

# 1           **Estimation of SARS-CoV-2 aerosol emissions from simulated** 2           **patients with COVID-19 and no to moderate symptoms**

3   A.A.Prof. Dr. Michael Riediker<sup>1</sup>, Dr. Dai-Hua Tsai<sup>1,2</sup>

4   1 Swiss Centre for Occupational and Environmental Health, Winterthur, Switzerland

5   2 Department of Child and Adolescent Psychiatry and Psychotherapy, University Hospital of

6   Psychiatry Zurich, University of Zurich, Zurich, Switzerland

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## 9    [Address for correspondence](#)

10   Michael Riediker

11   michael.riediker@alumni.ethz.ch

12   +41 77 431 08 58

13   Swiss Centre for Occupational and Environmental Health (SCOEH)

14   Binzhofstrasse 87

15   CH-8404 Winterthur

16   Switzerland

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**NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.**

## 18 Key Points

19 **Question:** How much SARS-CoV-2 virus is released from a case by breathing and coughing,  
20 and what is the resulting concentration in a room?

21 **Finding:** In this mathematical modelling study, both, breathing and coughing were estimated  
22 to release large numbers of viruses, which can lead to millions of virus copies/m<sup>3</sup> in a poorly  
23 ventilated room with a coughing emitter.

24 **Meaning:** These results may explain the important rate of transmissions and implies the  
25 need for strict respiratory protection when people are in the same room with a case with  
26 COVID-19.

## 27 Abstract

28 **Importance:** Cases of the coronavirus disease 2019 (COVID-19) with no or mild symptoms  
29 were reported to frequently transmit the disease even without direct contact. The severe  
30 acute respiratory syndrome virus (SARS-COV-2) was found at very high concentrations in  
31 swab and sputum of such cases.

32 **Objective:** We aimed to estimate in a mathematical modeling study the virus release from  
33 such cases into different aerosol sizes by normal breathing and coughing, and what exposure  
34 can result from this in a room shared with such as case.

35 **Data Sources and Model:** We combined the size-distribution of exhaled breath  
36 microdroplets for coughing and normal breathing with viral sputum concentrations as  
37 approximation for lung lining liquid to obtain an estimate of emitted virus levels. The  
38 resulting emission data fed a single-compartment model of airborne concentrations in a  
39 room of 50 m<sup>3</sup>, the size of a small office or medical exam room.

40 **Results:** The estimated viral load in microdroplets emitted by simulated patients while  
41 breathing normally was on typical 0.0000049 copies/cm<sup>3</sup> and could go up to 0.637  
42 copies/cm<sup>3</sup>. The corresponding numbers for coughing simulated patients were 0.277  
43 copies/cm<sup>3</sup> and 36,030/cm<sup>3</sup>, respectively, per cough. The resulting concentrations in a room  
44 with a coughing emitter were always very high, up to 7.44 million copies/m<sup>3</sup>. However, also  
45 regular breathing microdroplets from high emitters was modelled to lead to 1248 copies/m<sup>3</sup>.

46 **Conclusions and Relevance:** In this modelling study, breathing and coughing were estimated  
47 to release large numbers of viruses, ranging from thousands to millions of virus copies/m<sup>3</sup> in  
48 a room with an emitter having a high viral load, depending on ventilation and microdroplet  
49 formation process. These findings suggest that strict respiratory protection may be needed  
50 when there is a chance to be in the same room with a patient - whether symptomatic or not  
51 - especially for a prolonged time.

## 52 Introduction

53 The novel Coronavirus disease 2019 (COVID-19), emerged in late 2019 in Wuhan, China <sup>1</sup>  
54 from where it spread to the entire world. COVID-19 is caused by a novel type of Coronavirus,  
55 the severe acute respiratory syndrome virus (SARS-COV-2) <sup>2</sup>. The host-receptor for SARS-  
56 CoV-2 was found to be Angiotensin I converting enzyme 2 (ACE2), which is present in cells of  
57 the lungs and airways <sup>3</sup>. In the early phase of the outbreak, a large number of patients  
58 hospitalized for other reasons <sup>4</sup> and a considerable proportion of the medical staff <sup>5</sup>  
59 contracted COVID-19. However, the attack rate among medical staff corresponded to  
60 community rates when respiratory personal protective equipment (PPE) was used at work  
61 <sup>6,7</sup>. Also a series of community-transmissions were reported from cases that had no apparent  
62 symptoms <sup>8-11</sup>. The estimates for community and household attack rates are currently in the  
63 range of 1 % and 10 %, respectively <sup>12-15</sup>. However, during super-spreading events in

