



Original research

# Identification of the source events for aerosol generation during oesophago-gastro-duodenoscopy

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## ABSTRACT

**Objective** To determine if oesophago-gastro-duodenoscopy (OGD) generates increased levels of aerosol in conscious patients and identify the source events.

**Design** A prospective, environmental aerosol monitoring study, undertaken in an ultraclean environment, on patients undergoing OGD. Sampling was performed 20 cm away from the patient's mouth using an optical particle sizer. Aerosol levels during OGD were compared with tidal breathing and voluntary coughs within subject.

**Results** Patients undergoing bariatric surgical assessment were recruited (mean body mass index 44 and mean age 40 years, n=15). A low background particle concentration in theatres (3 L<sup>-1</sup>) enabled detection of aerosol generation by tidal breathing (mean particle concentration 118 L<sup>-1</sup>). Aerosol recording during OGD showed an average particle number concentration of 595 L<sup>-1</sup> with a wide range (3–4320 L<sup>-1</sup>). Bioaerosol-generating events, namely, coughing or burping, were common. Coughing was evoked in 60% of the endoscopies, with a greater peak concentration and a greater total number of sampled particles than the patient's reference voluntary coughs (11 710 vs 2320 L<sup>-1</sup> and 780 vs 191 particles, n=9 and p=0.008). Endoscopies with coughs generated a higher level of aerosol than tidal breathing, whereas those without coughs were not different to the background. Burps also generated increased aerosol concentration, similar to those recorded during voluntary coughs. The insertion and removal of the endoscope were not aerosol generating unless a cough was triggered.

**Conclusion** Coughing evoked during OGD is the main source of the increased aerosol levels, and therefore, OGD should be regarded as a procedure with high risk of producing respiratory aerosols. OGD should be conducted with airborne personal protective equipment and appropriate precautions in those patients who are at risk of having COVID-19 or other respiratory pathogens.

## INTRODUCTION

The COVID-19 pandemic, caused by SARS-CoV-2, has led to dramatic and widespread changes in the way hospital medicine is practised. SARS-CoV-2 has the potential to be spread by three main routes: droplet, contact and airborne. The extent of airborne transmission of SARS-CoV-2 remains debated<sup>1–4</sup> but is of increasing concern especially

## Significance of this study

### What is already known about this subject?

► Oesophago-gastro-duodenoscopy (OGD) is currently classified as an aerosol-generating procedure. Recent aerosol sampling studies have demonstrated increased particle concentration above the background during OGD but not identified the source events.

### What are the new findings?

► An uneventful OGD (without coughing or burping) does not generate aerosol above that associated with tidal breathing. More specifically, insertion and removal of an endoscope for OGD does not generate an increase in aerosol concentration. However, the process of OGD frequently triggers coughs in conscious patients. Such OGD-evoked coughs generate higher aerosol concentration than volitional coughs, and the resultant plumes of airborne particles are likely to be associated with an increased risk of transmission of respiratory pathogens. Our study puts the aerosol generated during endoscopy into a meaningful context of normal respiratory events and identifies the index risk events.

### How might it impact on clinical practice in the foreseeable future?

► OGD-evoked coughs are common. Therefore, OGD should be treated as having a high risk of aerosol generation and should be conducted with airborne personal protective equipment and appropriate precautions in those patients who are at risk of having COVID-19 or other respiratory pathogens. Strategies to reduce coughing and eructation would reduce aerosol generation.

with the advent of new strains of the virus (eg, B.1.1.7) that have increased transmissibility.<sup>5–6</sup> Infectious respiratory aerosols are considered by the WHO as being composed of particles <5 μm in diameter,<sup>7</sup> which remain in suspension in the air for many minutes or hours, potentially leading to distant transport of viral particles.<sup>8–9</sup> Importantly, particles of this dimension are respirable, enabling

deposition deep within the human respiratory tract leading to transmission of disease.<sup>8</sup>

A number of medical interventions have been designated 'aerosol-generating procedures' (AGPs). These AGPs are considered to carry the highest risk of airborne transmission of respiratory pathogens to healthcare workers. The interventions currently categorised as AGPs are based predominantly on epidemiological data from the 2003 SARS-CoV-1 epidemic.<sup>10–11</sup> The WHO list of AGPs has been adopted or adapted by many national healthcare organisations such as the Centers for Disease Control and Prevention<sup>12</sup> and Public Health England.<sup>13</sup> Oesophago-gastro-duodenoscopy (OGD) is classified as an AGP, and this designation has led to the development of joint guidelines for safe endoscopy by the gastroenterological societies in the UK,<sup>14</sup> Europe<sup>15</sup> and the USA.<sup>16</sup>

Current national and international guidance recommends the use of airborne precaution personal protective equipment (PPE) when undertaking AGPs, which includes the use of respirators (eg, FFP3 or N95 masks). Other recommendations include performing AGPs in a closed space with good ventilation<sup>17–18</sup> and allowing a sufficient 'fallow' interval such that aerosol may disperse after the procedure.<sup>19</sup> These precautions inevitably slow the turnover within an operating room or procedural suite, and the wearing of PPE may impact on the quality of care delivered due to physical and communication difficulties.

