

# **Review of evidence** on testing on arrival schemes

Prepared for Virgin Atlantic, IAG, TUI, Heathrow, MAG, Collinson, Airlines UK and

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### 1 Executive summary

Since June, the UK has required all international travellers to the UK, except those arriving from a list of exempt ('travel corridor') countries, to quarantine for 14 days. Unlike a number of other countries, the UK has not introduced any form of scheme to test travellers for COVID-19. We understand that part of the basis for this policy is evidence presented in a paper by Public Health England (PHE) that concluded testing on arrival at an airport would identify only 7% of virus cases.<sup>1</sup>

Oxera and Edge Health have been commissioned by a consortium of airlines, airports and industry organisations to undertake an independent review of the PHE paper, as well as two other studies on the effectiveness of testing schemes from the London School of Hygiene and Tropical Medicine (LSHTM) and the Animal and Plant Health Agency (APHA). We have benefited from input from Dr Kit Yates, a Senior Lecturer in mathematical biology and Co-director of the Centre for Mathematical Biology at the University of Bath. The outputs of our work are intended to feed into the work of the recently established Global Travel Taskforce as it considers how a testing regime for international arrivals could be implemented to boost safe travel to and from the UK.

There are three main areas where we consider that the current evidence base supporting the policy for quarantine rather than a testing scheme should be improved.

First, the key conclusion of the PHE analysis is that testing on arrival would identify only 7% of virus cases. However, this figure is significantly understated. This 7% assumes that all infected travellers who are symptomatic or detectable with a test on departure do not board flights to the UK and therefore only travellers who become detectable during the course of their flight are included in the 7%. Including travellers who are detectable on departure increases the detection rate to between 33% and 63%. These values are more consistent with those reported in the LSHTM and APHA papers.

Second, all three papers are based on theoretical simulation models. As with all models, the outputs are only as good as their inputs. The assumptions in the three papers vary considerably and, in a number of cases, are not based on the most recent empirical evidence. For example, none of the papers account for actual virus prevalence rates among travellers. In some cases there may be no consensus in the empirical evidence regarding certain assumptions; it is very important, therefore, that outputs are calibrated with real-world evidence from established airport testing regimes. However, none of the papers consider this evidence.

Third, it is important to consider the effectiveness of airport testing schemes in the context of an understanding of the level of acceptable risk for travellers and how this would change with testing. All three papers assume that the risk of travellers spreading the virus is reduced to close to zero with a mandatory 14-day quarantine requirement. However, this is unlikely to be the case given that returning travellers are currently permitted to quarantine with other individuals (who do not have to quarantine) and there is evidence to show that compliance with quarantine may be as low as 20%.

<sup>&</sup>lt;sup>1</sup> Public Health England (2020), 'Investigation into the effectiveness of 'double testing' travellers incoming to the UK for signs of COVID-19 infection', 17 June.

Following this report, Oxera and Edge Health will review the evidence on airport testing from other countries and seek to update the modelling completed to date with more recent data that can be aligned to real-world evidence.

## 2 Introduction

Oxera and Edge Health have been commissioned by Virgin Atlantic, IAG, TUI, Heathrow, MAG, Collinson, Airlines UK and IATA to undertake a review of three papers that seek to model the effectiveness of testing travellers for COVID-19. Our review focuses on the assumptions and approaches used in the models in each of these papers, as well as the scientific evidence supporting the analysis.

The UK government recently set up the Global Travel Taskforce to consider how a testing regime could be implemented in order to increase safe travel to and from the UK.<sup>2</sup> An understanding of the effectiveness of different types of testing schemes (e.g. pre-arrival, on arrival and a certain number of days after arrival), is therefore important in determining the government policies that could be introduced in order to safely re-open international travel.

The three papers that we have reviewed are as follows:

- Public Health England (2020), 'Investigation into the effectiveness of 'double testing' travellers incoming to the UK for signs of COVID-19 infection', 17 June. We refer to this as the PHE paper in this note. We have also reviewed the code accompanying the model.<sup>3</sup>
- Clifford et al. (2020), 'Strategies to reduce the risk of SARS-CoV-2 reintroduction from international travellers', 25 July. The authors of this paper are affiliated with the London School of Hygiene and Tropical Medicine (LSHTM), and we therefore refer to this paper as the LSHTM paper in this review. We have also reviewed the code accompanying this paper.<sup>4</sup>
- Taylor, R.A. et al. (2020), 'The risk of introducing SARS-CoV-2 to the UK via international travel in August 2020', 9 September. The main authors of this paper are affiliated with the Animal and Plant Health Agency (APHA), so we refer to this as the APHA paper in this note.

This note is structured as follows:

- section 3 sets out the overall conclusions from our review of the three papers;
- sections 4 to 6 contain more detailed reviews of each of the PHE, LSHTM and APHA papers in turn.

The Appendix sets out a table which compares the assumptions used in each of the three papers.

<sup>&</sup>lt;sup>2</sup> See https://www.gov.uk/government/groups/global-travel-taskforce, accessed 16 October 2020.

<sup>&</sup>lt;sup>3</sup> This can be found at: https://github.com/publichealthengland/SIRA, accessed 15 October 2020.

<sup>&</sup>lt;sup>4</sup> This can be found at: https://github.com/cmmid/travel\_screening\_strategies, accessed 15 October 2020.

## 3 Overview of key findings

#### 3.1 Due to a number of methodological concerns with the PHE paper, we do not consider that PHE's estimates for the effectiveness of testing schemes can be relied upon

The PHE paper estimates that only 7% of travellers would be detected by a testing on arrival scheme. This value is derived from a theoretical model, which, by design, artificially lowers the rate of detection from airport testing on arrival.

The PHE paper does not state that any testing on departure or exit screening is considered in the analysis. However, the paper mentions that a potential traveller who is symptomatic or detectable prior to boarding their flight does not make it onto their flight. This suggests that there is a form of exit screening in the country of origin that prevents asymptomatic but detectable, or symptomatic travellers from boarding the plane. However, the PHE paper does not count the share of the infected travellers that are prevented from travelling due to departure testing towards the 7% figure. As these individuals would also be detected if they flew to the UK, they need to be accounted for in considering the effectiveness of a testing regime.

The way in which the PHE model is set up therefore means that only a very small proportion of passengers—those who become symptomatic or detectable by a PCR test during the flight—can be detected on arrival. Passengers who are symptomatic and therefore do not travel, or who are asymptomatic but can be detected by a test before departure, are not counted in determining the effectiveness of a testing scheme.

Even if we continue to exclude all symptomatic passengers who are detectable before flying, as PHE has done, if detectable asymptomatic passengers are included in estimating the effectiveness of a testing scheme, the 7% figure becomes approximately 33%.<sup>5</sup> This figure is more consistent with, although still lower than, the equivalent figures in the LSHTM and APHA papers. If all infected passengers (i.e. including detectable symptomatic passengers) who attempted to enter the UK population but were prevented from doing so were to be included in the estimate, this estimate would be 63%.