64 situations where many people engaged in loud voice activities gathered in closed rooms for  
65 prolonged time, such as a restaurant <sup>16</sup>, a call-center <sup>17</sup>, a dermatologists scientific board  
66 meeting <sup>18</sup>, and a choir rehearsal <sup>19</sup> attack rates above 75% were reported. Notably, the choir  
67 rehearsal participants tried to follow social distancing and hand washing rules. These super-  
68 spreading events suggest that the airborne route may represent a virus transmission form in  
69 some indoor situations. Indeed, a study conducted in a Wuhan hospital found low airborne  
70 concentrations of the virus in the intensive care unit and in medical staff rooms <sup>20</sup>.  
71 Correspondences about the viral load in samples from patients with COVID-19 having no or  
72 only mild symptoms reported very high concentrations of SARS-CoV-2 in samples taken in  
73 the nose, throat and saliva <sup>11,21-23</sup>, and high during antiviral treatment <sup>24</sup>. This all raised the  
74 question whether transfections could occur via the air.

75 When coughing, humans release thousands of microdroplets per cubic-centimeter in the size  
76 range of 0.6 to 15  $\mu\text{m}$ , with the droplet concentration increasing strongly with cough flow  
77 rate <sup>25</sup>. But also normal breathing will lead to some microdroplet production, which is  
78 attributed to fluid film rupture in the respiratory bronchioles during inhalation leading to the  
79 formation of droplets that are released during exhalation <sup>26</sup>. The size of these droplets is  
80 mostly below 1  $\mu\text{m}$  <sup>27</sup>. The mode of droplet generation implies that they consist of lung lining  
81 liquid including dispersed viruses. Indeed, human volunteers exposed to virus-sized  
82 nanoparticles show nano-scaled particles in their exhaled breath <sup>28,29</sup>. Also, the described  
83 size distribution of particles emitted from coughing as well as normal respiration suggests  
84 that an important proportion of them will be able to remain airborne for many hours in  
85 turbulent conditions <sup>30</sup>.

## 86 Objectives

87 This study aimed to estimate the cumulative viral load released from simulated patients with  
88 COVID-19 with no to moderate symptoms in different microdroplet sizes via respiration and

89 coughing. We then used this information to make a risk appraisal for the situation of a low,  
90 typical or high emitter that is either breathing normally or coughing in a room operated at  
91 different air exchange rates. We chose a room size that is similar to a medical examination  
92 room or an office shared by two to three people.

## 93 Design and Methods

### 94 Concept:

95 The release of viruses from individual simulated patients was modeled by first calculating  
96 the viral load per exhaled microdroplets formed during normal breathing and while  
97 coughing. The resulting size-distribution provided an initial estimate of the concentration of  
98 SARS-CoV-2 virus copies released by a regularly breathing or coughing simulated patient.  
99 This viral emission factor was then fed into a well-mixed one-compartment model to  
100 simulate the situation in a closed room with different ventilation air exchange rates. This  
101 study follows the concept of Strengthening The Reporting of Empirical Simulation Studies  
102 (STRESS) guideline<sup>31</sup>. This mathematical modelling corresponds to a meta-analysis and was  
103 as such exempt from ethics approval.

### 104 Data sources:

105 Data on the number of viral copies present in sputum and swab samples were used to  
106 estimate the SARS-CoV-2 viral load present in the lining liquid of respiratory bronchioles in  
107 patients published before the here presented modelling (May 2020)<sup>11,21-24,32</sup>, specifically  
108 1,000 copies/ml representing a low-virus producing patient ("low emitter"), a "typical  
109 emitter" producing  $10^6$  copies/ml, and a "high emitter" producing  $1.3 \cdot 10^{11}$  copies/ml.  
110 Exhaled microdroplet size distributions and numbers were retrieved from published studies  
111 on healthy persons coughing<sup>25</sup> and breathing normally<sup>26</sup>. Both studies assessed the size-  
112 number distribution of freshly emitted microdroplets. The concentration of viral copies in

113 each microdroplet size was calculated from the volume of the microdroplets, the actual  
114 count number in each size and the above-mentioned virus-load per ml sputum. The viral  
115 load in the actual microdroplet counts in each microdroplet size was then used to calculate  
116 the total viral concentration. The cumulative emissions in the PM<sub>10</sub> fraction were summed  
117 up after applying the standard size fractionation curves<sup>33</sup> to the microdroplet distribution.

