Editorial

Safety of aerosol-generating procedures in COVID-19 negative patients: binomial probability modelling of intubateCOVID registry data

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Accepted: 23 July 2020
Keywords: COVID-19; modelling; risk; safety
This editorial accompanies an article by El-Boghdadly et al., Anaesthesia 2020; 75: 1437–47.

A central response to the COVID-19 pandemic was to create NHS capacity in part by suspension of elective services, as has been described elsewhere [1]. Now that the pandemic’s peak appears to have passed, attention has focused on restoring these services. Common to most hospital plans is the separation of patient pathways into COVID-19 test-positive (red) and test-negative (green) cohorts; patients in the latter also as a precaution having been in isolation for 14 days up to now (https://icmanaesthesiacovid-19.org/clinical-guidance). However, a key concern remains the infectious risk posed to staff undertaking aerosol-generating procedures in those patients who are test-negative. If this risk is negligible, limited or no personal protective equipment (PPE) precautions may be necessary, and in turn this will increase the turnover of cases by reducing or eliminating the considerable time taken to don and doff PPE.

In this article, we show how knowing the risk posed by patients who are COVID-19 positive can quantify the risk posed by COVID-19 test-negative patients, using binomial modelling. For the purposes of this article, we regard the relevant ‘COVID-19 test’ as being the polymerase chain reaction (PCR) antigen test for presence of virus [2].

Estimating aerosol-generating procedure risk from COVID-positive patients

In this issue of Anaesthesia, El-Boghdadly et al. present data from the intubateCOVID registry on the proportion of staff testing antigen-positive or, as a composite endpoint, also falling sick with symptoms after a COVID-positive aerosol-generating procedure. We can regard the latter as an upper bound for risk, since some of these may never have had COVID-19; and the former as a lower bound, since not all staff had access to tests, there is a false-negative rate, and a delay in a test becoming positive [2]. In their study, staff were followed-up for 21 days after their first COVID aerosol-generating procedure. Staff worked normally during this time (notwithstanding those who fell ill and isolated) and managed both some further COVID intubations (median (IQR [range]) of 2 (1–3 [1–42]) in this period) and also presumably non-COVID-19 patients. In total, 8.5% were reported to become symptomatic (composite risk) and 3.1% to become COVID-19 test-positive [3].

The specific data of interest to us are in their cumulative incidence plot (Fig. 4a in their paper for symptoms; data for test-positivity obtained from authors) and it is notable that this is linear over time (Fig. S1). This is significant, because a linear relationship in this data range would be predicted.
using binomial probabilities (Fig. 1) [3,4], the application of which can be explained as follows.

Let us suppose a practitioner undertakes a COVID aerosol-generating procedure on Day 1. We can regard this action as conferring a certain baseline risk (x%) of later contracting COVID-19 at some undefined future time-point. This risk cumulates over each day of work, given a certain average mix of work undertaken, which can include, as in El-Boghdadly et al.’s study, some further aerosol-generating procedures in COVID-positive patients. From the binomial perspective, the risk at each day of such ‘average’ work can be viewed as if tossing a weighted coin. Each day of the hypothetical coin toss (e.g. heads for infection) there is x% chance of the individual contracting COVID-19, cumulating binomially over time (see online Data S1 for the standard equations). After 21 working days, the reported cumulated risk by El-Boghdadly et al. was 8.5% for symptoms (composite), and 3.1% for test-positivity [5]. The original value of x in the binomial model at end of the first day (baseline risk) is therefore 0.42% (1 in 240; symptoms) and 0.15% (1 in 670; COVID-test positivity).

In other words, if we knew these values for risk in advance, and applied binomial probabilities, we would predict the same cumulated risk (linear rise) at 21 days as observed by El-Boghdadly et al. [5]. El-Boghdadly et al. did not express baseline or cumulative aerosol-generating procedure risk in this way – they simply reported what they observed – but the binomial model can be extended over prolonged periods of time, assuming the same mix of work as studied by El-Boghdadly et al. in their cohort (Fig. 1).

