPTIDE is a prospective, two-arm RCT that is underway at Peking Union Medical College Hospital (PUMCH), a tertiary medical centre in Beijing, China. Recruitment began in June 2022 and is expected to end in June 2023, and PEPTIDE is expected to be completed in December 2023.

Participants

Patients who are admitted to the digestive endoscopy centre of PUMCH and have planned to undergo OGD under general anaesthesia will be invited to consider participating in the RCT and screened for eligibility according to the following inclusion criterion and exclusion criteria. All eligible participants will be invited to provide their informed consent to participate (online supplemental additional file 2) and will be allowed sufficient time to ask any questions they may have. Those who are willing to participate will provide written informed consent and will then be enrolled. Subsequently, their basic information will be collected.

Inclusion criterion

1. Patients (aged ≥18) who plan to undergo OGD under general anaesthesia in the digestive endoscopy centre of PUMCH.

Exclusion criteria

1. Patients who have ever been allergic to a saline solution of the non-toxic fluorophore vitamin B_2.
2. Patients who are receiving antitumour therapies.
3. Patients with poor general conditions, such as those with severe cardiopulmonary diseases, coagulation disorders or a total platelet concentration less than 50×10^9/L.

4. Patients with structural pulmonary disease (eg, chronic obstructive pulmonary disease or asthma) or a history of airway or pulmonary surgery.
5. Patients with an intolerance of or contraindications to undergoing OGD under general anaesthesia.

Randomised allocation

The participants will be randomised in an allocation ratio of 1:1 to either the intervention group or the control group. In the measurement stage, those in the intervention group will undergo OGD in the presence of the anthropomorphic model wearing a surgical mask, whereas those in the control group will undergo OGD in the presence of the anthropomorphic model not wearing a surgical mask, respectively. The baseline information of the participants will be collected and used to stratify the participants for further analysis, with stratification based on factors that may influence participants' production capacity of infectious particles and exhalation processes, such as age, sex, body mass index (BMI) and their number of years of smoking. Due to the nature of the intervention, it will not be possible to blind the participants or medical staff performing OGD. However, the researchers who determine the dosage of the inhaled and deposited infectious particles will be blinded.

Intervention and OGD procedures

Considering three factors: (1) PEPTIDE was designed for evaluating the exposure risk of medical staff to infectious particles during OGD in a real-world scenario; (2) the need for accurate measurement of patient-derived aerosols; (3) the protective principle, vitamin B_2 (VB_2) was chosen to substitute as a viral surrogate marker that labels the participants' infectious particles.

A participant will be placed under total intravenous anaesthesia (propofol) without any invasive measures such as tracheal intubation by veteran anaesthesiologists according to the latest guideline of The ASGE.[41] The anaesthetised participant's oxygen mask will then be replaced with a nasal cannula to provide supplemental oxygen, and the participant will be fitted with a mouthguard. The patient's vital signs will be monitored throughout the whole examination by the veteran anaesthesiologist while paying attention to and preventing the patient from aspiration or choking. Subsequently, one fixed clinician, who is blinded to the overall protocol and purpose of this study, will use a needle-removing 2.0 mL syringe to slowly drip 1.5 mL VB_2 in saline solution (2.0 mg/mL, equivalent to 3.0 mg VB_2) into the participant's bilateral buccal mucosa. The whole dripping process will be strictly controlled for 1 min for all participants. The dosage of VB_2 is harmless and not irritating.[42–44] Next, a standard endoscopic examination (approximately 5–10 min) of the participant will be performed by either of the two settled experienced endoscopist, who do not get access to the overall protocol and purpose of this trial, using a GIF-HQ290 scope (Olympus Medical Systems, Tokyo, Japan), according to the participant's condition. Additionally, a series of standard examination requirements will be set, represented by prohibitions of negative pressure suction at the flexible gastroscopy-forward or outward. The anthropomorphic model will be placed at a fixed position beside the participant to simulate an endoscopist. The distance from the oral cavity of the participant to the oral cavity of the anthropomorphic model will be 0.8±0.1 m,[45 46] and the anthropomorphic model will wear or not wear a surgical mask, according to the group allocation of the participant being examined.

The details of the dripping procedure will be recorded by the fixed clinician as well as the OGD procedure (the type of anaesthesia, the dosage of anaesthetics and the contents and time of examination) will be recorded and reported by the anaesthesiologist and endoscopist. In addition, relevant events of the participant, such as sneezing, nausea, vomiting, and snoring and their time of occurrence during the examination, will also be recorded and reported. All medical staff and researchers will be required to wear contact-blocking and droplet-blocking PPE, in line with the national policy. Strict control strategies will be implemented for the number of staff in the closed endoscopic examination room and their movement within the room, to minimise extrinsic and artefactual interference.