# 3.2 As all three papers use theoretical models, it is important to check the model assumptions and outputs against real-world data

There are a number of assumptions in the three papers that are not calibrated to real-world data. First, the PHE paper does not consider actual infection rates in the country of origin of flights in its analysis; however, this is required in order to contextualise the risk of 'seeding' and spreading local infections. While country infection rates are considered in both the LSHTM and APHA papers, the estimation methodologies (COVID-19 prevalence is scaled from deaths data) may warrant further consideration of differing comorbidity levels between countries (e.g. to reflect higher levels of obesity).

Second, none of the papers take account of the demographics of infected people in a country compared with those of people who are likely to fly. COVID-19 infections have been higher in more deprived communities, which is the population that typically has a lower propensity to fly (particularly long-

<sup>&</sup>lt;sup>5</sup> This is the case using PHE's assumption that 50% of infected passengers are asymptomatic.

haul). If infection rates are corrected for demographics, the infection rates would be likely to be lower than those currently modelled.

Finally, it is important that the outputs of these models are calibrated to realworld data as far as possible. Benchmarking against real-world testing schemes in regions with extensive travel testing schemes in place, such as Jersey, will be considered in our forthcoming literature review and modelling reports.

#### 3.3 Variation in core modelling assumptions

All three papers are based on a simulation modelling technique known as Monte Carlo simulation. This modelling approach is highly parameterised, which means that the assumptions are critical to the outputs. The assumptions used vary substantially across the three papers. For example:

- the modelled detectability of passengers varies over time in different ways between the papers. The PHE paper assumes that the probability of being detected increases over time and peaks at the end of the 14-day quarantine period, which is not consistent with empirical evidence. In the LSHTM paper the probability of detection seems unreasonably low especially for asymptomatic travellers (only 48%), and in the APHA paper the probability of detection varies depending on who administers the test;
- passenger volumes are between 1% (LSHTM) and 40% (APHA) of 2019 levels;
- infected passengers in the PHE model remain infected forever, which is unlikely to be the case as some people will cease to become infectious in the days after they land. The LSHTM and APHA papers include different measures, such as infectious days.

For some of these assumptions, there is no consensus in the empirical evidence on the correct values. For this reason, it is critical to consider the sensitivity of the model results to changes in assumptions. The APHA paper is the only paper that includes a sensitivity analysis for key parameters, such as COVID-19 prevalence.

# 3.4 Non-compliance with quarantine restrictions is not properly considered

Only the APHA paper considers non-compliance with quarantine requirements (20% non-compliance), although this does not vary over time (i.e. non-compliance is as likely on day one as on day 13). Both PHE and LSHTM assume 100% compliance, which is inconsistent with evidence regarding compliance with quarantine. For example, SAGE has cited that only 'around 20% of those reporting symptoms of Covid-19 in England report fully self-isolating by staying at home.'<sup>6</sup> Assuming that all passengers comply with quarantine requirements will lead to an overestimation of the benefit of a 14-day quarantine period relative to alternative scenarios that include testing.

#### 3.5 There is no clarity on what level of risk should be tolerated

The papers assume that the objective of the testing strategy would be to reduce the risk of seeding community transmissions from passengers to zero. This appears to be the basis of the model used by PHE for its paper, which

<sup>&</sup>lt;sup>6</sup> Scientific Advisory Group for Emergencies (2020), 'Multidisciplinary Task and Finish Group on Mass Testing', 11 September, para 9.

was developed prior to 2020 and references only passengers from China as being a risk of introducing infection.

This is an understandable starting point, particularly as the initial premise of the modelling would have been to prevent infection reaching the UK. However, completely removing the risk of COVID-19 associated with travellers is inconsistent with the sustained level of community transmission in the UK and policies that have been implemented in other sectors, such as for leisure activities. It is also inconsistent with the government policy of establishing travel corridors and therefore allowing individuals from countries with certain levels of COVID-19 to enter the UK without quarantining. Furthermore, introducing a testing scheme in place of travel corridors could reduce the risk of transmission from passengers as some individuals who would otherwise not have had to quarantine would be required to do so if they have a positive test.

We therefore consider that the risk posed by travellers needs to be assessed in the context of the risk these infectious travellers pose to the UK population over and above the pre-existing community transmission risk and the level of risk accepted by the implementation of other government policies.

We also note that if the UK is seeking to pursue an elimination strategy, such as that in place in Australia, then arriving passengers should not be permitted to quarantine with other people (e.g. household members). Under the current rules this is permitted in the UK, even though quarantine rules do not apply to other household members. However, the papers do not consider the potential for infections to spread to other household members from an arriving passenger, or vice versa. In some cases, the risk of a returning passenger catching the disease from members of their household will be a higher risk than them having and transmitting the disease.

## 4 Review of the Public Health England paper

#### 4.1 Introduction

The PHE paper uses a Monte Carlo simulation model to assess the effectiveness of requiring all incoming travellers to the UK to undergo two rounds of PCR-type testing. PHE notes that it considers one test at arrival at the UK border and one test at another point before the end of the person's quarantine. Three different isolation periods of 7, 10 and 14 days are assessed, with tests administered after 5, 8 and 10 days respectively. This is compared against a baseline of performing PCR testing only on arrival. The paper also considers different flight types, categorising flights into short, medium- and long-haul.

PHE finds that testing on arrival would detect only 7% of infected travellers. The detection rate is significantly improved when second tests are administered 5, 8 and 10 days after arrival to 85%, 96% and 98% respectively.

We consider that there are some significant methodological concerns with the analysis undertaken in this paper, which lead to an underestimation of the proportion of infected travellers that are detected on arrival. In addition, there are several assumptions used in the modelling of detection rates that do not appear to be based on the most recent empirical evidence. Below, we set out our key concerns with the analysis in the PHE paper.

#### 4.2 Effect of testing on departure and arrival

We note that the PHE paper does not state that any testing on departure or exit screening is considered in the analysis. However, the paper mentions that a potential traveller who is symptomatic or detectable 'prior to boarding their flight [...] does not make it onto their flight' because of '*exit screening* or the traveller being too ill to fly' (p. 6, emphasis added). Although not mentioned at the outset of the PHE paper, this suggests that there is a form of exit screening in the country of origin that prevents asymptomatic but detectable travellers from boarding the plane. Therefore, the results in the paper should be interpreted as the effect of testing on arrival and exit. However, as detailed in the next section, the PHE paper does not count the share of the infected travellers that are prevented from travelling due to departure testing towards the 7% figure. The effectiveness of a departure and arrival testing regime is therefore significantly understated.

#### 4.3 Model set-up leads to low detection rates for testing on arrival

While the PHE paper assumes that all individuals intending to fly are infected (see section 4.5 below), only a proportion actually board the plane and travel to the UK. This is because the PHE paper makes the assumption that 100% of the symptomatic as well as the asymptomatic passengers who are detectable at the time of boarding do not fly. As these potential travellers are identified before exiting their country of origin, they are not counted towards the percentage of passengers detected (the 7% figure). However, this part of the infected population would also be detected if they flew to the UK and therefore need to be accounted for in considering the effectiveness of a testing regime. Hence, the paper bases its results on a false premise by assuming, but not accounting for, departure testing.