The categorisation of OGD as an AGP was not based on evidence demonstrating aerosol generation from this intervention, nor from being associated with an increased incidence of SARS-CoV-2 transmission to healthcare workers conducting the procedures. Recent work directly measuring aerosol levels in the clinical environment has questioned the validity of inclusion of several procedures defined as 'aerosol generating' including tracheal intubation and extubation<sup>20</sup>, percutaneous tracheostomy<sup>21</sup> and respiratory supportive treatments such as continuous positive airway pressure delivered via a facemask.<sup>22–24</sup>

Two recent proof-of-concept studies reported increased levels of aerosol measured during OGD and concluded that the procedure is an AGP.<sup>25–26</sup> However, these studies have been unable to definitively identify the specific source event responsible for the aerosol generation (ie, endoscope insertion/removal, coughing, deep breathing, GI eructation or retching) nor were they able to place the findings in the context of the risk of aerosol generation by natural respiratory events (tidal breathing and coughing). This is important as respiratory events such as coughing, speaking and breathing have been shown to generate measurable concentrations of aerosol.<sup>27–31</sup> To strengthen the evidence base underlying designation of AGPs and the rationale for stringent airborne transmission-based precautions, it is essential to determine how much aerosol these procedures generate compared with natural respiratory events. We therefore quantitated the extent to which OGD, performed in conscious patients, generates aerosols and compared this to the aerosol generated by coughing and tidal breathing in the same patients in an ultraclean ventilation (UCV) operating theatre.

## METHODS

### Ethics

A prospective environmental sampling study was undertaken to measure the amount and size distribution of particles generated by conscious patients undergoing OGD in a UK hospital (North Bristol NHS Trust).

### Selection of patients

Study participants were over 18 years of age and undergoing diagnostic OGD as part of a bariatric surgical assessment. The indication for endoscopy was in line with the International Federation for the Surgery of Obesity and Metabolic Disorders Position Statement,<sup>32</sup> which recommends consideration of OGD in patients without upper GI symptoms prior to bariatric and metabolic surgery procedures. All patients had self-isolated for 2 weeks, had a negative SARS-CoV-2 PCR test in the 72 hours before admission and gave written informed consent before entry to the study.

### Study conduct

The objective of the study was to measure aerosol generated during the routine conduct of OGD. To sensitively detect aerosols generated by either natural respiratory events or AGPs, the measurements must be undertaken in an environment where background airborne particle concentrations are very low. Therefore, recordings were undertaken in operating theatres with an UCV system (Exflow 32, Howorth Air Technology, Farnworth, UK) with high-efficiency particulate air (HEPA) filtration. The UCV system provides an environment that is both ultraclean and highly ventilated. We have previously demonstrated that the UCV ensures a very low background particle concentration, enabling detection of aerosols generated by natural respiratory events and AGPs.<sup>20–21–31–33</sup>

The UCV was placed in standby mode during recordings to minimise any effect the high air change rate may have on particle detection.<sup>33</sup> When fully operational, the UCV system generates a 'surgical canopy' of clean air, which is directed vertically downwards over the operating table within a perimeter delineated by markings on the floor. The air handling unit runs at 50 Hz to generate this ultraclean zone that results in 500–600 air changes per hour within the perimeter. When the system is placed in 'standby mode', the frequency of the inverter in the air handling unit is reduced to 25 Hz, and the 'surgical canopy' of constrained laminar airflow is lost; this reduces the number of air changes to 25 per hour (equivalent to a standard operating theatre). The air flow velocity is 0.25 m s<sup>-1</sup> at 1 m above the ground. This still provides an ultraclean environment (minimising interference from background aerosol)<sup>33</sup> but without the high number of air changes, ensuring any findings are generalisable to more typical operating theatre settings.

All healthcare workers, and members of the investigating team, wore contact and droplet precaution PPE in line with both trust, and national policy. The number of staff in the room and their movement were kept to a minimum throughout the study to minimise extrinsic and artefactual aerosol generation.