Outcomes

Primary outcome

The primary outcome of this RCT will be the anthropomorphic model's airway dosage of the infectious particles exhaled by the participants during OGD procedures with or without a surgical mask, where airway dosages comprise infectious particles deposited in the oral cavity, nasal cavity or oropharynx or inhaled into the small airway.

Secondary outcome

The secondary outcome of this RCT will be the anthropomorphic model's non-surgical mask-covered facial mucosa dosage of the infectious particles exhaled by the participant during OGD procedures. In real-life scenarios, these mucosae are typically the ocular mucosa of the medical staff.

Outcome measures

The sampling duration will be 20±5 min, with the time adjusted according to the duration of a given OGD procedure. The anthropomorphic model will mimic an additional medical staff close to the patients. The anthropomorphic model's airway dosage and non-surgical mask-covered facial mucosa dosage of the infectious particles exhaled by the participants during the procedure will be measured as the cumulative fluorescent particle mass (μg) over the exposure time and will be quantified by fluorspectrophotometry.

Adverse events

The participants in this RCT will undergo OGD under general anaesthesia. The use of 3.0 mg of VB_2 will not create any extra risk to those associated with anaesthesia

and endoscopic procedures. The patients will lie on the left side and the respiration will also face to the side. Dripping VB_2 in bilateral buccal mucosa will not irritate the patients and provoke additional coughing, since VB_2 will not enter the throat and respiratory tract by gravitational driving forces. To ensure that the participants suffer no adverse effects, potential participants with a history of VB_2 allergy or who are taking anticancer therapy will be excluded. Any adverse events (AEs) and serious adverse events (SAEs) occurring throughout the entire examination, namely, during the dripping, the anaesthesia, the OGD procedure and any other steps that prove necessary, will be managed appropriately. In addition, all AEs and SAEs will be recorded and reported. As the anthropomorphic model mimics the human respiratory function and the shape of the human respiratory tract, it may serve as an aural or visual disturbance to participants during the OGD procedure. The probability of such disturbance will be reduced by anaesthesia, which decreases patients' auditory and visual sensitivity. Moreover, if necessary, participants' discomfort will be reduced by, for example, the use of noise reduction devices or the adjustment of the position of the model. We will endeavour to protect participants' privacy and eliminate the risk of data leakage. Accordingly, none of the personal data of the participants will be disclosed, and the analysis results will be anonymised. Thus, no individual participant will be identifiable and data will only be used for statistical analysis.

Equipment and assessors

Anthropomorphic model

We have developed an anthropomorphic model that mimics a medical staff member's inhalation exposure to the infectious particles exhaled by patients during OGD procedures. The anthropomorphic model is based on a male volunteer in his 30s with no history of smoking or lung disease and recapitulates the natural morphological structure of the human face, oropharynx, trachea, G0–G5 bronchi and lung cavity. A small electric heater is used to simulate the thermal plume of the human body. A vacuum pump with an adjustable flow rate is used to simulate the sinusoidal inhalation process of the human body.[47 48] The features of the anthropomorphic model can be referred to figure 1 and our previous study.[45] The external ventilator is connected to the outlets on both sides of the lungs to provide sinusoidal respiratory airflow. The airflow rate will be adjusted to 15.0±1.0 L/min, which is the average inhalation rate of a standing male.

The face, oropharynx, trachea, G0–G5 bronchi and lung cavity are constructed based on 560 two-dimensional orthogonal slices from the head to the diaphragm, which