By suggesting that 100% of asymptomatic passengers who are detectable at the time of boarding do not fly, the PHE paper implicitly assumes that there are exit strategies in place to prevent these individuals from boarding, which are not only 100% accurate but also take place right before take-off. For asymptomatic passengers, this would mean that there is no gap between a test being administered and a passenger getting on a flight. If departure testing were made to be reflective of current processes, the paper would need to account for a gap of several hours or days between these two events. In this case, there would be the potential for an individual to become detectable while waiting for the results to arrive and hence board while being infected. Passengers who become detectable while waiting for departure test results would increase the detection rates on arrival.

We also note that PHE assumes that 100% of symptomatic passengers do not fly. We consider that this may actually be an overestimation and is inconsistent with the assumption included in the LSHTM paper that only 70% of symptomatic passengers do not fly. APHA also assumes that only a subset of symptomatic passengers do not fly; the exact percentage depends on the country of origin, type of exit screening, symptoms (cough, fever, etc.) and incubation period. Assuming that a proportion of symptomatic passengers board a plane to the UK would further increase the detection rates on arrival.

Essentially, the PHE paper uses the wrong denominator to calculate the effectiveness of pre-departure and on-arrival testing without any mandatory quarantine scheme. Instead of considering only the number of people successfully boarding an airplane, the more appropriate denominator would be all infected passengers aiming to fly to the UK. This is especially true for asymptomatic passengers, who would—without an exit screening test— board the airplane.

The set-up of the model used by PHE therefore considers that only individuals who meet the following characteristics are detected on arrival.

• First condition:  $t_{0+t_{dep}} < t_{symp}$ 

i.e. at the time of departure  $(t_{dep})$ , the time since exposure to virus is less than the incubation period until the onset of symptoms  $(t_{symp})$ , which the PHE paper assumes is the point in time at which an infection is detectable (by means of either a patient becoming symptomatic or a PCR test). This represents the proportion of passengers whose infection cannot be detected *before* departure.

• Second condition:  $t_{0+t_{dep}} + t_{flight} \ge t_{symp}$ 

i.e. the time since exposure to the virus plus a flight time between three to 13 hours is greater than the incubation period. This represents the proportion of passengers whose infection can be detected *on arrival*.

Therefore, only passengers who become symptomatic/detectable **during the flight** can be detected on arrival. Clearly, this is a very small proportion of all passengers. Detection rates on arrival are therefore low based on the way the model is constructed. One of the key variables affecting detection rates in this model set-up is the flight time ( $t_{flight}$ ), which is the reason why detection times on long-haul flights appear to be almost triple those of short-haul flights (see PHE paper, results table, p. 4).

To illustrate this, consider a plane with 100 seats. The incubation/detection period density used by PHE indicates that around 50% of passengers will have become symptomatic/detectable after 5 days (see Figure 4.1). Using a uniform distribution of time since exposure over the 14 days prior to boarding, this implies that around 60 passengers will have developed symptoms or will be

detectable at the time of departure.<sup>7</sup> All of these passengers are prevented from boarding and are therefore not counted towards the percentage of infected passengers that are prevented from entering the UK population without a quarantine scheme (and therefore the effectiveness of a testing on arrival scheme). A more appropriate representation of the usefulness of a testing regime would be to calculate the percentage of infected passengers that attempted to enter the UK population but were prevented from doing so. In this example, that percentage would be 63% instead of 7%.<sup>8</sup>

The results presented in the PHE paper contradict the results of other studies. The LSHTM paper, for instance, quotes detection rates of about 45% for a testing on arrival scheme (see Figure 4 (A) on p. 13). The APHA paper quotes detection rates of 39.6% (CI 35.2 - 43.7%) for a testing on arrival scheme.

## 4.4 Application of an incubation period density function to model detection rates

The PHE paper uses detection and incubation periods as key inputs into the analysis. The incubation period ( $T_{inc}$ ) describes the length of time that passes between infection ( $t_0$ ) and the onset of symptoms ( $t_{symp}$ ) for patients with COVID-19, conditional on patients being symptomatic. The incubation period density function used by PHE measures the probability that an individual with COVID-19 will develop symptoms at a given point in time.

The detection period  $(T_d)$  describes the length of time that passes between infection  $(t_0)$  and detectability  $(t_{detec})$  of COVID-19. A detection period density function is used to determine the probability that an individual with COVID-19 will test positive at any given point in time after contracting the virus.

The PHE paper incorrectly uses an incubation curve to model both the incubation and detection probabilities, rather than using a separate detection curve to model the probability of detection. While there is a correlation between incubation and detectability, the probabilities assigned to detection are likely to be incorrect as a result of using the incubation curve.

For example, for symptomatic travellers the incubation curve assumes that individuals cannot be detected before they have symptoms. Because this curve is then also used as the detection curve, it assumes that the probability distribution of asymptomatic travellers being detected is the same as the probability of symptomatic travellers developing symptoms (i.e. if there is a 10% likelihood that symptomatic travellers will develop symptoms on day 4, then there is a 10% likelihood that asymptomatic travellers would be detected by a test on day 4.)

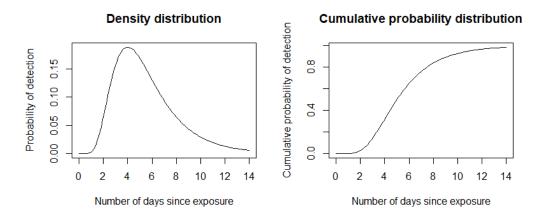
Figure 4.1 plots the incubation period density function and corresponding probability function that the PHE paper uses to model detection rates. This curve implies that the probability of returning a positive test for a randomly selected infected patient after 5 days is about 40%. However, it also assumes that detectability is increasing over time. As can be seen on the right hand chart of Figure 4.1, an infected traveller would be 100% detectable after 14 days of contracting the virus. This conflicts with empirical evidence that has

<sup>&</sup>lt;sup>7</sup> This follows the assumptions provided by the PHE paper (see p.7). The fact that approx. 60% of travellers are filtered out by some form of departure testing, exit screening or self-selection is supported by the figures cited in the results table, column 'non-flyers' (PHE paper, p.4).

<sup>&</sup>lt;sup>8</sup> This assumes that an additional 7% of on-flight passengers are detected upon arrival, as suggested by PHE. Based on the PHE results table (p.4), this is equal to 3% of the total population that intended to fly.

shown that detectability peaks around the time of symptom onset (at least for symptomatic patients), when the viral load is greatest, and reduces thereafter.<sup>9</sup>

Figure 4.1 Incubation period probability density and cumulative probability distribution



Source: Oxera and Edge Health based on incubation density provided in PHE paper, p.7.

