



# 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,<sup>1,2</sup> Zhiyu Yan ,<sup>1,2,3</sup> Yuheng Zhang,<sup>1,2</sup> Xi Wu,<sup>1,2</sup> Li Liu,<sup>4,5</sup> Aiming Yang,<sup>1,2</sup> Mengjie Duan <sup>4,5,6</sup>

**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



© Author(s) (or their employer(s)) 2023. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

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

## 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<sub>2</sub>, will be used to label patients' exhaled infectious particles and their dispersion.
- ⇒ Efficacy of wearing surgical masks during OGD procedures will be quantitatively evaluated.
- ⇒ Exposure assessment based on such surrogates does not reveal the overall infection risk due to unrealistic aerosolisation and inoculation mechanisms.

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.

## 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.<sup>1–3</sup> 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.<sup>4–5</sup> The risks of transmission of SARS-CoV-2 are particularly high in confined spaces,<sup>6</sup> especially in medical

facilities, as these may house patients with COVID-19 or who are asymptomatic carriers of SARS-CoV-2.<sup>7,8</sup>

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.<sup>9–11</sup> 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.<sup>12–14</sup> 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.<sup>15</sup>

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),<sup>16–19</sup> 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.<sup>9, 20–23</sup> In addition, wearing PPE does not affect the objective physiological state of medical staff during OGD procedures or the success of such procedures.<sup>24, 25</sup> 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.<sup>26</sup> 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.<sup>27–31</sup>

However, although the efficacy of surgical mask/N95 respirators or equivalent has been proven based on clinical observations and metrics such as infection rate,<sup>32–34</sup> 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,<sup>35–39</sup> 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).<sup>40</sup>

### 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  $\geq 18$ ) 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<sub>2</sub>.
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  $50 \times 10^9/L$ .

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<sub>2</sub> (VB<sub>2</sub>) 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.<sup>41</sup> 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<sub>2</sub> in saline solution (2.0 mg/mL, equivalent to 3.0 mg VB<sub>2</sub>) 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<sub>2</sub> is harmless and not irritating.<sup>42–44</sup> 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  $0.8\pm 0.1$  m,<sup>45 46</sup> 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  $20\pm 5$  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 ( $\mu\text{g}$ ) over the exposure time and will be quantified by fluorospectrophotometry.

#### Adverse events

The participants in this RCT will undergo OGD under general anaesthesia. The use of 3.0 mg of VB<sub>2</sub> 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  $\text{VB}_2$  in bilateral buccal mucosa will not irritate the patients and provoke additional coughing, since  $\text{VB}_2$  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  $\text{VB}_2$  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