#### 118 Model:

119 A one-compartment model<sup>34</sup> estimated the virus load concentration C for a perfectly mixed  
120 room of volume V<sub>R</sub> of 50 m<sup>3</sup> with one simulated patient as source, using the following mass-  
121 balance (equation 1):

$$122 \quad V_R * \frac{dC}{dt} = c_{PM10} * RR * V_t - V_R * ER * C(t) - \frac{\ln(2)*V_R}{t_{1/2}} * C(t) \quad (1)$$

123 The emission rate was calculated from the concentration c<sub>PM10</sub>, the viral load in the PM<sub>10</sub>-  
124 size range, which are particles collected with a 50% efficiency cut-off at 10 μm aerodynamic  
125 diameter; and a respiratory rate of 15 breaths per minute (RR) at a tidal volume of V<sub>t</sub> of 500  
126 ml per breath. Air exchange rates (ER) used were 1-, 3-, 10- and 20-times per hour. The virus'  
127 half-life t<sub>1/2</sub> of 1.1 hours was obtained from an experimental study about the persistence of  
128 SARS-CoV-2 on surfaces and when airborne<sup>35</sup>, tested by assessing the 50% tissue culture  
129 infective dose (TCID<sub>50</sub>).

130 The model for coughing was identical, except that coughing was assumed to happen every  
131 30 seconds at a volume of 250 ml, as described for chronic dry cough patient (not having  
132 COVID-19)<sup>36</sup>.

133 All statistics and models were calculated using Stata/SE 15.1 (Mac 64-bit Intel, Rev. 03 Feb  
134 2020, StataCorp, College Station, TX, USA). Robust data reported include estimated averages  
135 and ranges. The models and code are available on request.

## 136 Results

### 137 Emissions from normal breathing simulated patients

138 To estimate the virus emissions from simulated patients breathing normally, we first  
139 calculated the viral load for the microdroplet size distribution. Figure 1 shows that the  
140 highest virus load is present in the largest microdroplet size. The cumulative total emission  
141 per breath was 0.0000000049 copies/cm<sup>3</sup>(air) for a low emitter, 0.0000049 copies/cm<sup>3</sup> for a  
142 typical simulated patient, and 0.637 copies/cm<sup>3</sup> for a high emitter. The cumulative emissions  
143 in the PM<sub>10</sub> fraction were approximately 1/3 of these values with 0.0000017 copies/cm<sup>3</sup>  
144 (typical) and 0.226 copies/cm<sup>3</sup> (high) per breath.

### 145 Emission from coughing simulated patient

146 We then estimated the virus emissions from a coughing simulated patient (Figure 2). The  
147 cumulative total emission per cough was 0.000277 copies/cm<sup>3</sup> for a low emitter, 0.277  
148 copies/cm<sup>3</sup> for an typical simulated patient, and 36,030 copies/cm<sup>3</sup> for a high emitter. The  
149 cumulative emissions in the PM<sub>10</sub> fraction were about 1/2 of these values with 0.156  
150 copies/cm<sup>3</sup> (typical) and 20,221 copies/cm<sup>3</sup> (high) per cough.

### 151 Exposure estimation for bystanders

152 To estimate the exposure of bystanders spending time in the same room as a person with  
153 COVID-19, we calculated the time-course of the viral load in the thoracic size fraction for  
154 small droplets released from a high-emitter either breathing normally or coughing. Figure 3  
155 shows the results for a high-emitting simulated patient coughing frequently.

156 For a typical hospital ventilation situation of 10 air exchanges per hour, the concentration  
157 plateaus after about 30 minutes, while for a typical office with 3 air exchanges/hour,  
158 concentrations continue to rise for over one hours. In the used model, concentrations scale

159 linearly with the simulated patient emission rate, the plateau concentrations for different  
160 emitting simulated patients and ventilation types are summarized in Table 1.