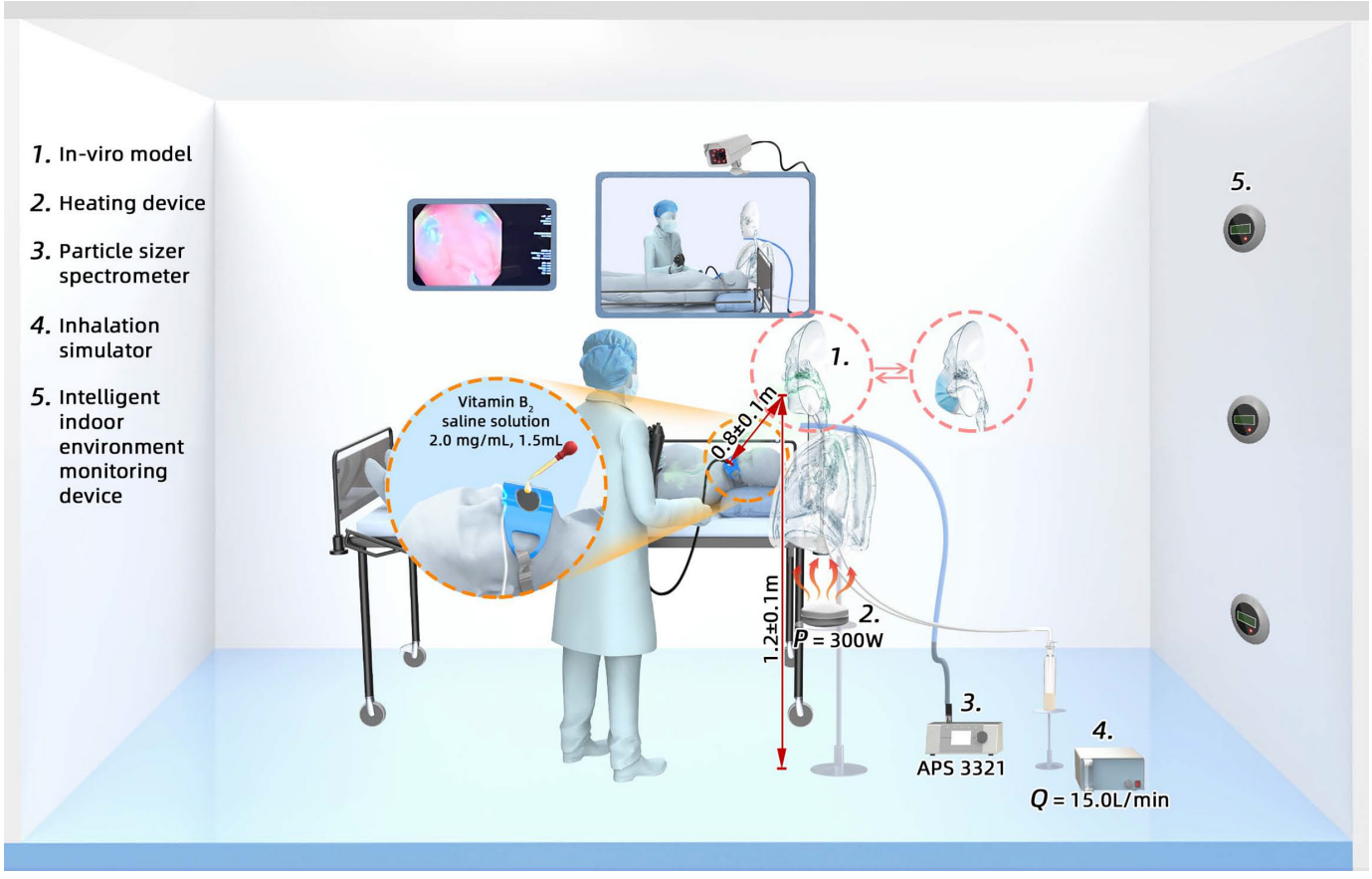

Figure 1 Three-dimensional layout illustration of the real oesophagogastro-duodenoscopy procedure scene that will be implemented in this RCT. RCT, randomised controlled trial.

was obtained by scanning the volunteer using a Philips Brilliance iCT scanner (Koninklijke Philips NV, Netherlands). The slices were processed with commercial software (Intrasense Myrian V1.12, France) to extract and restore the three-dimensional regions of interest. Please see our previous studies for detailed processes and model information.[45 46] The facial mucosal deposition dosage and small airway inhalation dosage to infectious particles can be collected and sampled. Though we can only reconstruct the first five generations of the bronchial due to the limitation of CT scan resolution and 3D print technique, we are still able to measure the total quantity of infectious particles leaving the fifth-generation bronchi or the total quantity of particles arriving at sixth-generation bronchi, that is, the small airway.

RCT environment

The RCT will be conducted in the digestive endoscopy centre of PUMCH, which complies with the national building standards of China (GB) and has passed quality inspections. All of the rooms will be ventilated in a manner similar to that used in our previous study (such as in terms of relative parameters, airflow organisation and the location of the diffusers and purifier).[46] The specific environments of rooms will be adjusted to suit the actual conditions of this RCT.

The location information of a medical staff member, a participant, and the anthropomorphic model is demonstrated in figure 1, which represents a real clinical working scene.

Sampling the inhaled VB_2 and the VB_2 deposited on facial mucosa not covered by a surgical mask

The anthropomorphic model's airway dosage of infectious particles exhaled by the participants during the OGD procedure will be represented by the cumulative mass of VB_2 (in μg) deposited in the oral cavity, nasal cavity and oropharynx as well as inhaled into the small airway. The oral cavity, nasal cavity and oropharynx of the anthropomorphic model will be wiped five times with a sterile swab and then a further three-to-four times with three-to-four additional swabs to recover deposited VB_2. These swabs will be extracted in a collection medium. The anthropomorphic model's small airway dosage of infectious particles exhaled by the participants during the OGD procedure will be represented by the cumulative mass of VB_2 (in μg) penetrating the several-generation bronchi into both lung voids throughout the sampling duration of one OGD procedure. It will be determined by measuring the airborne VB_2 in lung voids and VB_2 deposited on the inner surfaces of both lung voids. Airborne VB_2 will be collected into a liquid-impinging medium in a solution-based sampler (SKC, USA), which will be connected to the outlets of the left and right lung voids. VB_2 deposited on the inner surfaces of both lung voids will be recovered using the same protocol applied to recover VB_2 deposited on the oral cavity, nasal cavity and oropharynx.