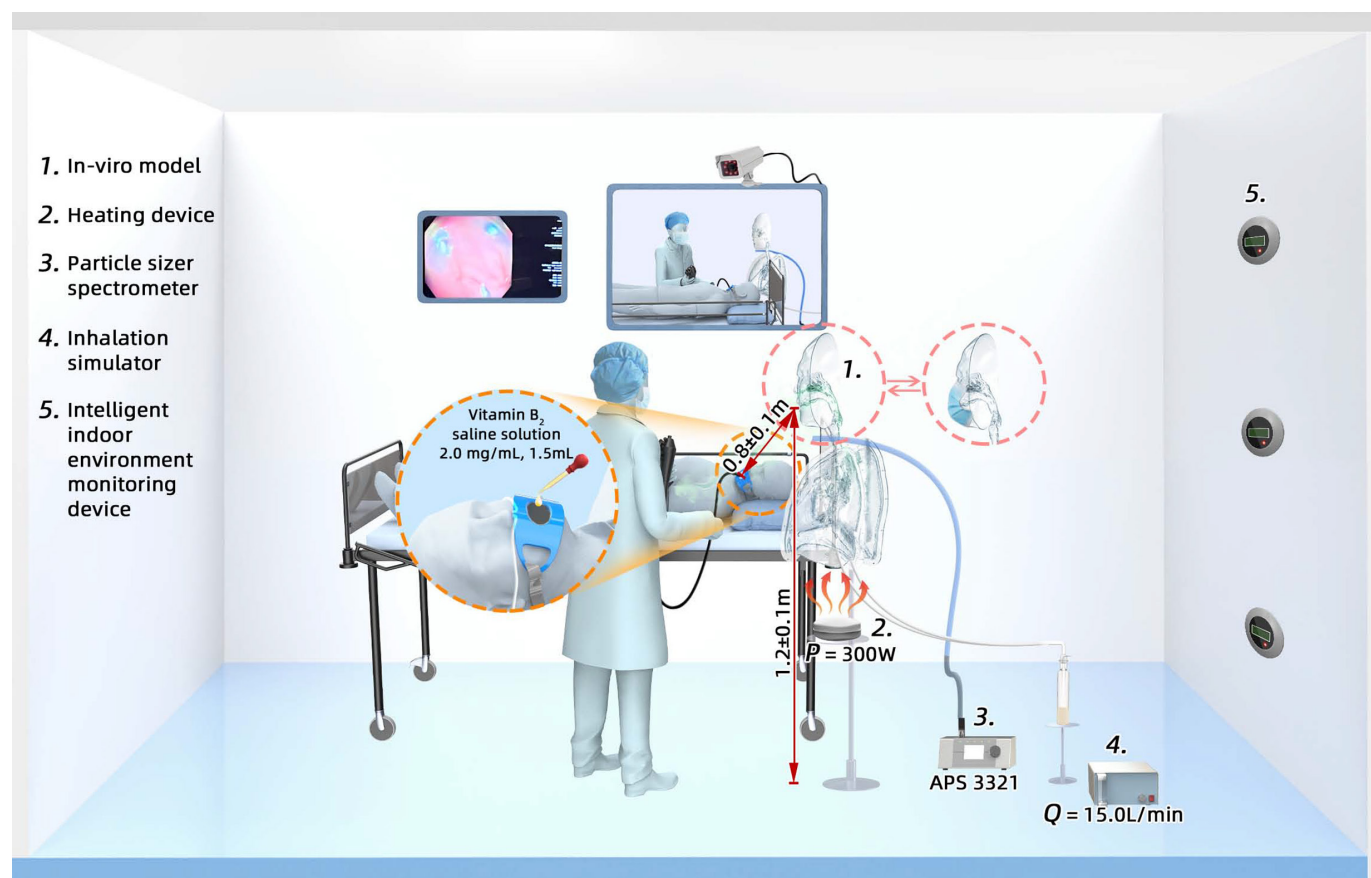
will be anonymised. Thus, no individual participant will be identifiable and data will only be used for statistical analysis.

## 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.<sup>47 48</sup> The features of the anthropomorphic model can be referred to [figure 1](#) and our previous study.<sup>45</sup> 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  $15.0 \pm 1.0 \text{ L/min}$ , 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 VI.12, France) to extract and restore the three-dimensional regions of interest. Please see our previous studies for detailed processes and model information.<sup>45 46</sup> 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).<sup>46</sup> 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<sub>2</sub> and the VB<sub>2</sub> 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<sub>2</sub> (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<sub>2</sub>. 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<sub>2</sub> (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<sub>2</sub> in lung voids and VB<sub>2</sub> deposited on the inner surfaces of both lung voids. Airborne VB<sub>2</sub> 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<sub>2</sub> deposited on the inner surfaces of both lung voids will be recovered using the same protocol applied to recover VB<sub>2</sub> 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<sub>2</sub> (µg) deposited on the model's eyes, which will be recovered using the same protocol applied to recover VB<sub>2</sub> 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.<sup>45</sup>

All dosages will be measured by fluorospectrophotometry 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<sub>2</sub> 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<sub>2</sub>. 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  $1.47 \times 10^{-1} \mu\text{g}$ , 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  $1.12 \times 10^{-1} \mu\text{g}$ , one patient's oropharynx was positive with a total of  $7.40 \times 10^{-2} \mu\text{g}$ , 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  $(7.36 \pm 5.20) \times 10^{-2} \mu\text{g}$  and  $(4.66 \pm 5.60) \times 10^{-2} \mu\text{g}$ , 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  $\chi^2$  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  $\pm$  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<sub>2</sub> 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<sub>2</sub>, 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 best. 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<sub>2</sub> 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<sub>2</sub> 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 multi-phase 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

<sup>1</sup>Department of Gastroenterology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

<sup>2</sup>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

<sup>3</sup>4+4 M.D. Program, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

<sup>4</sup>Department of Building Science, Tsinghua University, Beijing, China

<sup>5</sup>Laboratory of Eco-Planning & Green Building, Ministry of Education, Tsinghua University, Beijing, China