Furthermore, some empirical evidence suggests that detection periods of PCR tests for COVID-19 infections do not coincide with incubation periods as the PHE paper assumes.<sup>10</sup> The LSHTM paper sets out a detection curve that shows that 5 days after contact with an infected person, already over 60% of COVID-19 infections can be detected with a PCR test.<sup>11</sup>

Using the incubation curve to model the detection curve as PHE has done might understate the detection rates. As has been shown elsewhere, presymptomatic patients can also be detected using PCR tests.<sup>12</sup> Moreover, the PHE paper incorrectly suggests that detectability strictly increases and peaks at the end of the infection, in spite of what empirical evidence indicates.<sup>13</sup>

#### 4.5 The model is not based on actual infection rates

The PHE paper does not take account of actual infection rates in the country of origin or destination. Instead, it models a hypothetical situation in which all passengers intending to fly to the UK are infected with COVID-19. Therefore, the results presented have only limited direct applicability to real-world decision making, where it is likely that only a small proportion of travellers would be infected.

It is important that the analysis takes account of the percentage of infected passengers, based on the prevalence of COVID-19 in the country of origin. Indeed, this approach has been adopted by a number of similar studies (including the LSHTM and APHA papers discussed below). More specifically, it

 <sup>&</sup>lt;sup>9</sup> For instance: Walsh, K. A., et al. (2020), 'SARS-CoV-2 detection, viral load and infectivity over the course of an infection: SARS-CoV-2 detection, viral load and infectivity', *Journal of Infection*, June.
 <sup>10</sup> Arons, M. (2020), 'Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility',

The New England Journal of Medicine, April.

<sup>&</sup>lt;sup>11</sup> See LSHTM paper, p. 9, figure 2(A).

<sup>&</sup>lt;sup>12</sup> Arons, M. (2020), 'Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility', *The New England Journal of Medicine*, April; Sakurai, A. et al. (2020), 'Natural History of Asymptomatic SARS-CoV-2 Infection.', *New England Journal of Medicine*, August.

<sup>&</sup>lt;sup>13</sup> For instance: Walsh, K. A., et al. (2020), 'SARS-CoV-2 detection, viral load and infectivity over the course of an infection: SARS-CoV-2 detection, viral load and infectivity.', *Journal of Infection*, June; Sakurai, A. et al. (2020), 'Natural History of Asymptomatic SARS-CoV-2 Infection.', *New England Journal of Medicine*, August. Sakurai et al. finds that the median number of days between the first positive and two consecutive negative PCR tests was 9 days (with an interquartile range of 6 to 11 and a range of 3 to 21) in asymptomatic patients.

would be useful to take account of local/regional infection rates and infection rates among the groups of people likely to travel. This is because COVID-19 rates in the 'traveller' population may not be the same as in the 'general' population.

It is also important to assess the risk arising from infectious travellers in the context of the local infection incidence in the destination country. The PHE paper does not put its results in the context of infection rates in the destination country and therefore does not assess whether travellers are likely to lead to an increase in infection rates.

#### 4.6 Empirical evidence for assumptions used in the model

Many of the assumptions used by PHE in assessing the probability of detection on arrival are not based on empirical evidence, or are not based on the most recent scientific evidence. We note that in some cases there are a wide range of estimates in the literature for certain parameters. It is therefore important to undertake sensitivity analysis to consider the impact of using different estimates on the results. For instance:

- Without reference to empirical evidence, the PHE paper assumes a test sensitivity of 100% (see p. 7). According to PHE, the probability of detecting an infected patient after his/her incubation time has passed is always equal to one. This contradicts empirical evidence, which shows that detectability varies across the period of COVID-19 infection.<sup>14</sup>
- The risk of transmission from an international traveller infected with COVID-19 depends on how infectious that person is and how long that individual's infectious period lasts upon entry into the UK population. The PHE paper does not perform any analysis of infectiousness or the amount of remaining infectious days. It thereby treats an infected passenger who contracted COVID-19 13 days prior to the flight and is only infectious for a very limited period of time upon entry (or not infectious at all) exactly the same as a passenger who contracted the virus an hour before departure and will spend the majority of their infectious period in the UK.
- Without providing any reference to empirical evidence, the PHE paper assumes that 50% of travellers become symptomatic. The scientific literature provides a range of estimates for the proportion of asymptomatic COVID-19 patients. Whereas a World Health Organization publication from March 2020 suggested that 80% of COVID infections are asymptomatic,<sup>15</sup> more recent evidence from the Centers for Disease Control and Prevention (CDC) in September 2020 estimated that the proportion of asymptomatic COVID-19 patients was 40%.<sup>16</sup> Furthermore, a meta-study published in the *Journal of Medical Virology* from July 2020 found that 16% of COVID-19 infections did not lead to any symptoms.<sup>17</sup> Given the uncertainty around this assumption, we consider that it would be important to conduct sensitivity analysis.

 <sup>&</sup>lt;sup>14</sup> For instance: Walsh, K. A., et al. (2020), 'SARS-CoV-2 detection, viral load and infectivity over the course of an infection: SARS-CoV-2 detection, viral load and infectivity', *Journal of Infection*, June.
 <sup>15</sup> WHO (2020), 'Coronavirus Disease 2019 (COVID-19), Situation Report – 46', 6 March, accessed October

<sup>15, 2020.</sup> 

<sup>&</sup>lt;sup>16</sup> COVID-19 Pandemic Planning Scenarios', updated 10 September 2020. Available at:

https://www.cdc.gov/coronavirus/2019-ncov/hcp/planning-scenarios.html, accessed 15 October 2020. <sup>17</sup> He, J. et al. (2020), 'Proportion of asymptomatic coronavirus disease 2019: A systematic review and metaanalysis', 21 July, accessed 15 October 2020.

• The incubation period probability density function is based on a paper from the very early period of the COVID-19 pandemic (February 2020).<sup>18</sup> While more recent evidence may not change the probability density function substantially, the assumptions on incubation periods should be updated to reflect more recent studies and available meta-analyses.<sup>19</sup>

<sup>&</sup>lt;sup>18</sup> The PHE paper extracts the incubation period distribution from Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data, by N. Linton et al., from

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7074197/, accessed October 15, 2020.

<sup>&</sup>lt;sup>19</sup> For instance see McAloon, C., Collins, A., Hunt, K., et al. (2020), 'Incubation period of COVID-19: a rapid systematic review and meta-analysis of observational research', *BMJ Open 10(8)*, August.; or Li, Q., Guan, X., Wu, P., et al. (2020), 'Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia', *New England Journal of Medicine*, March; or Lauer, S.A., Grantz, K.H., Bi, Q., et al. (2020), 'The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application', *Annals of Internal Medicine* 172(9), May.

## 5 Review of the LSHTM paper

#### 5.1 Introduction

Like the PHE paper, the LSHTM paper uses a Monte Carlo simulation methodology to assess the effectiveness of testing and quarantine policies in preventing the introduction of COVID-19 infections into the UK through international travel. The paper focuses on passengers travelling to the UK from the EU or the USA. It compares the effects of passengers quarantining for 6, 8 and 14 days and being tested at the airport and at a later point during the period of quarantine, with a scenario of no quarantine and no test on arrival. The paper finds that quarantining travellers for 6 days with a test on day 5 reduces the number of infectious travellers released into the community by (a median of) 88%. Quarantining for 8 days with a PCR test on day 7 can reduce the number of infectious arrivals released into the community by (a median of) 94%, while quarantining for 14 days leads to a (median) reduction of 99%. Results are also expressed in terms of infectious travellers screened per 10,000 travellers.