The anthropomorphic model's surgical mask-uncovered facial mucosa dosage of infectious particles exhaled by the participants will be represented by the cumulative VB_2 (μg) deposited on the model's eyes, which will be recovered using the same protocol applied to recover VB_2 deposited on the oral cavity, nasal cavity and oropharynx. This method was validated for measuring the dosage of infectious particles exhaled by participants on the facial mucosa of an anthropomorphic model in our previous study.[45]

All dosages will be measured by fluorspectrophotometry on a Fluoro Max-4 fluorophotometer (HORIBA, Japan).

Sample size calculation

Fifteen patients who had provided written informed consent were recruited from 1 July 2022 to 29 July 2022, for preliminary experiments, at which time ethical approval had been obtained and registration of the RCT had been completed. Preliminary experiments were performed with nine of these participants to explore and refine the experimental parameters. In particular, two of these nine participants were treated in accordance with the examination procedure but with 1.5 mL of the saline solution instead of 1.5 mL of a solution of VB_2 in saline. This enabled the elimination of environmental interferences, such as those from participants' saliva, environmental particles and solvents from OGD procedures, as well as the determination of the limit of detection (LOD) of fluorescent signals. Preliminary experiments involving the remaining six participants were used to guide sample size calculations.

As mentioned, given the realistic morphological structure of the anthropomorphic model, the model's airway dosage of infectious particles exhaled by the participants comprises the dosage on the oral cavity, nasal cavity, oropharynx and small airway with/without a surgical mask (filtration efficiency=63.31% based on the results of the preliminary experiments with fifteen patients), and the model's surgical mask-uncovered facial mucosa dosage comprises the dosage on the eyes. These exposures were measured separately, and the highest fluorescent intensity was 567 counts per second (cps). The fluorescent intensities of buffer solutions that will be used in this RCT are less than 100 cps, and, thus, these solutions will not interfere with the fluorescence of VB_2. Accordingly, given the experimental error (comprising a 20% individual difference error, a 2% measurement error and a 10% manual sampling random error), the LOD was determined to be 800 cps, which means that fluorescent intensities of less than 800 cps will be considered as negative and not included in further analyses.

Given that the primary outcome of this trial was concentrated at infectious particles exposure through the airway, represented by the oral cavity, nasal cavity or oropharynx or small airway, the average dosages of the intervention group's and control group's anthropomorphic model in

the above niches were referred to calculate the sample size.

In terms of details, there were two patients in the control group without a surgical mask, one of whom was positive for the oral cavity, nasal cavity and oropharynx with a total of 1.47×10^{-1}μg, while another one was of <LOD in all niches. As regards the intervention group with a surgical mask, there were four patients, one patient's oral cavity, nasal cavity and oropharynx were positive with a total of 1.12×10^{-1}μg, one patient's oropharynx was positive with a total of 7.40×10^{-2}μg, and the remaining two patients were all of <LOD. Therefore, the average airway exposure dosage of the anthropomorphic model in the control group and the intervention group was $(7.36\pm5.20)\times10^{-2}$μg and $(4.66\pm5.60)\times10^{-2}$μg, respectively. Thus, it was calculated (http://powerandsamplesize.com) that to obtain a two-sided confidence level of 95%, a power of 80%, and an allocation ratio of 1:1, a sample size of 59 participants per group (118 in total) will be needed.

As participants have the right to drop out at any time after enrolment and as this RCT's primary and secondary outcomes will not involve follow-up, it was assumed that the dropout rate will be 10%. Thus, the final sample size for each group was set as 65 participants (130 in total) to ensure that this RCT's primary outcome will be statistically and clinically significant. What's more, considering that the estimated experiment time will be 5 hours per participant, the total experiment time will exceed 700 hours when accidental factors are taken into account. Thus, to ensure the feasibility of this study, the number of patients recruited is not further increased.