<sup>6</sup>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.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is

properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### ORCID iDs

Zhiyu Yan <http://orcid.org/0000-0003-4673-6489>

Mengjie Duan <http://orcid.org/0000-0003-4585-1901>

#### REFERENCES

- Richard M, van den Brand JMA, Bestebroer TM, et al. Influenza A viruses are transmitted via the air from the nasal respiratory epithelium of ferrets. *Nat Commun* 2020;11:766.
- Yan J, Grantham M, Pantelic J, et al. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a College community. *Proc Natl Acad Sci U S A* 2018;115:1081–6.
- Kutter JS, Spronken MI, Fraaij PL, et al. Transmission routes of respiratory viruses among humans. *Curr Opin Virol* 2018;28:142–51.
- Jayaweera M, Perera H, Gunawardana B, et al. Transmission of COVID-19 virus by droplets and aerosols: a critical review on the unresolved dichotomy. *Environ Res* 2020;188:109819.
- Prevention CDC. How COVID-19 spreads. Available: <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/how-covid-spreads.html> [Accessed 11 Aug 2022].
- Liu Y, Ning Z, Chen Y, et al. Aerodynamic analysis of SARS-cov-2 in two wuhan hospitals. *Nature* 2020;582:557–60.
- Moon J, Ryu BH. Transmission risks of respiratory infectious diseases in various confined spaces: A meta-analysis for future pandemics. *Environ Res* 2021;202:111679.
- Tang JW, Bahnfleth WP, Bluysen PM, et al. Dismantling myths on the airborne transmission of severe acute respiratory syndrome coronavirus-2 (SARS-cov-2). *J Hosp Infect* 2021;110:89–96.
- Zhang S, Wu X, Pan H, et al. Gastrointestinal endoscopy infection control strategy during COVID-19 pandemic: experience from a tertiary medical center in china. *Dig Endosc* 2021;33:577–86.
- Friedrich K, Scholl SG, Beck S, et al. Respiratory complications in outpatient endoscopy with endoscopist-directed sedation. *J Gastrointest Liver Dis* 2014;23:255–9.
- Gregson FKA, Shrimpton AJ, Hamilton F, et al. Identification of the source events for aerosol generation during oesophago-gastro-duodenoscopy. *Gut* 2022;71:871–8.
- Herfst S, Böhringer M, Karo B, et al. Drivers of airborne human-to-human pathogen transmission. *Curr Opin Virol* 2017;22:22–9.
- van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-cov-2 as compared with SARS-cov-1. *N Engl J Med* 2020;382:1564–7.
- Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019-ncov infection from an asymptomatic contact in Germany. *N Engl J Med* 2020;382:970–1.
- Wang M-K, Yue H-Y, Cai J, et al. COVID-19 and the digestive system: a comprehensive review. *World J Clin Cases* 2021;9:3796–813.
- Soetikno R, Teoh AYB, Kaltenbach T, et al. Considerations in performing endoscopy during the COVID-19 pandemic. *Gastrointest Endosc* 2020;92:176–83.
- Gralnek IM, Hassan C, Beilenhoff U, et al. ESGE and ESGENA position statement on gastrointestinal endoscopy and the COVID-19 pandemic. *Endoscopy* 2020;52:483–90.
- Lui RN, Wong SH, Sánchez-Luna SA, et al. Overview of guidance for endoscopy during the coronavirus disease 2019 pandemic. *J Gastroenterol Hepatol* 2020;35:749–59.
- Chiu PWY, Ng SC, Inoue H, et al. Practice of endoscopy during COVID-19 pandemic: position statements of the Asian Pacific Society for digestive endoscopy (APSDE-COVID statements). *Gut* 2020;69:991–6.
- Mariani A, Capurso G, Marasco G, et al. Factors associated with risk of COVID-19 contagion for endoscopy healthcare workers: a survey from the italian society of digestive endoscopy. *Dig Liver Dis* 2021;53:534–9.
- Bor R, Szántó KJ, Fábíán A, et al. Effect of COVID-19 pandemic on workflows and infection prevention strategies of endoscopy units in hungary: a cross-sectional survey. *BMC Gastroenterol* 2021;21:98.
- Say DS, de Lorimier A, Lammers CR, et al. Addendum to: risk stratification and personal protective equipment use in pediatric endoscopy during the COVID-19 outbreak: a single-center protocol. *J Pediatr Gastroenterol Nutr* 2020;70:755–6.
- Zhang S, Wu X, Feng Y, et al. Gi endoscopy infection control strategy after COVID-19 peak: changing strategy for a changing epidemic. *Gastrointest Endosc* 2021;93:530–2.
- Chisholm PR, Smith ZL. Behind the mask: physiologic effects of facial personal protective equipment during endoscopy. *Gastrointest Endosc* 2021;94:169–71.