A portable Optical Particle Sizer (OPS, Model 3330, TSI, Shoreview, Minnesota, USA) was used. The OPS samples air at 1 L min<sup>-1</sup> and detects particles by laser optical scattering, reporting the particle number concentration and size distribution within the range 300 nm to 10 µm diameter, with a sampling bin width of 1 s. All air sampled was via a 3D-printed funnel (formed of polylactic acid on a RAISE3D Pro2 Printer, 3DGBIRE, Chorley, UK) with a maximum diameter of 150 mm and cone height of 90 mm with a 10 mm exit port. Conductive silicone sampling tubing (3001788, TSI, 1 m length and 4.8 mm internal diameter) connected the funnel to the OPS. The silicone tube had an internal volume of 72.5 mL giving a transit lag between the funnel and the particle sizer (with a flow of 1 L min<sup>-1</sup>) of 4.3 s, which was taken into account in the time registration of measurements. In previous work, we have established that the

transmission sampling loss of particles  $<5\ \mu\text{m}$  diameter with this set up is  $<10\%$ .<sup>31</sup> It should be noted that we cannot report the absolute number of particles generated, only the number sampled and detected, recognising that we do not sample all of the air from the activity into the OPS instrument.

Reference aerosol generation was measured in each patient before endoscopy with the patient positioned supine on the operating table in the theatre. The sampling funnel was handheld by the investigator approximately 20 cm in front and directed towards the patient's face. The reference sequences consisted of 1 min quiet tidal breathing, followed by three maximal voluntary coughs at 30 s intervals, with tidal breathing in between. Background aerosol was then measured with the funnel at 1 m distance, facing away from the patient (and any other staff) but still within the central area of the UCV system while the patient was prepared for the endoscopy as below.

All patients had topical anaesthesia of their oropharynx with lidocaine 10% (Xylocaine, 50 mL/500 spray, AstraZeneca, Sweden). The OGD was performed in the left lateral position, with conscious sedation achieved with intravenous midazolam as necessary by the endoscopist, according to their normal practice. A mouthguard was inserted prior to insertion of the endoscope (8.9 mm GIF-H290 Video Gastrointestinal Scope with EVIS X1 CV-1500 Video System, Olympus, Tokyo, Japan).

Aerosol generation during endoscopy was measured with the sampling funnel, handheld 20 cm from the patient's mouth. This enabled insertion of the endoscope between the funnel and the mouth. The aerosol generated during OGD was analysed for all periods between endoscope insertion through the mouthguard until endoscope removal. These periods were aggregated for those patients where more than one endoscope insertion was undertaken. Aerosol sampling commenced for reference recordings, undertaken prior to initial endoscope insertion, and was continuous until after final endoscope removal. All events of significance were timestamped (ie, endoscope insertion, endoscope removal, coughs burping). Cough events (both voluntary and evoked during endoscopy) were averaged within subject and then aggregated across the whole group.

Data were exported from the OPS, processed in the TSI Aerosol Instrument Manager software and analysed in OriginPro (OriginLab, Northampton, Massachusetts, USA) and Prism V.8 (GraphPad, San Diego, California, USA). We report the sampled

mean aerosol concentration as well as the peak concentration over 1 s sampling time, reported as mean (SD). We used paired or unpaired t-tests or Mann-Witney and Wilcoxon tests to conduct statistical comparisons as appropriate. The criterion for statistical significance was set at  $p < 0.05$ .

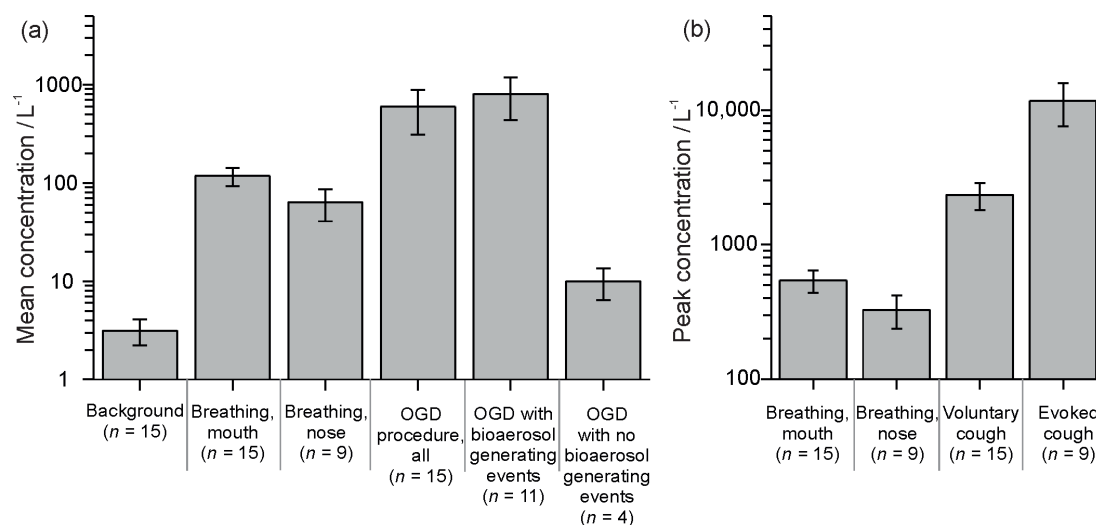
## RESULTS

Fifteen patients were recruited: fourteen were being assessed before bariatric surgery, and one patient attended for assessment 2 years after gastric bypass surgery. There were two men and thirteen women with a mean body mass index (BMI) of  $46 \pm 9.3\ \text{kg/m}^2$  and an average age of 42 years old (range 21–75). Four patients requested and received additional conscious sedation with endoscopist-administered midazolam.