## 161 Discussion

162 An elevated number of viruses is expected to be released by patients with COVID-19 having  
163 high viral load in the form of airborne microdroplets, especially when they are coughing.  
164 While the bigger portion of the emitted viral load is in the form of large droplets that can  
165 deposit rapidly, there is also an important portion in the smaller size fractions. Small  
166 microdroplets can remain airborne for an extended time<sup>30</sup> and are very effective at reaching  
167 the lungs<sup>37</sup>.

168 One study assessed airborne SARS-CoV-2 levels in a hospital in Wuhan, China and found  
169 concentrations in the range of 20 copies/m<sup>3</sup> in medical staff offices and meeting rooms<sup>20</sup>,  
170 concentrations that our modelling would suggest for a small room with a regularly breathing  
171 non-symptomatic person having a viral load above a typical emitter.

172 A typical person breathes about a half m<sup>3</sup> per hour in resting state<sup>38</sup>, which can rapidly  
173 increase to several m<sup>3</sup> during exercise<sup>39</sup>. Thus, a person spending time in a room with a  
174 typical emitting patient breathing normally has the chance of inhaling only a few copies of  
175 the virus when keeping distance from that person. However, the situation is worse in the  
176 presence of a high emitter and worst if the patient is a coughing high emitter. A review of a  
177 wide range of respiratory viruses suggests that the infective dose is often quite low.

178 Sometimes as few as few hundred units of active virus (TCID<sub>50</sub>)<sup>40</sup> seem sufficient to provoke  
179 a disease. Thus, our modelling suggests that there is a clear risk of infections for a person  
180 spending an extended time in the room with an infected person having an elevated viral  
181 load, even if the distance is too large for direct transmission. The situation is worse if the  
182 person is coughing.



183 High emitters are not very frequent in the population. However, if such a person is engaged  
184 in activities such as loud speaking or singing, microdroplet formation and thus viral  
185 emissions can rapidly increase by one to two orders of magnitude <sup>41</sup>. This may help explain  
186 the occasional superspreading events in crowded situations involving loud voices <sup>16-19</sup>.

187 The occasionally very high virus load in exhaled respiratory microdroplets proposed by our  
188 assessment may be an explanation why COVID-19 was associated with more transfusions to  
189 hospital staff than what was expected from SARS <sup>4</sup>. While having everybody wear a surgical  
190 face mask can be an effective source control <sup>42</sup>, the protective factors may still be  
191 insufficient if an extended amount of time is spent in the same room with a coughing high  
192 emitter, especially if the room is small and the ventilation low. Increasing ventilation can  
193 help to some extent but is not sufficient in a room of the size of a typical office or medical  
194 exam room. Note also that ventilation design for hospitals is complex and not always  
195 functioning as intended <sup>43</sup>.

196 The implications for the normal life and the workplace are that the risk of infection is real  
197 when being near an infected person with high viral load in a room for more than a few  
198 minutes and this even when keeping distance to that person. Sharing a workplace in a small  
199 room with a non-symptomatic case seems not advised. This implies that workplaces should  
200 not be shared as long as there are no rapid tests to differentiate between healthy and non-  
201 symptomatic cases. Medical staff is advised to wear the best possible respiratory protection  
202 whenever in the same room as a patient, especially when this person is coughing, in which  
203 case eye protection is advised as well <sup>44</sup>. In addition, every patient, also non-symptomatic  
204 ones, should wear a well-fitting surgical face mask to reduce emissions, which will increase  
205 the overall protection for the medical staff <sup>42</sup>.