Statistical analysis

Statistical analysis will be performed using SPSS, V.26.0 (IBM Corporation, Armonk, New York) and RStudio, V.1.3.959 (2009–2020 RStudio, PBC). Descriptive statistics will be used to represent the characteristics of each group and the baseline variables, primary outcomes and secondary outcomes. Categorical variables will be summarised and reported by case number and proportion and compared using Pearson's χ^2 test or Fisher's exact test (according to the characteristics of the data). Quantitative variables will first be subjected to a Shapiro-Wilk test. Then, they will be expressed as means±SDs and subjected to t tests, or as medians with an IQR and subjected to Wilcoxon rank-sum tests, depending on whether the variables are normally distributed. Relative risk will be calculated as needed and will be reported with the accompanying 95% CI and p value.

Additional model-based analyses, represented by multiple linear regression, logistics regression and Cox regression, will be conducted. The response variable will be the airway dosage and the surgical mask-uncovered facial mucosa dosage of the anthropomorphic model, whereas the explanatory variables will be the grouping of participants, the duration and relevant events of the OGD procedure, and baseline variables collected before the procedure, such as age, sex, BMI and the number of years of smoking. The estimated fixed effects will be reported for the model, with the accompanying 95% CI and p values. $p<0.05$ will indicate statistical significance, and $p<0.01$ and $p<0.001$ will indicate higher levels of statistical significance.

PUMCH has many patients on daily basis, and, thus, it is expected that enough potential participants will be identified during the RCT period to ensure that a sufficient sample will be obtained. In addition, we will carefully collect and store each participant's data to minimise the risk of confusion, disclosure or loss. If these problems occur, proxy information or appropriate imputation methods will be considered, if needed.

Data management and monitoring

The randomised group allocation of enrolled participants will be managed by an independent full-time research assistant in the Department of Gastroenterology at PUMCH. The RCT-related data will be collected, entered and managed by another independent full-time research assistant at Tsinghua University. A third dedicated research assistant in the Department of Gastroenterology at PUMCH, independent of the two mentioned above, will periodically perform reconciliation. All of them will be blinded except for the necessary information about their work.

Withdrawals

The participants will be informed that they will be able to withdraw from the RCT at any time without needing to provide a reason.

Ethics and dissemination

Ethical approval for this RCT was received from the Ethics Committee of PUMCH (ZS-3377) in February 2022. The RCT will comply with the clinical trial protocol, the Declaration of Helsinki, and Good Clinical Practice and will be reported according to the Consolidated Standards of Reporting Trials 2010 statement.

The results of this RCT will be disseminated to other digestive endoscopists or other interested parties through presentations at scientific conferences and publications in peer-reviewed journals.

DISCUSSION

Airway inhalation and facial mucosa deposition are major routes of exposure to infectious particles, especially during OGD procedures where medical staff are in close proximity to patients. However, there have been no quantitative assessments of occupational exposure to potentially pathogen-laden infectious particles exhaled by patients during OGD procedures. This RCT aims to quantify the airway dosage and the surgical mask-uncovered facial mucosa dosage of infectious particles by anthropomorphic fluorescent dosimetry to reflect and assess medical staff's occupational infection risk during OGD procedures.

Instead of characterising the emission of infectious particles exhaled by patients, this RCT will focus on determining the exposure of medical staff during OGD, when these patients are under general anaesthesia, by employing an anthropomorphic model, a fluorophore and fluorospectrophotometry. Thus, a direct outcome of this RCT will be a dimensionless exposure ratio, which will be easily derived as the ratio of collected fluorescent dosage from the anthropomorphic model to the original dosage of VB_2 administered to the participants. This exposure ratio will later be indexed to factors such as specific pathogens, detailed procedures, participants' health conditions, environment dilution and air filtration. We regard this approach as a generic methodology for estimating occupational exposure to infectious particles exhaled by patients during OGD procedures, no matter what pathogen the infectious particles carry. To the best of our knowledge, no such methodology has been developed.

There are two main innovations of this RCT. The first innovation is that it will use a non-toxic fluorophore, VB_2, to label participants' exhaled infectious particles and serve as the signal for fluorescent dosimetry. This will enable accurate and reliable data to be obtained with minimal background interference from ambient particles. The second innovation is that the anthropomorphic model has realistic respiratory-related morphology, respiratory function and body plume, so it will simulate a medical staff member to the bast. This will allow the measurement of airway inhalation exposure and facial mucosal deposition exposure to participants' infectious particles without the limitations of real human experiments, which will give this RCT good reproducibility.

Another research focus of this RCT is to perform a quantitative comparison of the dosage of infectious particles from an anthropomorphic model wearing a surgical mask during OGD procedures with this dosage on an anthropomorphic model not wearing a surgical mask during OGD procedures. This will enable scientific evaluation of the protective efficacy of a type of PPE that is commonly used in endoscopy, thereby revealing whether additional masks are required in endoscopic settings. This, together with the results of the models' surgical mask-uncovered facial mucosa dosage of infectious particles exhaled by the participants during OGD procedures, will reveal whether other PPE such as medical safety goggles should be worn by medical staff during such procedures.