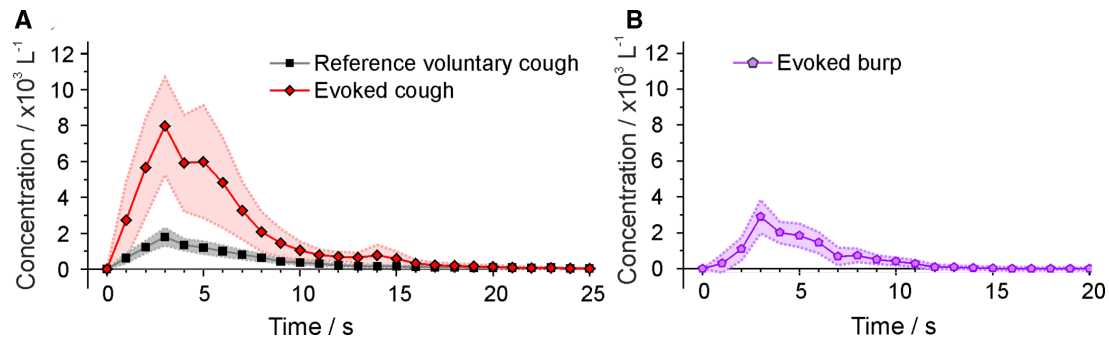
Background sampling showed the air was very clean with a mean aerosol number concentrations, referred to below simply as the *concentration*, of  $3.1\ (3.7)\ \text{particles L}^{-1}$  (corresponding to approximately three particles detected each minute of sampling). The patient's tidal breathing, via the mouth, generated a mean particle concentration of  $118\ (97.2)\ \text{L}^{-1}$  and an average peak particle concentration of  $540\ (410)\ \text{L}^{-1}$  ( $n=15$  patients) (figure 1). In nine patients, a further minute of nasal breathing was recorded; this generated a mean particle concentration of  $63.5\ (72.0)\ \text{L}^{-1}$  and a peak particle concentration of  $327\ (283)\ \text{L}^{-1}$  ( $n=9$ ). Nasal breathing produced a lower aerosol concentration than mouth breathing ( $p=0.008$ , Wilcoxon test).

The expulsive phase of a cough typically lasts less than 1 s,<sup>34</sup> and the aerosol concentration rises rapidly to a sharp peak, with a subsequent decay as the remaining aerosol reaches the sampling funnel, dissipates and becomes diluted by clean background air (figure 2). The reference voluntary coughs for the 15 patients each generated an aerosol concentration profile clearly detectable above the baseline with a mean peak concentration of  $2330\ (2120)\ \text{L}^{-1}$ , an average total number of particles detected per cough of 192 (183) and mean duration of 19.8 (5.8) s.

The mean aerosol particle concentration measured during endoscopy was  $595\ (1110)\ \text{L}^{-1}$  ( $n=15$ , figure 1A), and the average duration of endoscopy was 222 s (range 129–457 s). This aerosol concentration was well above background levels but was not significantly higher than the level of aerosol measured during mouth breathing (vs  $118\ \text{L}^{-1}$ ,  $p=0.17$ , Wilcoxon test).



**Figure 1** (A) Mean particle concentrations and (B) peak particle concentrations generated during the recording protocol. Note log scale for concentrations plotted as mean  $\pm$  SEM. OGD, oesophago-gastro-duodenoscopy.