In addition to considering the effect of two separate tests on arrival, including one a certain number of days after arrival, LSHTM considers the effectiveness of just one test on arrival compared with a no-test, no-quarantine scenario. It finds that testing on arrival reduces the number of infectious travellers released into the community by about 45% (see Figure 4 (A) on p. 13). This can be directly compared with the 7% figure from the PHE paper, which claims to estimate results based on the same scenario.

There are a number of assumptions used in the LSHTM paper that could be refined. We consider these below.

#### 5.2 Infection rates

The paper calculates the rate of infection in the origin country using a scaling methodology based on reported deaths. While the resulting infection prevalence estimates generally perform well against studies on seroprevalence,<sup>20</sup> LSHTM does note that they do not account for differing underlying age structures between countries.<sup>21</sup>

A follow-up study used in the APHA paper (see section 6) to estimate infection prevalence does account for underlying differences in age structures between countries.<sup>22</sup> However, neither study accounts for differing levels of comorbidities between countries. Earlier research has attempted to do this using life tables to scale infection fatality ratios (IFRs) between countries.<sup>23</sup> Initial results from this suggest the need for further benchmarking to seroprevalence data and investigation of the trade-offs of this approach. However, in countries such as the USA, with relatively higher levels of comorbidities relative to many European countries, not accounting for comorbidities would lead to the IFR being underestimated, which would in turn lead to an overestimation of COVID-19 prevalence in the USA. Given the

<sup>&</sup>lt;sup>20</sup> Studies on seroprevalence use antibodies as markers of pathogen exposure to estimate the proportion of the population infected to date.

 <sup>&</sup>lt;sup>21</sup> Russell, T.W., Golding, N., Hellewell, J., Abbott, S., Wright, L., et. al. (2020), 'Reconstructing the early global dynamics of under-ascertained COVID-19 cases and infections', *medRxiv*.
 <sup>22</sup> Patel, V., McCarthy, C., Taylor, R.A., Moir, R., et al. (2020), 'An improved methodology for estimating the

 <sup>&</sup>lt;sup>22</sup> Patel, V., McCarthy, C., Taylor, R.A., Moir, R., et al. (2020), 'An improved methodology for estimating the prevalence of SARS-CoV-2', *medRxiv*.
 <sup>23</sup> Bohk-Ewald C., Dudel, C., Myrskyla, M. (2020), 'A demographic scaling model for estimating the total

<sup>&</sup>lt;sup>23</sup> Bohk-Ewald C., Dudel, C., Myrskyla, M. (2020), 'A demographic scaling model for estimating the total number of COVID-19 infections', *medRxiv*.

uncertainty associated with estimating this parameter, we consider that a sensitivity analysis should be undertaken.

#### 5.3 Passenger mix

The LSHTM paper does not control or adjust for the demographics of infected people in a country compared with those of people who are likely to fly. COVID-19 infections are higher in more deprived communities, which is the population that typically has a lower propensity to fly. If infection rates are corrected for demographics, these would be likely to be lower than those currently considered or modelled. This is particularly the case for long-haul passengers.

#### 5.4 Sensitivity of PCR testing

The LSHTM paper assumes a *maximum* test sensitivity of approximately 77% for symptomatic travellers (see Figure 2A on p. 9). This is based on fitting a binomial Generalised Additive Model (GAM) to data collated by Kucirka, Lauer, Laeyendecker, Boon and Lessler (2020).<sup>24</sup> This is in contrast to other recent studies that have estimated maximum sensitivity to be approximately 91% (see Figure 1 in the supplementary appendix).<sup>25</sup>

For asymptomatic travellers, the paper assumes a sensitivity that is 38% lower than that of symptomatic travellers (see Table 3 on p. 8). This is based on a study reporting that asymptomatic individuals are 38% less likely to test positive at the beginning of their infection period. However, this does not mean that asymptomatic individuals are 38% less likely to test positive throughout their infection period, as assumed in the LSHTM paper.

The combination of these assumptions implies that *at most* 48% of asymptomatic infected travellers can be detected by a single test, however this is significantly lower than the maximum sensitivity found in recent studies.<sup>26</sup>

# 5.5 Assumptions around non-compliance with self-isolation guidelines

The current policy that individuals need to quarantine for 14 days when they arrive from certain countries assumes that infection is present in arriving passengers. While some people, particularly those with some symptoms, may quarantine properly for the full 14 days, others will not.

If there is no testing, combined with an absence of symptoms, travellers are more likely to mix more actively with their household (or people in their hotel), meet friends at home, and even break quarantine. A positive test result would reduce these cases where the infection is likely to be transmitted. Indeed, with limited enforcement of quarantine restrictions (from 8 June to 7 September, 34 fixed penalty notices for breaches of international travel measures were issued in the UK),<sup>27</sup> lower levels of compliance should be expected in the absence of a positive test to confirm an infection.

A survey commissioned by IATA and referenced in the LSHTM paper found that 17% of respondents would be unwilling to undergo quarantine. It is

<sup>&</sup>lt;sup>24</sup> Kucirka, L. et al., (2020), 'Variation in False Negative Rate of RT-PCR Based SARS-CoV-2 Tests by Time Since Exposure', 13 May.

<sup>&</sup>lt;sup>25</sup> Grassly, Nicholas C et al., (2020), 'Comparison of molecular testing strategies for COVID-19 control: a mathematical modelling study', The Lancet Infectious Diseases, Volume 0, Issue 0, 18 August.
<sup>26</sup> ibid.

<sup>&</sup>lt;sup>27</sup> Border Force (2020), 'Data on health measures at the UK border', 10 September. Available at: https://www.gov.uk/government/publications/data-on-health-measures-at-the-uk-border/data-on-health-measures-at-the-uk-border, accessed October 15, 2020.

possible that this number is an underestimation if people's revealed ability to quarantine is lower than stated in advance. A recent study by King's College London found that 70% of respondents who had not experienced COVID-19 symptoms over the past week intended to self-isolate if symptoms arose. However, only 18.2% of respondents who did report COVID-19 symptoms over the past week reported that they had in fact self-isolated.<sup>28</sup> More recently SAGE has cited that only 'around 20% of those reporting symptoms of Covid-19 in England report fully self-isolating by staying at home.'<sup>29</sup> The risk of non-compliance with quarantine rules is not included as a sensitivity in the LSHTM paper.

Equally, providing a false-negative test may result in overconfidence of an infected traveller who then chooses to mix more than normal and infects other people more than would otherwise have been the case. To assess this risk, the number of infected and asymptomatic arriving passengers with a false-negative test can be compared with the level of current infections in the UK population.

<sup>&</sup>lt;sup>28</sup> Smith L. et al (2020), 'Adherence to the test, trace and isolate system: results from a time series of 21 nationally representative surveys in the UK (the COVID-19 Rapid Survey of Adherence to Interventions and Responses [CORSAIR] study', 18 September.

<sup>&</sup>lt;sup>29</sup> Scientific Advisory Group for Emergencies (2020), 'Multidisciplinary Task and Finish Group on Mass Testing', 11 September, para 9.