## 206 Limitations

207 Our assessment has a number of limitations. Namely: 1) The estimated virus levels strongly  
208 depend on the number of virus copies produced by a case with COVID-19. We used sputum  
209 data from a well described peer-reviewed study<sup>21</sup> assuming that it is a reasonable  
210 approximation for the virus load in the respiratory bronchioles, the space where most  
211 respiratory microdroplets are formed. Our high-emitter estimates would be 100-fold higher  
212 if the most extreme viral data was combined with microdroplet super-emissions<sup>22,41</sup>. 2) We  
213 used information about virus copies but compare the results with TCID<sub>50</sub> infective dose.  
214 Research on other virus types suggests that the number of virus copies and TCID<sub>50</sub> are  
215 comparable<sup>45</sup>. However, it would be important to confirm this relationship for the case of  
216 SARS-CoV-2. 3) For breath and cough microdroplets release, we used data collected in  
217 experimental setups involving healthy young subjects. However, microdroplet formation is  
218 influenced by surface tension of the lung lining liquid<sup>46</sup>. It is likely that microdroplet  
219 formation will be altered in cases with COVID-19 but it is not clear in which direction. 4)  
220 Microdroplets will shrink in dry air<sup>47</sup>, resulting in a shift to smaller particle sizes. This will not  
221 directly change the number of copies in the PM<sub>10</sub> range but simply upconcentrate the viral  
222 load per microdroplet. While we addressed passivation of viruses in the air by using the  
223 documented half-life<sup>35</sup>, it is still possible that viruses in smaller droplets are quicker  
224 passivated because of shorter diffusion distances for airborne oxidants and faster increasing  
225 salinity. Our estimates would be slightly smaller if this was relevant. 5) The one-  
226 compartment model assumes perfectly mixed conditions. However, often, rooms are not  
227 perfectly mixed and also ventilation and room geometry will add spatiotemporal variability.  
228 The modelling provides an estimate, but exact concentrations will vary in function of the real  
229 circumstances. In multi-room situations, numerical flow simulations seem indicated to  
230 describe the microdroplet distribution<sup>48</sup>. 6) Finally, though our results suggest that in certain

231 situations, airborne transmission of COVID-19 may be possible, it is important to keep in  
232 mind that this was a modelling effort. While this route would provide a convenient  
233 explanation for several superspreading events<sup>16-19</sup>, and even though the virus was found in  
234 airborne microdroplets in hospital situations<sup>20</sup>, it still needs to be validated in clinical  
235 settings and animal models.

## 236 Conclusions

237 In conclusion, our mathematical modelling suggests that the viral load in the air can rapidly  
238 reach critical concentrations in small and ill-ventilated rooms, especially when the patient is  
239 a super-spreader defined as a person emitting large number of microdroplets containing a  
240 high viral load. Thus, strict respiratory protection is needed whenever there is a chance to be  
241 in the same room with such a patient - whether symptomatic or not - especially if this was  
242 for a prolonged time.

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386

## 387 [Figure legends](#)

388 Figure 1: Size distribution of exhaled microdroplets (left) and resulting viral emissions (right)  
389 during normal breathing.

390 The left panel shows the typical exhaled microdroplet concentration used as input for the  
391 simulation, the right panel shows the modelled viral emission per breath for typical (red),  
392 high and low emitters (spike-lines).

393 Figure 2: Size distribution of exhaled microdroplets (left) and resulting viral emissions (right)  
394 during coughing.

395 The left panel shows the typical exhaled microdroplet concentration used as input for the  
396 simulation, the right panel shows the modelled viral emission per breath for typical (red),  
397 high and low emitters (spike-lines).

398 Figure 3: Temporal course of airborne virus load in a perfectly mixed room of 50 m<sup>3</sup>.  
399 The simulation estimated the concentration in a closed room for different air exchange  
400 rates. The emitter was assumed to have a high virus-load in the lungs and to be coughing  
401 intermittently every 30 seconds.

402 Tables

403 Table 1: Plateau concentration for different combinations of air exchange rate, emission form and emitter type.

Air exchange rate (times / hour)	1 / hour	3 / hour	10 / hour	20 / hour
Time until 99% of plateau	169 minutes	77 minutes	26 minutes	14 minutes
Airborne viral concentration at plateau (copies/m <sup>3</sup> )				
Regular breathing				
Low emitter	0.00000960	0.00000431	0.00000147	0.00000076
Typical emitter	0.00960	0.00431	0.00147	0.00076
High emitter	1247.7	560.3	191.3	98.6
Frequent coughing (every 30 seconds)				
Low emitter	0.5725	0.2571	0.00878	0.00452
Typical emitter	57.250	25.709	8.779	4.524
High emitter	7 442 598	3 342 148	1 141 326	588 093