- Lee JY, Kang YW, Koh M, et al. The impact of face shields on the quality of gastrointestinal endoscopy during the COVID-19 pandemic. *BMC Gastroenterol* 2022;22:38.
- Khalid A, Romutis S, Ibinson J, et al. Acute physiologic effects of N95 respirator use on gastroenterologists performing simulated colonoscopy. *Gastrointest Endosc* 2021;94:160–8.
- Furukawa K, Sato K, Okachi S, et al. Surgical mask designed for endoscopic procedures to prevent the diffusion of droplets. *Acta Gastroenterol Belg* 2021;84:517–9.
- Qadeer MA, Abbas Z. A surgical mask worn by the patient in addition to the barrier box reduces the droplet spray during endoscopy. *J Pak Med Assoc* 2021;71:1703.
- Maehata T, Yasuda H, Kiyokawa H, et al. A novel mask to prevent aerosolized droplet dispersion in endoscopic procedures during the coronavirus disease pandemic. *Medicine (Baltimore)* 2021;100:e26048.
- Akahoshi K, Tamura S, Akahoshi K. Protection against aerosol droplets from the mouth using the mask plus vinyl bag method during esophagogastroduodenoscopy in the coronavirus disease-19 pandemic. *Dig Endosc* 2021;33:e100–1.
- Vahabzadeh-Hagh AM, Patel SH, Stramiello JA, et al. Patient-worn endoscopy mask to protect against viral transmission. *Laryngoscope Investig Otolaryngol* 2022;7:190–6.
- Verbeure W, Geeraerts A, Huang I-H, et al. Aerosol generation and droplet spread during nasogastric intubation in the COVID-19 era. *Gut* 2021;70:2017–9.
- Cheng Y, Ma N, Witt C, et al. Face masks effectively limit the probability of SARS-cov-2 transmission. *Science* 2021;372:1439–43.
- Tan X, Guo J, Chen Z, et al. Systematic review and meta-analysis of clinical outcomes of COVID-19 patients undergoing gastrointestinal endoscopy. *Therap Adv Gastroenterol* 2021;14:17562848211042185.
- Sharma D, Campiti VJ, Ye MJ, et al. Aerosol generation during routine rhinologic surgeries and in-office procedures. *Laryngoscope Investig Otolaryngol* 2021;6:49–57.
- Endo H, Koike T, Obara N, et al. Commercially available novel device to prevent the diffusion of droplets from subjects undergoing esophagogastroduodenoscopy: a pilot study with its prototype. *DEN Open* 2022;2:e36.
- Workman AD, Welling DB, Carter BS, et al. Endonasal instrumentation and aerosolization risk in the era of COVID-19: simulation, literature review, and proposed mitigation strategies. *Int Forum Allergy Rhinol* 2020;10:798–805.
- Sim ES, Dharmarajan H, Boorgu DSSK, et al. Novel use of vitamin B2 as a fluorescent tracer in aerosol and droplet contamination models in otolaryngology. *Ann Otol Rhinol Laryngol* 2021;130:280–5.
- Phillips F, Crowley J, Warburton S, et al. Aerosol and droplet generation in upper and lower gi endoscopy: whole procedure and event-based analysis. *Gastrointest Endosc* 2022;96:603–11.
- Chan A-W, Tetzlaff JM, Göttsche PC, et al. Spirit 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586.
- Early DS, Lightdale JR, et al. ASGE Standards of Practice Committee. Guidelines for sedation and anesthesia in gi endoscopy. *Gastrointest Endosc* 2018;87:327–37.
- RiboflavinDB. *Encyclopedia of toxicology*. Third Edition. Oxford: Academic Press, 2014: 128–9.
- Ding S, Lee JS, Mohamed MA, et al. Infection risk of SARS-cov-2 in a dining setting: deposited droplets and aerosols. *Build Environ* 2022;213:108888.
- Hachem M, Loizeau M, Saleh N, et al. Short-term association of in-vehicle ultrafine particles and black carbon concentrations with respiratory health in parisian TAXI drivers. *Environ Int* 2021;147:106346.
- Duan M, Liu L, Da G, et al. Measuring the administered dose of particles on the facial mucosa of a realistic human model. *Indoor Air* 2020;30:108–16.
- Duan M, Wang L, Meng X, et al. Negative ion purifier effects on indoor particulate dosage to small airways. *Int J Environ Res Public Health* 2021;19:264.
- Tang JW, Liebner TJ, Craven BA, et al. A schlieren optical study of the human cough with and without wearing masks for aerosol infection control. *J R Soc Interface* 2009;6 Suppl 6(Suppl 6):S727–36.
- Tang JW, Nicolle ADG, Pantelic J, et al. Qualitative real-time Schlieren and shadowgraph imaging of human exhaled airflows: an aid to aerosol infection control. *PLoS One* 2011;6:e21392.