## 6 Review of the APHA paper

#### 6.1 Introduction

The APHA paper uses a Monte Carlo methodology to assess the effectiveness of testing and quarantine policies in preventing the introduction of COVID-19 to the UK through international travel. The paper models the impact of various self-isolation policies on travel between the UK and the 25 countries with the highest air traffic volumes to the UK, estimating both: the effectiveness of different quarantine and testing policies, expressed as a percentage; and the number of cases detected by these policies.

In order to estimate the probability of a passenger being infected, the paper considers the following cohorts of travellers:

- non-UK travellers who were infected in the origin country prior to travel;
- returning UK travellers who were infected prior to travelling to the country;
- returning UK travellers who were infected during their trip.

Of the three papers we have reviewed, this paper takes the most granular approach to modelling the development of COVID-19 symptoms, assuming different probability distributions for different types of symptoms (e.g. cough, fever).

The paper examines several policies, including thermal imaging scanners, health checks, single RT-PCR taken at the airport or 4 or 7 days after arrival; double testing RT-PCR, first at the airport and then 4 days or 7 days after arrival; and self-isolation for 7, 10 or 14 days. In contrast to the PHE and LSHTM papers, the APHA paper does not assume 100% compliance with self-isolation, and instead uses a non-compliance rate of 20% until a positive COVID-19 test is received. Testing 4 days after arrival is estimated to reduce the number of infectious arrivals released into the community by 64.3%, a test on arrival and an additional test four days later is estimated to reduce the number of infectious arrivals released into the community by 68.9%, and 14-day quarantine measures are estimated to reduce the number of infectious arrivals released into the community by 78%.

Testing on arrival is estimated to reduce the number of infectious arrivals released into the community by 39.6%. This can be directly compared with the 7% figure from the PHE paper, which claims to estimate results based on the same scenario.

Overall, there are a number of assumptions used in the paper that could be refined or that may not be reflective of the most up-to-date evidence.

#### 6.2 Infection rates

The paper calculates the rate of infection in the origin country using a scaling methodology based on reported deaths. Unlike the LSHTM paper, the methodology used in this paper accounts for different age structures between countries. It also uses estimated prevalence as an input for a sensitivity analysis of the model. However, as with the LSHTM paper, this paper does not account for differing levels of comorbidities between countries. Earlier research attempts to do this using life tables to scale IFRs between countries.<sup>30</sup> Initial

<sup>&</sup>lt;sup>30</sup> Bohk-Ewald C., Dudel, C., Myrskyla, M. (2020), 'A demographic scaling model for estimating the total number of COVID-19 infections', *medRxiv*.

results from this study suggest the need for further benchmarking to seroprevalence data and investigation of the trade-offs of this approach. However, in countries such as the USA, with relatively higher levels of comorbidities relative to many European countries, not accounting for comorbidities would lead to the IFR being underestimated, which could in turn lead to an overestimation of COVID-19 prevalence in the USA.

#### 6.3 Passenger mix

The APHA paper does not control or adjust for the demographics of infected people in a country compared with those people who are likely to fly. COVID-19 infections are higher in more deprived communities, which is the population that typically has a lower propensity to fly. If infection rates are corrected for demographics, these would be likely to be lower than those currently modelled. This is particularly the case for long-haul passengers.

#### 6.4 Proportion of asymptomatic travellers

The APHA paper assumes that 50% of travellers are asymptomatic, referencing a paper on varying COVID-19 presentation levels based on age structure.<sup>31</sup> This would suggest that the percentage of asymptomatic travellers should vary depending on the country of origin and its age structure. However, only one parameter (50%) is used by APHA. As mentioned in section 4, the scientific literature provides a range of estimates for the proportion of infected individuals who are asymptomatic. Given the uncertainty around this assumption, we consider that it would be important to conduct sensitivity analysis.

#### 6.5 Sensitivity of PCR testing

Unlike the LSHTM paper, APHA assumes uniform sensitivity of PCR tests. This is set to 0.95 for the first test administered at the airport, and to 0.66 for the second test (if administered). The difference between the sensitivities is attributed to the fact that the first test is administered by a healthcare professional, while the second one is self-administered. It may be reasonable to assume different sensitivities between the first and the second PCR tests (although the evidence is limited), but the paper does not account for the fact that the detectability of the virus varies throughout the infection period. Infection is less detectable at the very early or very late stages of disease progression and this is not modelled.

### 6.6 Including UK travellers in infectious incoming traveller estimates

The APHA paper considers the scenario where passengers are infected in the UK, travel to another country, then return to the UK. While this represents a realistic scenario and this cohort should be reflected in the percentage of cases detected through different screening policies, the interpretation of the results including this cohort is important. When considering the total number of infections introduced to the UK through travel, this cohort should not be included as they would have spread the infection had they remained in the UK (perhaps even to a greater extent) even if they had not travelled.

<sup>&</sup>lt;sup>31</sup> Davies, N. et al (2020), 'Age dependent effects in the transmission and control of COVID-19 epidemics', 16 June, accessed 15 October 2020.

### A1 Overview of key assumptions in the papers

In the table below, we set out the key assumptions included in the PHE, AHPA and LSHTM papers. We also highlight how the estimates from the different papers compare, and note that in many cases the three papers have very different assumptions.

\* Denotes no source.

 Table A1.1
 Key assumptions in the PHE, AHPA and LSHTM papers

Model input		PHE	АРНА	LSHTM	Evaluation and comparison
Number of people intending to fly	Value	100,000*	40% of weekly volumes of August 2018 (non-EU) and August 2019 (EU) <sup>32</sup>	1% of July 2019 volumes <sup>33</sup>	By assuming that only 1% of July 2019 flights take place, the LSHTM paper is likely to understate the absolute number of infected travellers seeking to enter the UK. The current proportion of passengers entering the UK is significantly above 1% and is likely to further increase as quarantine restrictions are eased
Departure countries	Value	Does not consider specific departure countries*	Top 25 countries in terms of arriving passenger volumes that account for 86% of flights into UK airports in August <sup>34</sup>	EU and USA*	

<sup>&</sup>lt;sup>32</sup> 'Ryanair to restore 40% of scheduled flights from 1 July' Available from: https://corporate.ryanair.com/news/ryanair-to-restore-40-ofscheduled-flights-from-1-july/

<sup>&</sup>lt;sup>33</sup> Airport data 2020 05 | UK Civil Aviation Authority. Available from: https://www.caa.co.uk/Data-and-analysis/UK-aviation-market/Airports/Datasets/UK-Airportdata/Airport-data-2020-05/

<sup>&</sup>lt;sup>34</sup> Eurostat Bulk Download Listing. Available from: http://ec.europa.eu/eurostat/estat-navtree-portletprod/BulkDownloadListing.