There are limitations to this approach. There is no guarantee that the binomial model is the correct one. A simple linear model would also achieve the same result for the reported data, although it would not produce the asymptotic relationship in Figure 1 for more sustained prediction. Second, it would seem intuitive that undertaking more aerosol-generating procedures would confer higher risk, although no such association was apparent in their original data [5]. Third, based as it is on the intubateCOVID data, our model does not risk stratify patients or different aerosol-generating procedure interventions [5]. Fourth, although we present binomial predictions for very long time

![Figure 1](image-url)  
**Figure 1** Cumulative risk (binomial probabilities) by days of work. Red lines: calculated from data in [5], after the first COVID-positive aerosol-generating procedure. Green lines: cumulated risk in COVID-negative pathway where no PPE is used. There is also a line (not visible as near-superimposed on x-axis) representing the very small risk after aerosol-generating procedures in COVID-negative pathways where PPE is used (see Figure S2 for graph with expanded scale). Solid lines represent risk of staff acquiring test-positivity (lower bound); dotted lines represent risk of acquiring symptoms (upper bound). The individual symbols (filled and hollow) represent data from [5], yellow symbols data from [7] and [8] (for test-positivity), and the black symbols with 95% CI represent data from two different trusts cited in the text (filled symbols for test positivity; hollow symbols for symptoms). The line breaks enable the curvilinear shape of the binomial model to be seen, as the timescale extends to beyond a year. Data not shown for aerosol-generating procedures in COVID-19 status-unknown patients (these also near-superimposed on the x-axis; see Figure S2).
periods in Figure 1, it is unlikely that a single COVID aerosol-generating procedure at Day 1 would alone confer such prolonged risk, since COVID-19 has a finite (up to 14 day) incubation period [6]. It should be stressed that the extended plots in Figure 1 are based only on the continued average mix of work as studied by El-Boghdadly et al. [5]. Finally, we do not present calculated confidence intervals for each of our estimates, but rather use symptoms as the upper bound and test results as the lower bound (Fig. 1).

Regardless of these limitations, it is notable that data from one of our Trusts (unpublished) show that by the end of a 4-month period, 15/82 (18.3%) anaesthetists had developed a COVID-positive antigen test, closely matching the prediction from our binomial model of 16.5% (Fig. 1). In this same trust, 34 (41.5%) had isolated with COVID-19 symptoms, close to 39.7% predicted by our model for symptoms (Fig. 1). In a second trust, 16/240 (6.7%) anaesthetic staff became antigen-positive after 6 weeks, also closely matching the binomial model prediction of 6.1% (Fig. 1). Estimates are also available from non-anaesthetist aerosol-generating procedure exposure (in acute and intensive care [7] and ‘red’ area wards [8]) that broadly match the predictions (Fig. 1).

**Estimating aerosol-generating procedure risk from COVID-negative patients**

We now can use this derivation to assess the risk posed by COVID test-negative patients. The underlying principle is that the intubateCOVID data, subjected to a binomial model, define risk from a COVID-positive aerosol-generating procedure. Staff can only be infected by COVID-positive patients. Therefore, the only additional factor needed is the population prevalence of COVID-19 (active cases), which appears at time of writing to be approximately 1 in 2000 (0.05%; see https://www.ons.gov.uk). Thus, of say 100,000 people drawn at random, 50 will have active COVID-19. The false negative test rate for COVID-19 is approximately 20% [2]. Thus, of these 50 COVID-19 patients, 10 would have tested negative. Therefore, there will be 99,960 patients directed down a hospital’s COVID-negative (‘green’) pathway, 10 of whom would in fact be positive. The risk to staff is posed only by this COVID-positive proportion, approximately 1 in 10,000 (0.01%).

This represents the risk of encounter; we are more interested in the risk of infection. Some approaches try to assign a numerical value to the protective effect of PPE [9–11] but this is problematic, and one resulting estimate has offered an implausibly high infection risk of 1 out of 5 [11]. This approach is also unnecessary, because the data of El-Boghdadly et al. already tell us the baseline risk, taking all this into account (0.42% for symptoms and 0.15% for test). Therefore, the risk of infection is simply the product of the risk of encounter and the baseline risk from El-Boghdadly’s data. This is approximately 1 in 2.3 million (symptoms) or approximately 1 in 6.7 million (test). We can then apply binomial probabilities, as we did above, to estimate how this risk cumulates over time and Figures 1, 2 and S2 summarise some values for the respective patient pathways.

**Estimating the aerosol-generating procedure risk where COVID-19 status is unknown**

There is a third group, often emergency cases, whose status is unknown, sometimes termed an ‘amber’ pathway. There may not be time to conduct a COVID antigen test, but equally the patients have no symptoms to suspect disease. Logically, they should be regarded as a random sample from the population, so at worst the chance they have COVID–19 – the risk of encounter – is approximately 1 in 2,000; the same as the contemporaneous prevalence. Again, the risk of infection is the product of this and the baseline risk data of El-Boghdadly et al., which is approximately 1 in 1.3 million (test) and 1 in 480,000 (symptoms; Fig. 2).