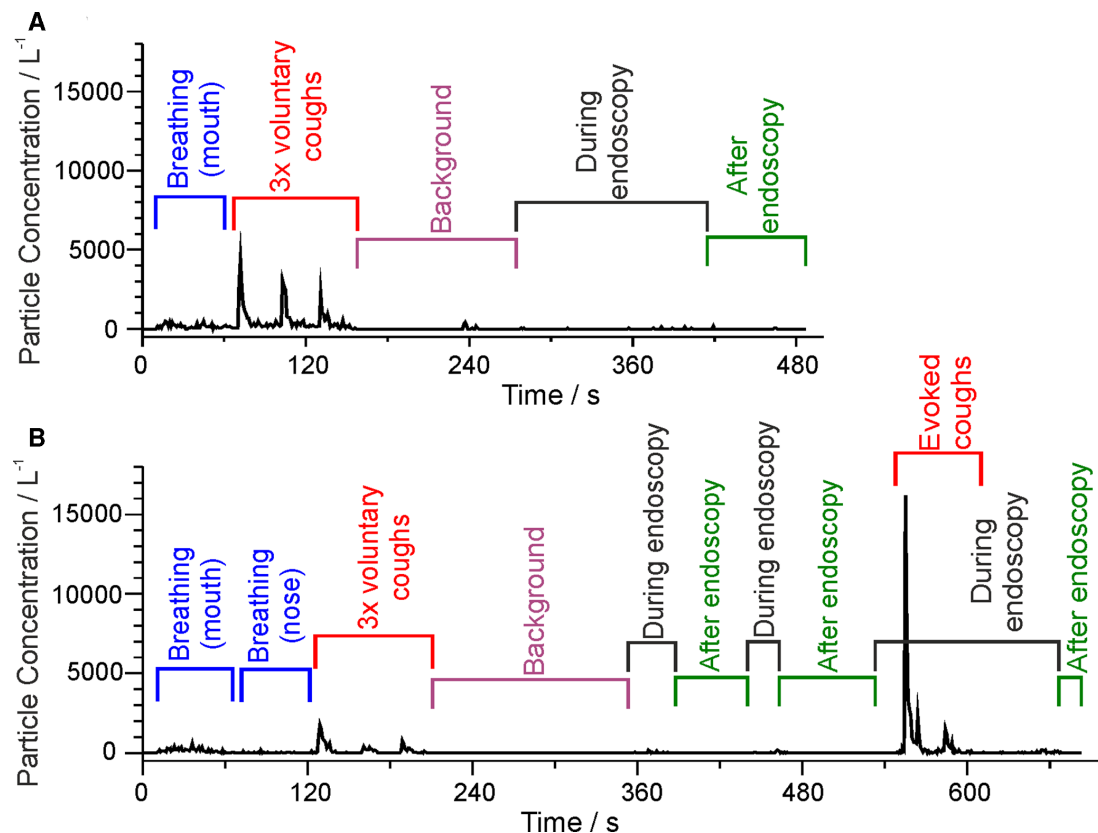
**Figure 2** Mean particle concentration sampled during reference voluntary coughs (n=15 patients) overlaid with those for coughs evoked during oesophago-gastro-duodenoscopy (OGD) (n=9 patients) and burps observed during OGD (n=4 patients). The shaded region represents SEM.

We noted that there were a very large range of average aerosol concentrations between endoscopy sessions from 3 L<sup>-1</sup> (indistinguishable from the background—see figure 3A) to 4320 L<sup>-1</sup> (figure 3B). Coughs were frequently evoked during the endoscopy (figure 3B; 9/15 subjects were observed to cough—with a median of four coughs (range 1–10)). Likewise, burps were induced during some procedures (figure 2B; 4/15 subjects burped—median of two burps per endoscopy (range 1–4)).

The OGD-evoked coughs generated high concentrations of aerosol (figures 2A and 3B) with a mean peak concentration of 11 710 (13 700) L<sup>-1</sup> and total number of particles detected per cough of 780 (1010). The total number of particles from evoked coughs was significantly greater than the volitional coughs recorded from the same patients (780 vs 191, n=9, p=0.008, Wilcoxon test), and the peak mass concentration was

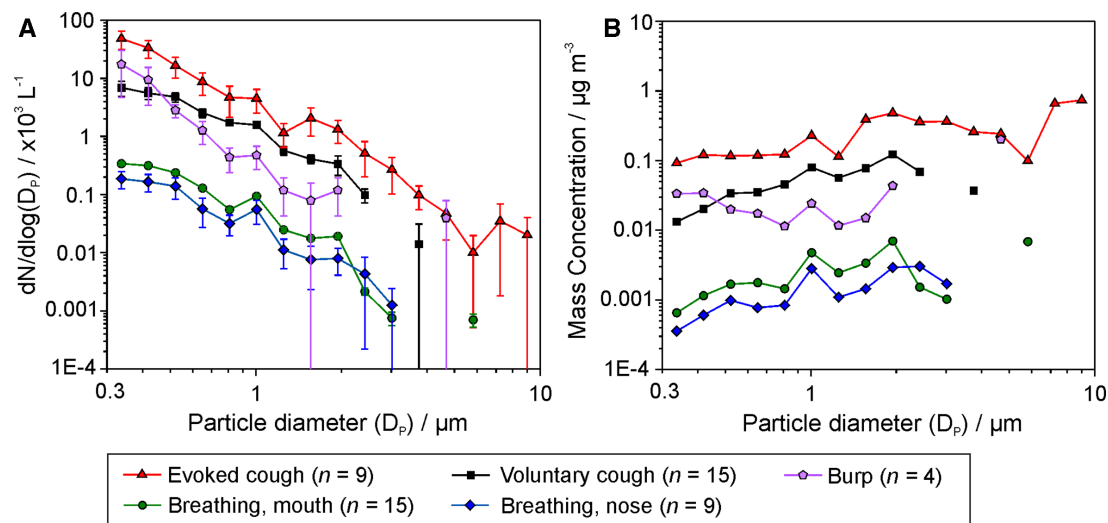
higher (4.51 vs 0.54 μg/m<sup>3</sup>, p=0.008, Wilcoxon test). Similarly, the peak particle concentration was greater for evoked versus volitional coughs (11 710 vs 2320 L<sup>-1</sup>, p=0.008, Wilcoxon test). The profile of the particle concentration generated by evoked coughs remained detectable above the baseline for a mean duration of 14.5 (4.8) s. Analysis of the size distribution of these evoked coughs showed them to have a similar profile to volitional coughs, reported as number of concentration distribution across the size-resolved bins of the OPS, but with an increase in the total numbers of particles in each size bin (figure 4).