Model input		PHE	АРНА	LSHTM	Evaluation and comparison
Duration of flight	Value	Sampled from a uniform distribution on the ranges [3,5], [7,9] or [11,13]*	Calculated based on the distance of each country to each UK airport and the average speed of a plane. While this does not take into account stopovers for longer journeys, it is a reasonable estimate of journey time. The distance is calculated using the latitude and longitude of UK airports and the centre of each country, as APHA does not know which airport in the country the flights are leaving from <sup>35</sup>	2 hours for EU flights and 8 for USA flights*	PHE does not consider flights of under 3 hours' duration, which are common within the EU. Additionally, when calculating the proportion of passengers testing positive PHE uses an unweighted passenger mix, rather than weighting the results across the different flight time categories
Proportion of infected passengers (prevalence estimates)	Value	100%*	Based on the prevalence in the departure country (if the traveller is non-UK or UK but was infected during the trip) and UK prevalence (for UK travellers who were infected prior to their departure from the UK). Assumes 51% of UK travellers <sup>36</sup>	Estimates of current COVID- 19 infection prevalence are derived from reported cases and death time series data while adjusting for reporting delays and under-reporting based on case-fatality ratio estimates. EU-wide prevalence is calculated as a population-weighted mean of available country-level estimates of the non-UK EU countries (except Malta, for which a prevalence estimate is not available) <sup>37</sup>	PHE's assumption is unrealistic and is not based on real-world data. LSHTM's and APHA's assumptions are based on prevalence in the departure country, where the prevalence is calculated based on deaths, cases (and in the case of APHA, age profiles) of the countries. None of the three papers account for comorbidity mix, i.e. some countries might have on average less healthy populations and hence a prevalence calculated based on only death rates and age profiles will lead to an overestimate

 <sup>&</sup>lt;sup>35</sup> Open Flights: Airport, airline and route data. 2006. Available from: https://openflights.org/data.html.
 <sup>36</sup> Patel V, McCarthy C, Taylor RA, Moir R, Kelly LA, Snary EL., (2020), 'An improved methodology for estimating the prevalence of SARS-CoV-2.' 19 August. Available from: https://medrxiv.org/cgi/content/short/2020.08.04.20168187v1; Horsfield G. (2020), 'Travel trends: 2019'. Office for National Statistics. Available from:

https://www.ons.gov.uk/peoplepopulationandcommunity/leisureandtourism/articles/traveltren <sup>37</sup> Russell TW, Joel Hellewell SA, Golding N, Gibbs H, Jarvi CI, Kevin van Zandvoort, et al. (2020), 'Using a delay-adjusted case fatality ratio to estimate under-reporting.' 25 June. Available from: https://cmmid.github.io/topics/covid19/global\_cfr\_estimates.html; Russell TW, Wu J, Clifford S, Edmunds J, Kucharski AJ, Jit M. (2020), 'The effect of international travel restrictions on internal spread of COVID-19.' Available from: https://www.medrxiv.org/content/10.1101/2020.07.12.20152298v1

Model input		PHE	APHA	LSHTM	Evaluation and comparison
Proportion of asymptomatic cases	Value	50%*	50% <sup>38</sup>	3-55% - Beta(1.9, 6.3), Median: 0.21, IQR: (0.12, 0.32), 95%: (0.03, 0.55) - derived from quantile matching, 95%:(0.03, 0.55) <sup>39</sup>	PHE's assumption is not supported by evidence. APHA's assumption appears to be an overestimation as there are multiple sources stating that the asymptomatic proportion is significantly lower
Infection start (i.e. the number of days between becoming infected and travelling)	Value	A start day for infection is modelled by uniform distribution (0,14)*	A start day for infection is modelled by uniform distribution (0,30)*	A start day for infection is modelled by uniform distribution (0,14)*	Neither the PHE paper nor the LSHTM paper considers the duration of the trip. If the trip was shorter than 14 days, it is likely that an infection could have originated in the UK and then returned back. PHE and LSHTM overlook these cases, which might lead to an overestimation of non-UK- originating infections detected on arrival
Incubation period (i.e. time from exposure to onset of symptom)	Value	Assume incubation period and model by log-normal distribution, with parameters $\mu$ = 1.6112, $\sigma$ = 0.47238 t <sup>40</sup>	Time from infection to developing cough is modelled by Gamma (4,1.375)), fever by Gamma (4,1.375), and getting severe symptoms by Gamma $(7,1)^{41}$	Gamma( $\mu$ = 5.5, $\sigma^{2}$ = 6.5) Median: 5.1 days IQR: (3.6, 6.9) days 95%: (1.7, 11.5) days; Derived from quantile matching with Median: 5.1 days, 97.5%: 11.5 days <sup>42</sup>	The PHE paper references a source from February 2020, which is outdated

<sup>&</sup>lt;sup>38</sup> Davies NG, Klepac P, Liu Y, Prem K, Jit M, Eggo RM. (2020), 'Age-dependent effects in the transmission and control of COVID-19 epidemics.'

<sup>&</sup>lt;sup>39</sup> Buitrago-Garcia DC, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. (2020), 'The role of asymptomatic SARS-CoV-2 infections: rapid living systematic review and meta-analysis.' Available from: https://www.medrxiv.org/content/10.1101/2020.04.25.20079103v2

<sup>&</sup>lt;sup>40</sup> Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data, by N. Linton et al. <sup>41</sup> Davies NG, Kucharski AJ, Eggo RM, Gimma A, Edmunds WJ. (2020), 'Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study,' Lancet Public Health, July (5):11–15.

<sup>&</sup>lt;sup>42</sup> Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. (2020), 'The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application'. May 5; 172(9): 577–82. Available from: http://dx.doi.org/10.7326/M20-0504

Model input		PHE	АРНА	LSHTM	Evaluation and comparison
Infectious period	Value	Assumed to be infinite for the purposes of the model*	Gamma (4,1.25) <sup>43</sup>	For symptomatic cases: Median: 7.1 days IQR: (5.7, 8.5) days 95%: (2.5, 11.6) days	PHE's assumption is highly theoretical and removes the possibility of individuals recovering throughout the flight/quarantine
				For asymptomatic cases: Gamma( $\mu$ = 6, $\sigma$ ^2 = 12) Median: 5.3 days IQR: (3.5, 7.8) days 95%: (1.2, 14.4) days <sup>44</sup>	
Symptomatic period (i.e. time after onset of symptoms until no longer symptomatic)	Value	An individual is assumed to be forever symptomatic (for the purposes of the model) after the incubation period*	Symptomatic period for cough is modelled by Gamma (4,0.875), and for fever by Gamma (4,0.875) <sup>45</sup>	Gamma( $\mu$ = 9.1, $\sigma^{2}$ = 14.7) Median: 8.6 days IQR: (6.3, 11.3) days 95%: (3.2, 18.0) days Derivation based on moment matching distributions <sup>46</sup>	PHE's assumption is highly theoretical and does not reflect the empirical evidence
PCR sensitivity	Value	The incubation period is assumed to be the period until detectability. Once detectable, a sensitivity of 1 is assumed*	Assumes a uniform sensitivity of 0.95 for the first PCR test carried out in the airport (assumed to be of high accuracy as performed by a health professional) and 0.66 for the second self- administered test. The sensitivity stays the same	Modelled as a function of the time since an individual's exposure by fitting a Generalised Additive Model (GAM), with a Binomial likelihood and penalised B-spline basis (P- spline), to the data collected by Kucirka et al. (2020). The	The PHE paper assumes that the virus becomes detectable at the same time as the person (if symptomatic) develops symptoms, and, in doing so, equates incubation and detectability. Assuming a sensitivity of 1 is overly optimistic. PHE also does not make a distinction between the sensitivity rates in symptomatic and asymptomatic cases, as well as between self-administered tests and tests administered by a healthcare

