Investigation of respiratory disease: risk of aerosolisation from spirometry, peak flow, and other associated tests.

Supplement 2 - Results

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Results

Demographics

33 healthy volunteers and ten patients were recruited; with demographics and lung function results reported in Table S1. Volunteers were young (median age 32), of normal weight (median BMI 23.6) and had normal lung function; as would be expected from this cohort. 16 (48%) were male, with 17 being female (52%). 10 patients were recruited with a median age of 71. 3 were female and 7 were male. The clinical diagnoses were asthma (5 patients), bronchiectasis (3 patients), allergic bronchopulmonary aspergillosis (1 patient), asthma/COPD overlap (1 patient).

Table S1: Demographics of the study cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Volunteers (n = 33)</th>
<th>Patients (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight in kg</td>
<td>72 (64, 79)</td>
<td>73 (63, 81)</td>
</tr>
<tr>
<td>Height in centimetres</td>
<td>174 (164, 179)</td>
<td>161 (158, 162)</td>
</tr>
<tr>
<td>BMI</td>
<td>23.6 (22.0, 25.5)</td>
<td>28.1 (24.0 – 31.0)</td>
</tr>
<tr>
<td>Age</td>
<td>35 (32, 40)</td>
<td>71 (62, 76)</td>
</tr>
<tr>
<td>Female (n, %)</td>
<td>17 (52%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>FEV1 (litres)</td>
<td>3.50 (3.17, 4.07)</td>
<td>1.48 (1.20 – 1.65)</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>105 (91, 111)</td>
<td>59 (56 -67)</td>
</tr>
<tr>
<td>FVC (litres)</td>
<td>4.28 (3.98, 5.27)</td>
<td>2.43 (1.76 - 2.81)</td>
</tr>
<tr>
<td>FVC (% predicted)</td>
<td>110 (105, 118)</td>
<td>75 (72 -80)</td>
</tr>
</tbody>
</table>

1 Median (IQR), unless stated

Aerosol emission during respiratory function testing

Table 1 (in the main document) describes the geometric mean and geometric standard deviation of aerosol number concentrations generated during FEV1, peak flow, and FENO, in comparison with speaking, breathing and coughing for all patients and volunteers. Figure 1 (in the main document) reports the data as a boxplot, comparing volunteers and patients with lung disease. As all of those
activities apart from breathing and speaking are sporadic activities, we report the maximum number of particles per cm$^3$ for those activities.

Patients with lung disease generated higher aerosol concentrations than volunteers when breathing (0.29 vs 0.04 particles/cm$^3$, p <0.01), and when speaking (0.20 vs 0.10 particles/cm$^3$, p = 0.04), but not when coughing (1.45 vs 1.61 particles/cm$^3$, p>0.2) although there was large individual variability, particularly in healthy volunteers. Figure S1 shows the aerosol emission for each individual patient.

Figure S1: Aerosol total concentration detected while speaking, breathing, and coughing for each patient with lung disease.

Of all the activities tested, voluntary cough produces by far the most particles, with an average of 1.61 particles/cm$^3$ in volunteers, and 1.45 particles/cm$^3$ in patients. However, adding a filter reduced this by an order of magnitude for both volunteers (0.76 unfiltered vs 0.09 particles/cm$^3$ filtered, p <0.01) and patients (0.37 unfiltered vs 0.01 particles filtered /cm$^3$, p <0.01). Therefore, compared to a filtered peak flow, voluntary cough produced factor of 18 more aerosol in volunteers (0.09 particles /cm$^3$ vs 1.61 particles/cm$^3$) and a factor of 145 more aerosol in patients (0.01 particles /cm$^3$ vs 1.45 particles/cm$^3$, both comparisons p<0.01).
For both patients and volunteers, filtered spirometry generated aerosol similar to a filtered peak flow (0.11 particles/cm$^3$ in volunteers and 0.10 particles/cm$^3$ in patients) at a concentration of one order of magnitude lower than a voluntary cough, with all participants except one healthy volunteer having >2-fold reduction in aerosol emission. On average, voluntary cough in healthy volunteers generated a factor of 56 more aerosol compared to spirometry in volunteers, with a factor of 22 in patients with lung disease (both comparisons $p < 0.01$).