Burps observed during OGD procedures generated a mean peak concentration of 3060 (3830) L<sup>-1</sup> and a total number of particles detected per burp of 205 (280). There was no significant difference between the peak particle concentration or total number of detected particles of a voluntary cough and burp by



**Figure 3** Continuous time series of aerosol detected during respiratory manoeuvres (tidal breathing and voluntary coughs) followed after a period of background monitoring by OGD. (A) Uneventful oesophago-gastro-duodenoscopy (OGD) without any significant aerosol generation. (B) A more challenging endoscopy requiring multiple attempts at scope insertion that triggered coughing during the final episode.





**Figure 4** (A) Particle size distribution of the events.  $dN/d\log(D_p)$  is the concentration sampled within each bin normalised by the logarithm of the bin width. The error bars represent the SE of the mean. (B) The size distribution of the average aerosol concentration generated by each activity represented in terms of a mass concentration, calculated assuming unit density.

the same patient. Analysis of the particle size distribution of these evoked burps showed them to have a different profile to coughs, with a decrease in the total numbers of particles in the size range between 0.5 and 1.5  $\mu m$  (figure 4).

As an evoked cough or a burp had a large effect on the particle concentration, our subsequent analysis split the patients into those who had such ‘bioaerosol-generating events’ (BGEs) versus those who did not. The mean aerosol number concentration sampled during the eleven endoscopies with BGEs was higher than that recorded during the four endoscopies where no cough or burp was triggered (808 (1240)  $L^{-1}$  vs 10.0 (7.2)  $L^{-1}$ , Mann-Whitney test,  $p=0.0015$ ). When these transient and discrete coughing or burping events were excluded from the analysis, the mean particle concentration during the rest of the endoscopy was 31.4 (33.9)  $L^{-1}$  identifying the discrete BGEs as being responsible for the overall elevation in aerosol during the procedure.

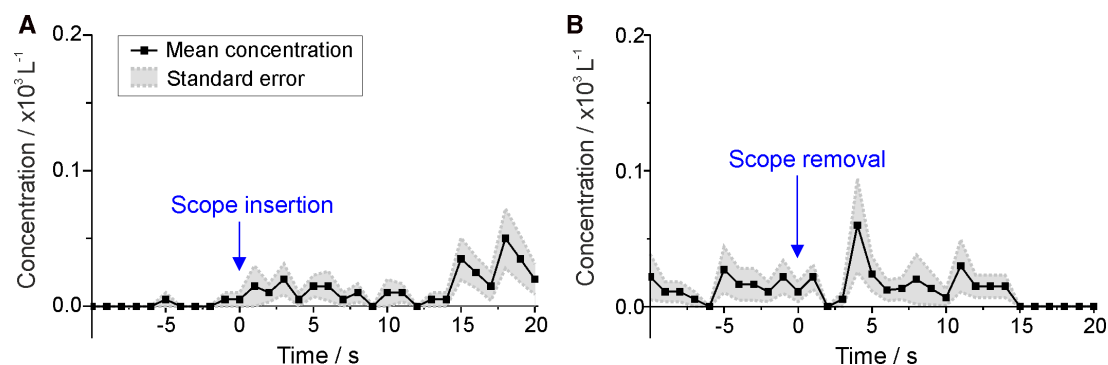
A focused analysis of aerosol concentration fluctuations during a 30s sampling window surrounding endoscope insertion ( $n=12$ ) and removal ( $n=11$ ) (starting 10s prior to insertion or removal), excluding those that triggered BGEs, showed a low concentration of aerosol that was not significantly different to the background and was less than both tidal breathing and voluntary

coughs (figure 5). No other significant aerosol-generating events were identified during the conduct of the OGDs.

## DISCUSSION

We have measured aerosol generation in patients undergoing OGD. In the patients who coughed during the procedure (60%), very high particle concentrations were detected—around fivefold higher than those seen during volitional coughs. This suggests that OGD meets the criterion for being a high-risk procedure for generating aerosol in those patients in whom endoscopy evokes a cough. This is consistent with the findings of recent studies that also concluded that OGD was associated with increased aerosol generation.<sup>25 26</sup> However, we specifically identify that evoked coughs and belches are the index risk events rather than the insertion and removal of the endoscope from the oesophagus.