The possible limitation of this RCT is that this trial will be conducted at a single centre, due to equipment, management and other practical factors. Besides, no surrogates can mimic the overall transmission process including aerosolisation, emission, dispersion, exposure and inoculation. This RCT cannot reveal the actual aerosolisation process in the respiratory tract, since we do not add VB_2 into the airway surface liquid (ASL). Adding surrogates into ASL demands invasive inhalation procedure that can cause significant discomfort. It is also difficult to estimate the total released amount of inhaled surrogates, which is the key to normalise the consequent exposure. Therefore, this RCT adds the same quantity of VB_2 into the oral cavity of patients after anaesthesia to avoid the variation of viral loads among patients. Since this RCT measures in the same room with the same equipment setups and very similar operation procedures, the fluctuation of observed exposure only consists of the turbulent nature of multiphase airflows and the stochastic exhalation behaviours/responses of patients. At this stage, these factors are assumed to have equal, if not more, contribution to the individual-varying feature of exposure and infection in clinical practices, compared with the contribution of the variation of individual viral load.

The results of this RCT will provide scientific evidence that may facilitate the targeted control and efficacious reduction of medical staff's risk of exposure to infectious particles exhaled by patients during OGD procedures. In addition, the results may aid in the rapid development of safe and effective methods of personal protection from exposure to infectious particles in future public health settings and disease outbreaks.

Author affiliations
[1]Department of Gastroenterology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China
[2]State Key Laboratory of Complex Severe and Rare Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China
[3]4+4 M.D. Program, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China
[4]Department of Building Science, Tsinghua University, Beijing, China
[5]Laboratory of Eco-Planning & Green Building, Ministry of Education, Tsinghua University, Beijing, China
[6]Vanke School of Public Health, Tsinghua University, Beijing, China

Contributors SZ, LL, XW, AY and MD conceived the project and are responsible for designing, adjusting and supervising the RCT. SZ, ZY, LL and MD drafted the RCT protocol. SZ, ZY, YZ and MD are responsible for conducting the RCT and statistical analysis. All of the listed authors listed provided critical reviews of the RCT protocol and approved the final version of this manuscript.

Funding This work is supported by National High Level Hospital Clinical Research Funding (2022-PUMCH-A-075), CAMS Innovation Fund for Medical Sciences (CIFMS, 2021-I2M-1-002), the National Key Clinical Specialty Construction Project (ZK108000) and Tsinghua Vanke School of Public Health Research Fund (2022BH001).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs
Zhiyu Yan http://orcid.org/0000-0003-4673-6489
Mengjie Duan http://orcid.org/0000-0003-4585-1901

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Reported on Page Number/Line Number	Reported on Section/Paragraph
Administrative information				
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	Page 1/Line 3-5	Title page/Paragraph 3
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	Page 4/Line 14-15	Abstract/Paragraph 5
	2b	All items from the World Health Organization Trial Registration Data Set	Page 4/Line 14-15	Abstract/Paragraph 5
Protocol version	3	Date and version identifier	N/A	N/A
Funding	4	Sources and types of financial, material, and other support	Page 29/Line 13-16	Footnotes/Paragraph 4
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	Page 1/Line 7-22	Title page/Paragraph 6-14
	5b	Name and contact information for the trial sponsor	Page 2/Line4-15	Title page/Paragraph 2-13
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	Page 29/Line 5-11	Footnotes/Paragraph 3
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	Page 23/Line 1-8	Data management and monitoring/Paragraph 1-2
Introduction				
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention		
	6b	Explanation for choice of comparators	Page 6/Line 1-34	Introduction/Paragraph 1-4
Objectives	7	Specific objectives or hypotheses	Page 7/Line 13-28	Introduction/Paragraph 5-6
			Page 8/Line 6-11	Introduction/Paragraph 7-8

Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	Page 9/Line 6-11	Method and analysis/ Paragraph 3-4
Methods: Participants, interventions, and outcomes				
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	Page 9/Line 6-11	Method and analysis/ Paragraph 3-4
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	Page 11/Line 8-24	Methods and analysis/Paragraph 9-18
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	Page 12/Line 17-41	Methods and analysis/ Paragraph 22-25
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N/A	N/A
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	Page 14/Line 18-38	Methods and analysis/ Paragraph 33-37
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N/A	N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	Page 13/Line 19-39	Method and analysis/ Paragraph 26-32
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Page 9/Line 5-14; Figure 1	Method and analysis/Paragraph 3-6
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	Page 19/Line 18-53	Method and analysis/ Paragraph 56-59
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	Page 22/Line 10-14	Method and analysis/Paragraph 63
Methods: Assignment of interventions (for controlled trials)				
Allocation:				
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	Page 12/Line 2-14	Method and analysis/ Paragraph 20-21
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	Page 12/Line 2-14	Method and analysis/ Paragraph 20-21