<sup>&</sup>lt;sup>43</sup> Davies NG, Kucharski AJ, Eggo RM, Gimma A, Edmunds WJ. (2020), 'Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study', Lancet Public Health, July (5):11–15

<sup>&</sup>lt;sup>44</sup> Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature [Internet]. 2020 May;581(7809):465–9. Available from: <u>http://dx.doi.org/10.1038/s41586-020-2196-x;</u> Byrne AW, McEvoy D, Collins A, Hunt K, Casey M, Barber A, et al. Inferred duration of infectious period of SARS-CoV-2: rapid scoping review and analysis of available evidence for asymptomatic and symptomatic COVID-19 cases [Internet]. Epidemiology. medRxiv; 2020. Available from: <u>https://www.medrxiv.org/content/10.1101/2020.04.25.20079889v1</u>

<sup>&</sup>lt;sup>45</sup> Davies NG, Kucharski AJ, Eggo RM, Gimma A, Edmunds WJ. (2020), 'Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study', Lancet Public Health, July(5): 11–15

<sup>&</sup>lt;sup>46</sup> Quilty BJ, Clifford S, Flasche S, Eggo RM, CMMID nCoV working group. Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV). Euro Surveill [Internet]. 2020 Feb;25(5). Available from: http://dx.doi.org/10.2807/1560-7917.ES.2020.25.5.2000080; Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med [Internet]. 2020 Mar 26;382(13):1199–207. Available from: http://dx.doi.org/10.1056/NEJMoa2001316

Model input		PHE	APHA	LSHTM	Evaluation and comparison
			throughout the infection period, i.e. an infection can be detected from day 0 <sup>47</sup>	probability of detecting an asymptomatic infection through PCR testing is 0.62 times that of a symptomatic individual's infection <sup>48</sup>	professional. The APHA paper assumes that the sensitivity of a PCR test is constant throughout the infection period (i.e. an infection is as likely to be identified at day 0 as it is at day 5). It does not account for the potential difference in detection rates between symptomatic and asymptomatic cases. The LSHTM paper does not account for the differences in sensitivity between self- administered tests and those administered by a healthcare professional
Proportion stopped from flying (symptomatic and asymptomatic)	Value	100%*	<ul> <li>Varies from country to country. It is assumed that a passenger will not fly due to:</li> <li>1) developing severe symptoms and hence choosing not to board;</li> <li>2) being symptomatic and hence identified by an exit health check.</li> <li>For 1), an individual needs to develop cough or fever AND those need to be severe enough to stop the passenger from boarding.</li> <li>For 2), different exit strategies have different sensitivities and hence will identify different proportions of infections. It is assumed that thermal imaging has a sensitivity of 0.86, and</li> </ul>	70% of travellers who are symptomatic at their intended departure time are either prevented from travelling or choose not to travel. 0% of asymptomatic infected travellers are stopped from boarding <sup>50</sup>	By assuming that all of the passengers with detectable infections do not fly, the PHE paper implies the use of exit strategies that are 100% accurate. These are never mentioned explicitly and the assumption about 100% sensitivity is optimistic. The exit strategies considered in the APHA paper seem to be overly sensitive. In addition, a uniform detection rate assumed for all the exit strategies means that once a symptom develops, it is equally likely to be detected at any point in time. The detectability rate of 70% of passengers assumed by the LSHTM paper might appear to be too high, although this cannot be supported by evidence as the symptoms would vary significantly between infected individuals

<sup>&</sup>lt;sup>47</sup> European Centre for Disease Prevention and Control. Methodology for estimating point prevalence of SARS-CoV-2 infection by pooled RT-PCR testing. Stockholm (Sweden): ECDC; 2020 May 28.; Kojima N, Turner F, Slepnev V, Bacelar A, Deming L, Kodeboyina Š, Klausner JD. SelfCollected Oral Fluid and Nasal Swabs Demonstrate Comparable Sensitivity to Clinician Collected Nasopharyngeal Swabs for COVID-19 Detection. MedRxiv 2020.04.11.20062372 [Preprint]. 2020 [cited 2020 Jun 9]. Available from: https://www.medrxiv.org/content/10.1101/2020.04.11.200623721 48 Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. (2020), 'Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction-Based SARS-CoV-2 Tests by Time Since Exposure' May 13; Available from: http://dx.doi.org/10.7326/M20-1495; Chau NVV, Thanh Lam V, Thanh Dung N, Yen LM, Minh NNQ, Hung LM, et al. (2020), 'The natural history and transmission potential of asymptomatic SARS-CoV-2 infection' Jun 4; Available from http://dx.doi.org/10.1093/cid/ciaa711

health checks have a

<sup>&</sup>lt;sup>50</sup> Gostic K, Gomez AC, Mummah RO, Kucharski AJ, Lloyd-Smith JO. Estimated effectiveness of symptom and risk screening to prevent the spread of COVID-19. Elife [Internet]. 2020 Feb 24;9. Available from: http://dx.doi.org/10.7554/eLife.55570

Model input		PHE	APHA	LSHTM	Evaluation and comparison
			sensitivity of 0.75. For 1), the proportion of individuals developing a cough is 0.777, and 0.601 for a fever. The proportion of individuals becoming severely ill is 0.185. The duration of these is also taken into account. For 2), different sensitivities are assumed for different exit check strategies (e.g. health checks and thermal scanners). The incubation period is also considered— this ensures that people who became infected earlier will be less likely to board <sup>49</sup>		
Exit strategies for preventing infected passengers from boarding and their sensitivities	Value	*	Country-specific data used to determine which detection measures are in place in the exit airports— primarily health checks (to identify a cough) and thermal imaging scanners (to identify a fever) <sup>51</sup>	*	The strategies considered by the APHA paper will be subject to constant changes and hence might be out of date
Non-compliance rate	Value	0%*	20%*	0%*	0% non-compliance rate is unrealistic, while 20% might be too low

<sup>&</sup>lt;sup>49</sup> Davies NG, Kucharski AJ, Eggo RM, Gimma A, Edmunds WJ. Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study. Lancet Public Heal. 2020;July(5):11–15 ; Boddington NL, Charlett A, Elgohari S, et al. COVID-19 in Great Britain: epidemiological and clinical characteristics of the first few hundred (FF100) cases: a descriptive case series and case control analysis. MedRxiv 2020.05.18.20086157 [Preprint]. 2020 [cited 2020 Jun 9]. Available from:

https://www.medrxiv.org/content/10.1101/2020.05.18.20086157v1 ; Priest PC, Duncan AR, Jennings LC, Baker MG. Thermal image scanning for influenza border screening: Results of an airport screening study. PLoS One. 2011;6(1)

<sup>&</sup>lt;sup>51</sup> iata.org [Internet]. COVID-19 Government Public Health Mitigation Measures; c2020 [cited 2020 Aug 13]. Available from: https://www.iata.org/en/programs/covid-19-resourcesguidelines/covid-govmitigation/.