Conducting aerosol sampling during OGD in a HEPA-filtered ultraclean environment provides an optimal setting for detecting aerosols due to the extremely low background concentration. Sampling in an adjacent operating theatre (non-UCV) revealed a baseline particle content of 16000 particles  $L^{-1}$  (compared with 3  $L^{-1}$ ).<sup>33</sup> Sampling in such a theatre would mean the aerosol detected in this study (eg, associated with tidal breathing) would



**Figure 5** Profile of aerosol concentration detected during endoscope (A) insertion ( $n=12$ ) and (B) removal ( $n=11$ ). A low mean concentration of aerosol was detected in the 30s time period around endoscope insertion (10.3 (9.5) particles  $L^{-1}$ ) and removal (15.1 (12.4) particles  $L^{-1}$ ) where the concentrations were not significantly different to the background. Note that endoscope insertions ( $n=3$ ) and removals ( $n=4$ ) that immediately triggered coughing or burping (ie, during this sampling window) were excluded from the pooled analysis.

be impossible to detect over background 'noise'. We note that a previous study of OGD aerosol generation also found high background counts (25–40 000 particles per cubic foot equating to ~900–1400 particles L<sup>-1</sup>) in their procedure room, which had a standard ventilation system.<sup>25</sup> This would preclude detection of the aerosol generated by breathing or even a volitional cough over the background particle count (likely mostly inorganic 'dust' rather than bioaerosol). Importantly, the high temporal resolution (1 Hz measurements of airborne particles) in combination with the low background aerosol concentration enables the definitive attribution of specific respiratory or procedural events as being the source of the aerosol (rather than attempting to make the link by inference when using a minute-by-minute analysis<sup>26</sup>).

A novel aspect of our study design is using each patient's own respiratory events as a comparator. This puts the aerosol measurements made during endoscopy into a meaningful biological context of normal respiratory events. This approach also reduces the impact of between-subject variation and so increases the power to detect significant changes even within a relatively small sample size. We used tidal breathing as a lower reference for natural aerosol generation and could reliably detect this aerosol concentration above the background (the first time such a measure has been possible in a study of patients). For the patients who did not cough during the procedure, lower concentrations were detected than during coughing or even normal tidal breathing. This may be due to the presence of the bite guard, attenuation by the endoscope itself or the endoscopist's hands or shallow/nasal breathing during the procedure.

The sampling method used in our study is appropriate to detect aerosol particles generated from the respiratory system, which are generally in the range of 10 nm to 20 µm, with a large predominance in the submicron range<sup>29</sup>; we do not detect droplets larger than 20 µm and can make no statement about their presence or absence from these procedures. We set out to study aerosol levels close to the source of generation. By sampling close to the patient (20 cm), we achieve an accurate measure of exposure risk for the endoscopist and assistant who will be within the near vicinity of the patient (within 1 m), so any emitted plumes of aerosol are highly relevant to their risk of transmission. The WHO has defined aerosols as being composed of particles <5 µm in size, but recently, such a strict delineation in size has been questioned: moist exhaled droplets smaller than 100 µm can decrease considerably in size, showing similar aerodynamic behaviour to aerosol such that they can present a transmission risk over many metres.<sup>35</sup> This is relevant particularly when considering the dispersal of particles within the room, which is currently not directly experimentally quantifiable for respiratory aerosols given the relatively low concentrations of particles and the enormous degree of dilution that occurs with dispersal even in a room with standard ventilation. We believe that the primary risk to the endoscopy team is from the close-quarters exposure to respiratory aerosol near the site of generation (the patient), but the issue of potential particle persistence and dispersal within the room as a route of transmission may also be a factor that merits further investigation (for review, see <sup>36</sup>).

Respiratory aerosols are considered to be well represented by a bimodal distribution, with mean aerodynamic diameters of the two modes in the range 800–1500 nm; the smaller mode is considered to arise in the lower respiratory tract, the bronchioles, and the larger is assigned as the laryngeal mode.<sup>29</sup> The OPS cannot intrinsically differentiate between respiratory and non-respiratory aerosols, but by timestamping events, minimising movement of the investigator, sampling close to the patient and

using a funnel to directionally focus on sources originating from the patient, we reduced the risk of artefactual particle detection or detection of aerosol from staff in the room. We did not take any specific precautions such as limiting staff movement or altering their routine care during the conduct of these endoscopies, and so, our results are characteristic of aerosol generated during typical clinical practice. The size distribution of the particles detected during the study was typical of respiratory aerosols; it formed a lognormal distribution of particles with the peak lying in the submicron size range<sup>20 29 30</sup> and had a similar profile for both voluntary and procedure-evoked coughs.<sup>20</sup> This suggests the mechanism generating the aerosol is similar in both cases and provides a characteristic fingerprint distinguishing respiratory aerosols from other potential particle sources (ie, from fabric/bedding dust released by movement of staff and patient).