			Page 23/Line 1-8	Data management and monitoring/Paragraph 1-2
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions		
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	Page 12/Line 2-14	Method and analysis/ Paragraph 20-21
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A	N/A
Methods: Data collection, management, and analysis				
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	Page 15/Line 17-81	Method and analysis/ Paragraph 38-55
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	N/A	N/A
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	Page 23/Line 1-8	Data management and monitoring/Paragraph 1-2
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	Page 21/Line 10-32	Method and analysis/ Paragraph 60-62
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)		
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Page 21/Line 10-32 Page 21/Line 10-32	Method and analysis/Paragraph 60-62 Method and analysis/ Paragraph 60-62
Methods: Monitoring				
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	Page 23/Line 1-8	Data management and monitoring/Paragraph 1-2
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial		
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N/A	N/A
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	Page 14/Line 18-38	Methods and analysis/ Paragraph 33-37
			Page 23/Line 1-8	Data management and monitoring/Paragraph 1-2

Ethics and dissemination				
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	Page 23/Line 14-18	Data management and monitoring/Paragraph 5-6
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	N/A	N/A
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	Page 11/Line 6-14	Methods and analysis/Paragraph 8-9
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A	N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	Page 15/Line 12-15	Methods and analysis/ Paragraph 37
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	Page 29/Line 18	Footnotes/Paragraph 5
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	Page 21/Line 15-19	Data management and monitoring/Paragraph 7
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N/A	N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	Page 23/Line 19-23	Data management and monitoring/Paragraph 7
	31b	Authorship eligibility guidelines and any intended use of professional writers		
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N/A	N/A
Appendices			Page 23/Line 19-23	Data management and monitoring/ Paragraph 7
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplemental Additional File 2	Supplemental Additional File 2
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N/A	N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

版本号：1.0

版本日期：2022.02.15

中国医学科学院北京协和医院
临床科研知情同意书

（适用于信息采集，不干预临床诊疗的研究：仅供参考，请研究者根据研究内容修订）

项目名称：胃镜检查产生气溶胶相关的暴露测量及干预措施

研究机构：中国医学科学院北京协和医院

研究负责人：张晟瑜

联系电话：17521679101

_____（受试者）：

您将被邀请参加一项临床研究。您参加本项研究是自愿的，本知情同意书提供给您一些信息以帮助您决定是否参加此项临床研究。请您仔细阅读，如有任何疑问请向负责该项研究的研究者提出。

1. 研究背景与目的：飞沫、气溶胶传播是引发呼吸道传染性疾病大规模暴发的主要传播途径，在患者聚集且封闭的医院诊疗场所，尤其是消化内镜中心等操作区域，气溶胶风险尤为突出。当感染患者或无症状感染者接受消化内镜检查时，咳嗽、嗳气等行为可能排放高浓度气溶胶飞沫，加之医护人员与患者的近距离暴露可能导致潜在的医源性感染。因此，明确消化内镜诊疗时呼出飞沫、气溶胶传播风险，阐明医护人员个体暴露水平，对优化消化内镜诊室环境控制策略，有效降低消化内镜医护人员职业暴露感染风险，具有积极意义。

为进一步探索上述所提出的问题，本研究融合建筑环境与医学领域前沿交叉技术，为明确消化诊室潜在的重点暴露区域，量化医护个体暴露水平，阐明呼出飞沫传播途径的暴露风险，提供科学依据。

2. 研究内容、方法及程序：如果您符合入组条件，并愿意参加本研究，请签署知情同意书。我们将在全麻胃镜操作开始之前，采用医用无毒荧光剂（符合我国每日营养推荐剂量的维生素 B_2 水溶液）标记于您的口腔中，之后按常规步骤进行胃镜检查，全程严格按照各项 SOP 和实验方案进行操作。

维生素 B_2 是一种机体必需的水溶性维生素：它能促进发育和细胞的再生；促使皮肤、指甲、毛发的正常生长；帮助预防和消除口腔内、唇、舌及皮肤的炎症反应；增进视力，减轻眼睛的疲劳等。因其水溶性特征，它不会蓄积在体内，所以时常要以食物或营养补品来补充。它广泛存在于酵母、肝、肾、蛋、奶、大豆中。**本研究在口腔内滴入的维生素 B_2，在胃镜检查结束后可由漱口去除，经**