**FENO device**

The FENO device does not have a clear exhalation port and the manufacturer does not make clear where exhaled breath leaves the device. We interrogated the device and measured aerosol concentration at all possible exhalation ports (see image in supplementary appendix). In all positions we did not find any significant aerosol emission from the FENO device.

**CPET mask**

We tested the use of a CPET mask with viral filter placed over the exhalation port to reduce aerosol emission on 5 healthy volunteers, with raw data shown in Table S2. Large reductions in aerosol emission during breathing (0.02 vs <.0001 particles/cm$^3$, $p = 0.08$, paired t-test for all comparisons), speaking (0.1 vs <0.001 particles/cm$^3$, $p = 0.06$) and coughing (1.12 vs 0.06 particles/cm$^3$, $p< 0.01$) were measured when using the CPET mask with a filter. Because of the small numbers this only met significance testing for coughing, although the average reduction in aerosol emission was by more than a factor of ten for speaking, and a factor of 20 for coughing and breathing.

Table S2: Raw data from the CPET mitigation strategy.

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Breathe (mean)</th>
<th>CPET breathe (mean)</th>
<th>Speak (mean)</th>
<th>CPET speak (mean)</th>
<th>Cough (peak)</th>
<th>CPET cough (peak)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.044</td>
<td>0.006</td>
<td>0.044</td>
<td>0.002</td>
<td>1.23998</td>
<td>0.06</td>
</tr>
<tr>
<td>2</td>
<td>0.03</td>
<td>0.002</td>
<td>0.15</td>
<td>0.006</td>
<td>0.91998</td>
<td>0.04</td>
</tr>
<tr>
<td>3</td>
<td>0.01</td>
<td>0.002</td>
<td>0.056</td>
<td>0.002</td>
<td>1.05998</td>
<td>0.1</td>
</tr>
<tr>
<td>4</td>
<td>0.042</td>
<td>0</td>
<td>0.46599</td>
<td>0.002</td>
<td>7.29986</td>
<td>0.12</td>
</tr>
<tr>
<td>5</td>
<td>0.008</td>
<td>0</td>
<td>0.06162</td>
<td>0</td>
<td>0.2</td>
<td>0.04</td>
</tr>
</tbody>
</table>

All figures represent the raw reported aerosol number concentration from the APS, with peak number concentration for cough, and average for breathing and speaking.
This is visualised in Figure S2. This mask can be worn before, during, and after spirometry and may be a potential mitigation technique as induced coughing is common during lung function.

In summary, formal lung function testing using a spirometer with a filter did not generate significant aerosol in comparison to a cough; with peak levels similar to average emissions during speaking.
Figure S2: CPET mask as a mitigation strategy

![Graph showing average particle number concentration recorded per 1 sample/cm³ for different activities: Breathe (mean), Speak (mean), Cough (peak). The graph compares activity without CPET mask and activity with CPET mask.]

$n=5$
**Peak flow with a filter**

To ensure peak flow results were reliable with a filter, we compared peak flow readings both with and without the protective filter for 9 participants. The measured flow rates are shown in Figure S3 and are strongly correlated with a R of 0.966. Therefore, although there may be a slight reduction in recorded FEV1 with the peak flow monitor when used with a filter, this is likely clinically insignificant.

Figure S3: Correlation between unfiltered and filtered peak flow
Aerosol emission pre and post-spirometry, and the effect of salbutamol

There is a concern that lung function testing itself may generate aerosol. Therefore, for all patients, we measured aerosol number concentrations from breathing, speaking, coughing both pre- and post-spirometry. Results are shown in Figure S4 and S5: no quantitative or qualitative difference in aerosol number concentration is reported between pre- and post-spirometry. For four patients, we assessed the impact of salbutamol nebulisation on aerosol emission, and again found no difference in aerosol emission post-salbutamol reversal (Figure S6).

Figure S4: Aerosol total concentration detected pre and post spirometry in patients with lung disease.

Figure S5: Aerosol size distribution detected pre and post spirometry in patients with lung disease.
Figure S6: Aerosol total concentration detected pre and post reversal in patients with lung disease.