The increased number of particles produced by OGD-evoked coughs, above those produced by a volitional cough, may relate either to a more forceful reflexively generated protective cough, to the presence of fluid in the oropharynx associated with the endoscopy or to partial occlusion of the oropharynx during endoscopy reducing the diameter of the airway and increasing the amount of turbulent flow. Interestingly, burps (eructations) also produced measurable aerosol, but this had a different size distribution to coughs (with an order of magnitude fewer particles in the size range from 0.5 to 1.5 µm) reflecting the different site of origin of the aerosol. However, although the gastric source of the BGE is unlikely to represent a reservoir for SARS-CoV-2 (unlike the lungs), the passage of turbulent gas flow over the oropharyngeal and nasopharyngeal membranes still could result in generation of virus containing aerosol so should not be discounted as a risk.

Our study was not designed to look at the potential mitigating effect of using sedation to reduce coughing. Midazolam was administered to four patients for conscious sedation at patient request. All of the patients receiving midazolam coughed compared with 50% of the remainder. A subsequent exploratory study of the incidence of coughing in patients having upper GI endoscopy in our institution showed similar findings with 67% (n=8/12) coughing with midazolam sedation and 40% without (n=4/10). This fits with the known lack of antitussive properties of benzodiazepines, which tend to preserve airway reflexes (generally considered a safety advantage for endoscopy in reducing the incidence of aspiration and hypoxia). Likewise, both of the previous studies of aerosol generation during endoscopy<sup>25 26</sup> found no association with either the presence or quantity of sedation on aerosol generation (both with midazolam). A randomised controlled study would be needed to answer the question as to whether conscious sedation can be used to reduce aerosol generation during endoscopy. However, we also note that this would be a difficult trial to translate into change in guidelines as even a large reduction in the incidence of coughing (of say 50% as has been noted for combinations of midazolam and opiate<sup>37 38</sup>) could not exclude the possibility that any individual patient would cough or burp, and hence, airborne PPE would still be needed. This would also have to be balanced against the possible detrimental effect of suppression of protective airway reflexes, which could increase the risk of hypoxia.

There are several limitations to our study. Our sample size was relatively small, and 14 out of the 15 participants had a BMI >40 kg m<sup>-2</sup>. It is possible that these patients with higher BMI may have generated more aerosol than leaner patients (as was suggested by the study of Sagami and colleagues),<sup>26</sup> but this effect is likely to apply both for the baseline cough measurements and

during endoscopy and so is controlled for in our study design looking at relative levels of airborne particles. It is not possible to extrapolate our findings to patients with active respiratory disease or COVID-19 infection as all participants were screened for COVID-19 and had no acute illness. Our study cannot be used to determine the risk of COVID-19 transmission during endoscopy where the risk status of the patient (ie, the likelihood of having COVID-19) is the major determinant. Our sampling methodology does not detect aerosols smaller than 300 nm (approximately three times the diameter of the SARS-CoV-2 virus); however, respiratory particles less than 300 nm in diameter are extremely unlikely to carry viable virions unless the patient's viral titre is extremely high. This lower size limit excludes aerosols of subvirus size that cannot contain the virus<sup>39</sup> but are always present in any environment at the highest concentration and number—so our sampling method reduces this irrelevant 'noise' signal. Similarly, aerosols greater than 10 µm are not detected using our techniques. However, particles larger than 5 µm are classified as droplets, and protection is afforded by droplet precaution PPE (ie, fluid-resistant surgical facemasks).

Our findings are clinically relevant, particularly in the context of the COVID-19 pandemic. Performing an OGD may unpredictably trigger coughing whenever the oropharynx is instrumented, and such OGD-evoked coughs generate more aerosol than either breathing or volitional coughs. Based on our observations, OGD should continue to be designated an aerosol-generating procedure in conscious patients. Therefore, airborne protection PPE including a FFP3/N95 facemask and eye protection should be used in the care of any patient known or suspected to have COVID-19. These precautions will likely have to continue while SARS-CoV-2 is still in circulation in the community and beyond for the management of any patients with respiratory pathogens. We also note there is currently an absence of epidemiological evidence demonstrating that OGD is associated with an increased risk of COVID-19 transmission, but this may reflect the widespread adoption of airborne PPE and precautions by endoscopists and endoscopy staff. Given the increased risk of aerosol generation, we suggest that upper GI endoscopy should be conducted in an environment with a high level of air changes and carefully designed air flows to ensure rapid clearance and dispersal of aerosol.<sup>19</sup> We find no evidence for any other sources of increased aerosol generation during the OGD, and therefore, if a patient does not cough or belch during the OGD, then consideration may be given to decreasing the time interval for air changes in the room between cases. In addition, strategies to reduce the incidence of coughing and eructation should be explored as a means to decrease the risk of aerosol generation.

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