口腔吸收的微量维生素 B_2 不会对您的健康状态及疾病后续诊治计划产生影响。

3. 预期收益：尽管参加本次研究可能不会给您带来直接益处，但通过对您胃镜操作过程中呼出飞沫→环境迁移→医护暴露过程的监测和研究将有助于明确消化内镜诊疗时环境物表间接接触、呼出飞沫、气溶胶传播风险，阐明医护人员个体暴露水平，对优化消化内镜诊室环境控制策略，有效降低消化内镜医护人员职业暴露感染风险，保护医护人员诊疗安全，为未来医学事业发展做出贡献。

4. 可能风险：该研究所涉及的干预为体外仿生系统（模拟医护）是否佩戴标准个人防护装置，就患者而言除使用医用无毒荧光剂标记口腔外无任何额外处理（入组时已排除维生素 B_2 水溶液过敏者），内镜操作医师均按常规步骤进行胃镜检查，全程严格按照各项 SOP 和实验方案进行操作，**不会对疾病后续诊断和治疗计划产生影响。故理论上不存在可能的风险。**

5. 有关费用和赔偿：本研究基于科学需求，仅涉及采用医用无毒荧光剂（维生素 B_2 水溶液）标记于受检者口腔，不会产生额外的费用，且不会给患者带来额外风险，故不存在赔偿问题。

6. 作为研究受试者，您有以下职责：提供有关自身病史和当前身体状况的真实情况，以及是否有医用无毒荧光剂（维生素 B_2 水溶液）过敏史或潜在过敏风险，是否在接受抗肿瘤药物治疗；告诉研究医生自己在最近是否曾参与其他研究，或目前正参与其他研究。

7. 保密隐私问题：如果您决定参加本项研究，您的隐私非常重要，本临床研究收集到的所有信息都被保密。

在本临床研究中，您的医疗记录档案将保存在有锁的档案柜中，为了保护您的隐私，会分配给您一个研究专用代码，仅通过研究专用代码来识别您。监管部门、伦理审查委员会成员、研究中心的工作人员和申办方的代表将获准会访问可能识别您身份的原始医疗记录等数据（包括直接访问您的原始医疗记录）以确保提供信息的正确性。签署了这份同意书，就表明您允许前述这些组织的人员直接查看您的医疗记录。根据法律规定，您的医疗记录不会公布。

如果研究结果公开发表，您的个人身份将被保密。签署了这份同意书，就表明您同意我们使用您的信息。

为了科学研究之目的，收集的信息可能会发送给其它合作单位或公司，以及监管机构，还可能会将您的信息与研究伙伴分享。与研究伙伴进行分享之前，会在您的信息上标注一个不同于您的研究编号的代码。您的信息中不会带有任何个人身份识别信息。你的信息不会被出售、出借或赠予任何其它独立团体供其自行使用。与申办方合作的研究伙伴不得将您的信息与未获申办方授权的任何人分享。申办方将控制对您的信息进行的操作。

8. 退出：您可以选择不参加本项研究，或者在任何时候通知研究者后退出，您的任何医疗待遇与权益不会因此而受到影响。

9. 伦理原则说明：本项研究的研究人员及工作程序将遵守《赫尔辛基宣言》、

《涉及人的生物医学研究伦理审查办法》、GCP 及中国相关法律法规。

10. 联系：您可随时了解与本研究有关的信息资料和研究进展，如果您有与本研究有关的问题，或您在研究过程中发生了任何不适与损伤，或有关于本项研究参加者权益方面的问题您可以联系电话 17521679101；如果在研究过程中您有关于伦理方面的问题，可以联系伦理委员会办公室，地址：北京市东城区帅府园 1 号；联系电话：010-69156874

知情同意书签字页

在签署这份知情同意书之前，我已经阅读过本知情同意书，研究者已经向我解释过知情同意书的内容。我确认已有充分的时间考虑，我有机会提问而且所有问题均已得到解答。我可以随时向医生咨询更多信息，我可以选择不参加本项研究，或者在任何时候通知研究者后退出，我的任何医疗待遇与权益不会因此而受到影响。

如果我没有遵守研究计划，或者发生了与研究相关的损伤或者有任何其它原因，研究医生可以终止我继续参与本项研究。

我自愿参加本项研究，且已自愿签署这份知情同意书，并与研究者全面合作。

受试者姓名（正楷）：_____

受试者签名：_____ 联系电话_____

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（如适用：如果受试者系无民事行为能力或部分民事行为能力人时则需法定代理人签名。见证人是否需要签字，视情况而定）

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姓名（正楷）：_____

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日期：_____年_____月_____日

我已准确地将这份文本告知受试者，他/她准确地阅读了这份知情同意书，并证明该受试者有机会提出问题。我证明他/她是自愿同意的。

研究者姓名（正楷）：_____

研究者签名：_____研究者联系电话：_____

日期：_____年_____月_____日

胃镜检查产生气溶胶相关的暴露测量及干预措施

附录 1 体外仿生测量系统