404

Figure 1

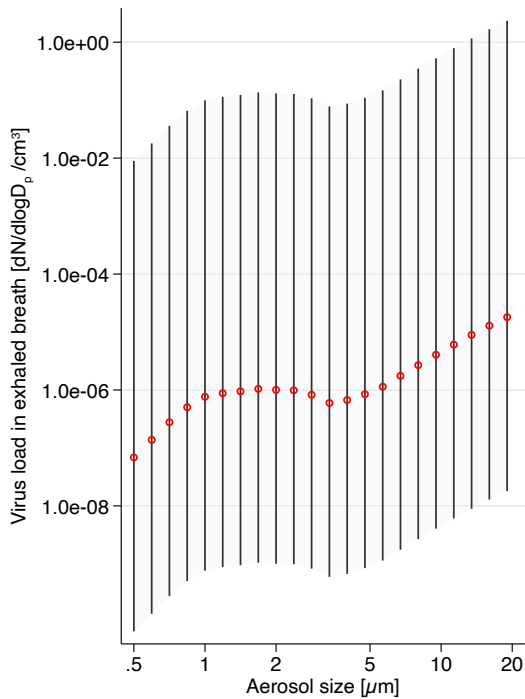
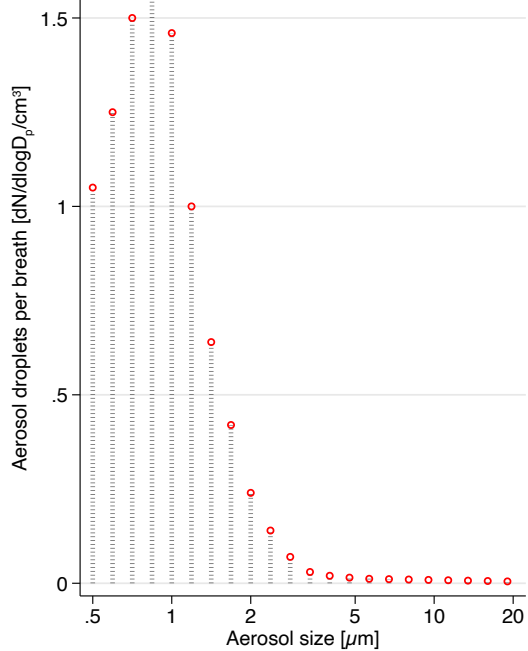


Figure 2

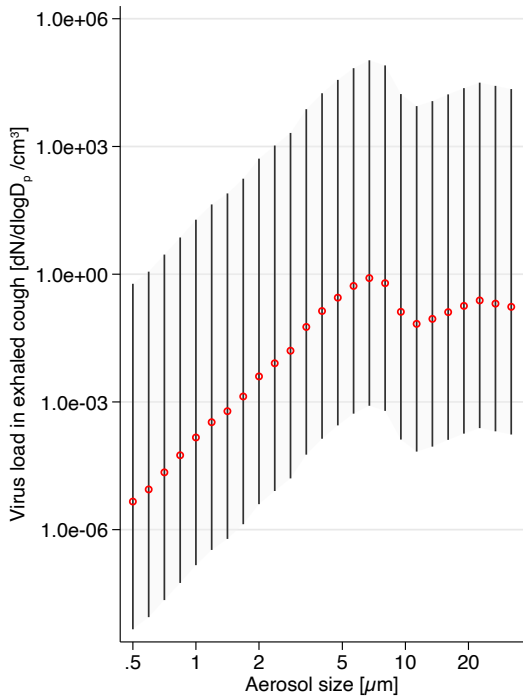
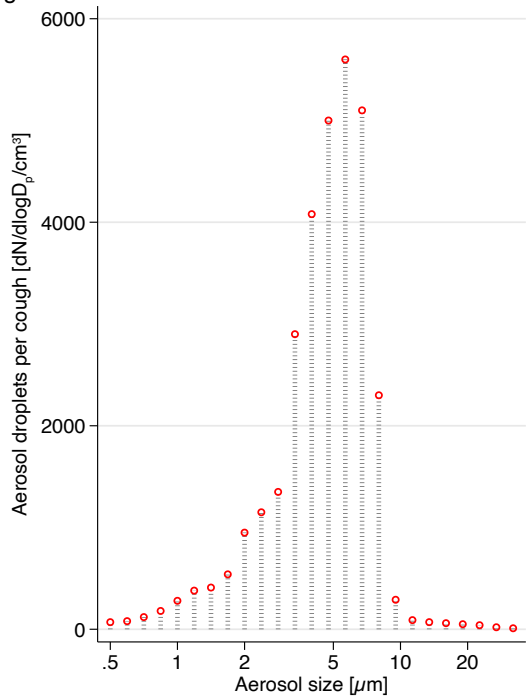


Figure 3

Airborne virus load for high emitter cough  
[copies/m<sup>3</sup> in PM<sub>10</sub>]

— 1/hour    - - 3/hour    ··· 10/hour    - · - 20/hour