**Implications for planning**

Our analysis reveals a huge gulf of risk between managing known (or suspected) COVID-19 test-positive patients vs. that of managing COVID-19 test-negative patients (Fig. 2). Although the rate of false-negative COVID testing is reportedly as high as 30% (we use 20% as a conservative estimate in our calculations [2]), the low disease prevalence makes it unlikely that a patient in the COVID-negative pathway will transmit infection at a level of risk that should cause great concern. Staff working at some distance from aerosol-generating procedures have even less to fear. This reassuring analysis is strongly contingent upon rigorously separate pathways of care, based on testing and isolation of patients before elective surgery. Although we cannot comment on the optimum number of tests or duration of isolation before surgery, the low risks presented by the ‘green’ pathways may help facilitate the safe return to work of some vulnerable staff currently shielding.

Our results might tempt some to relax or abandon the requirements for high-level PPE in COVID-19 test-negative patients; something which if worn otherwise greatly slows down surgical case turnover. However, if we assume a worst case of 100% risk of transmission after the aerosol-generating procedure with minimal or no PPE, then the risk of infection is the same as that of encountering a COVID-
Applying the binomial model, this baseline risk of 1 in 10,000 after 1 day translates to risks of 1 in 500 (0.2%) after 21 days and 1 in 83 (1.2%) at 120 days (see Fig. 1, green lines, for risks at other time-points). However, one mathematical model estimates the risk of infection with no barrier protection to be 38%, so these are very much worst-case scenarios [12]. These risks remain considerably lower than those of an aerosol-generating procedure when wearing PPE in a COVID-positive patient (Fig. 1; red lines). Whether these risks justify changing current PPE guidance probably depends on individual perception, vulnerability, and attitude to risk.

At the same time as providing reassurance in the COVID-19 test-negative pathway, the data of El-Boghdadly et al. [5] combined with our model predictions, raise real concerns about managing COVID-positive patients, even when using PPE. The reported rates of infection in staff seem high enough to suggest that staff should not work indefinitely in the average mix of work representative of that study (Fig. 1). Otherwise, sickness rates could reach 50% after a few months, which is incompatible with current aspirations for service delivery. The model implies that maximum lengths of duty should be set for staff undertaking this mix of work, with perhaps a month being a reasonable upper limit (Fig. 1). This would approximate the risk (upper bound 10%) that currently seems to justify the isolation of members of the public in track-and-trace systems, after COVID-positive contact in the community [10]. However, setting such 'maximum duty periods' will itself have significant workforce implications.

**Conclusions**

We have applied binomial probability to the intubateCOVID data to estimate a baseline (Day 1) risk after a COVID-positive aerosol-generating procedure. Forward-binomial modelling yields cumulative risk estimates, which match some real datasets. The infection risk from patients in a
‘green’ pathway is the product of this baseline risk and disease prevalence. Our analysis is generally reassuring, so long as separate pathways based on testing and prior isolation are maintained. However, the same analysis underlines the much greater risk posed by COVID-positive aerosol-generating procedures, despite use of PPE. Setting maximum periods of duty, based on cumulated risk, may be advisable. The precise numerical values generated by our model (displayed in Figures 1 and 2) will depend on: disease prevalence (predicted to fluctuate as a ‘logistic map’ [13]); false-negative test rate [2]; and updated data from intubateCOVID, this being an ongoing database [5].

Acknowledgements
We thank Ms R. Owen, Research Fellow in Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK and Dr K. El-Boghdadly, Consultant Anaesthetist, Guy’s and St Thomas’ NHS Foundation Trust, for clarifying aspects of the intubateCOVID data. JP is an elected member of the Council of the Royal College of Anaesthetists and Chair of the Safe Anaesthesia Liaison Group (SALG). PK serves as special advisor to the Care Quality Commission (CQC). The views expressed are personal and not of these organisations. No other competing interests declared.

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Supporting Information
Additional supporting information may be found online via the journal website.

Figure S1. Data from reference [5] re-plotted to show cumulative (linear) rise in infection (%) for symptoms and COVID-19 test-positive.

Figure S2. Same plot as Figure 1, but with an expanded y-axis to reveal the data for COVID-test negative patients and COVID status-unknown patients.

Data S1. Equations for the binomial distribution.