Air Travel, Public Health Measures and Risk in the context of COVID-19

A Brief Summary of Current Medical Evidence

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Introduction / Purpose of the document

This summary is intended to provide the scientific foundation to assessing risk related to air travel during COVID-19. As the pandemic continues, and as vaccination programmes are under way in most countries, the considerations behind decisions regarding travel will continue to change. This document aims to provide an up to date evaluation of those considerations, based on available scientific evidence. It should be read with attention to the date of the latest revision, as the state of knowledge will continue to evolve rapidly.

It is prepared in the context of vaccination progress being at different stages in different countries. Despite the best efforts by WHO to aim for vaccine equity, countries are achieving vaccination at wildly different rates and it appears likely that this will continue to be the case. Additionally, regulatory approval differs between states both between vaccine type and even within the same type, depending on place of manufacture. As a result, the risk assessment around travel between one pair of countries may be very different from the assessment for another pair of countries.

Part 1: Risk

Risk Assessment Frameworks

- An assessment of risk needs to consider both likelihood and consequence. Risk cannot be avoided but the risk of a process can be balanced against the benefits, and against the risks of the counterfactual, to assist those who are tasked with making decisions. In particular the risks of international travel must be balanced against the risks of maintaining restrictions which include economic, employment, social and health risks. Part of the risk assessment process for a country will be determining how much risk, related to importing cases of COVID-19, can be accepted; this in turn may depend on the state of the public health system to detect (contract tracing, testing facilities) and manage (isolation and health care system) those cases. It may also be influenced by political considerations in each state.

Flight-associated transmission

- Information on in-flight transmission is incomplete, but several published papers have examined instances of probable and possible flight-associated transmission. Documented instances are very few [Bae, Chen J, Choi EM, Eichler, Eldin, Freedman, Hoehl, Khanh, Murphy, Nir-Paz, Pavli, Schwartz, Speake, Swadi, Thompson HA] compared with the total numbers of travellers, and while it must be assumed that these reports greatly underestimate the actual incidence, there appears sufficient evidence to conclude that this risk is low, particularly when masks are worn. The papers referred to describe instances of probable/suspected transmission associated with flight: some had little or no evidence of flight-related transmission compared with other origins [Eldin, Murphy, Schwartz] and most described flights with 1 or 2 presumed secondary cases in close proximity to the index case [Bae, Chen, Hoehl, Pavli]. In the more recent studies the transmission was supported by whole genome sequencing [Choi EM, Eichler, Speake, Swadi].

- Since the start of the pandemic many protections have been added to commercial air travel aimed at preventing transmission [Khatib], and collectively have been referred to as the "Public Health Corridor" [ICAO]. One of the most obvious changes on-board is the implementation of mask wearing by passengers. There were few instances of suspected transmissions on flights when masks were worn by passengers [Nir-Paz, Swadi, Thompson, Eichler]. Universal wearing of face coverings appears to be an effective protection against spread via aerosols [Cheng]. Of all the presumed secondary cases in these published studies, half were from just two flights [Bhuvan, Khanh, Speake], on which mask-wearing by passengers was not yet normal practice. This finding is in keeping with other studies showing that the majority of spread in the population originates from a small minority of cases [Yang Q]. The mechanism in those unusual cases with multiple secondaries is likely to be related to airborne carriage of fine aerosols [Chen, Davis, Fennelly, Klompas].

- In terms of risk the airline cabin compares favourably with other indoor environments [Hadei, Rivera-Rios] including restaurants [Lu], buses [Shen], churches [James, Kateralis], gymnasiums [Jang], and high-speed trains [Hu]. The mechanism presumed in such indoor environments is aerosol transmission [Allen, Kateralis]. There is even a well-documented transmission in a quarantine facility where the only contact between primary and secondary (linked by genome sequencing) was non-simultaneous opening of their room doors to the same corridor [Eichler], once again pointing to suspended aerosols. It has been suggested [Allen] that the characteristics of airline cabin air supply (rapid air flow, increased air changes, and HEPA filtration) should be applied to these other indoor environments.

- In the aircraft environment, although some earlier studies (pre-COVID) pointed to the possibility of spread particularly across rows [Chen, Olsen, Wang&Galea, Wilder-Smith], supporting evidence for low transmission risk in flights comes from modelling with computational fluid dynamics [Davis, Davis, Pang] and a large experimental study using actual aircraft cabins [Kinahan]. A modelling study reinforces the gradient of risk with distance from source, suggesting lower relative risk with the "empty middle seat" [Dietrich] but does not account for mask wear, and conflicts with the more complex analysis above [Davis]. Finally, note that other factors may be relevant, and of particular note is that speech, particularly loud speech, may be an underestimated determinant of aerosol transmission [Andersson], and one which could be relevant to the apparent low risk of on-board spread.

- Travel encompasses an entire journey including not only aircraft but also surface transport (road/rail etc) and airports. Any discussion of air travel, or of its risk, needs to have all of those elements considered. In some of the studies above, it is not clear at what part of the journey transmission may have occurred.

- Most of the studies referred to above were undertaken prior to the appearance of more transmissible variants, which are discussed in part 3 of this report. In the absence of evidence to the contrary, it must be assumed that flight-related transmission of variants could be increased proportionately.

- Even if transmission during travel was completely eliminated, the much more challenging problem to solve is the risk of importation of cases which are incubating at the time of travel [Pana]. The main focus of this document is on factors relevant to importation risk. This is the risk to be weighed by countries in seeking to allow increased international travel, one which in many countries is managed with mandatory quarantine after arrival [Kiang].

- The surface route of transmission has been assessed as low when compared with droplet and aerosol routes – and dealt with by standard cleaning and disinfection practices. A US CDC report [CDC] suggested that "the risk of fomite transmission can be reduced by wearing masks consistently and correctly, practicing hand hygiene, cleaning, and taking other measures to maintain healthy facilities."

Part 2: Vaccinations and immunity – effect on risk

Impact of vaccines on severe disease/mortality, and transmission

- There is abundant evidence from clinical trials and real-world data that vaccination reliably prevents severe disease, hospitalisation, and death [Dagan, Pawlowski, Tenforde, Vahidy, Vasilieou] – even in the small minority who become infected after vaccination [Bernal]. What is less clear is the degree to which vaccination can prevent mild or asymptomatic infection – the likely pathway being that viral colonisation of the upper respiratory tract could result in shedding of virus before the immune response has fully been triggered and effected. Even in the scenario of a strong vaccine-mediated immune response [Lustig], the possibility remains that a proportion of mild or asymptomatic cases may not be prevented [Bleier]. Therefore, since asymptomatic transmission is an important contributor to transmission [Johansson, Letizia, Oran, Rasmussen, Ren], it is necessary to determine the extent to which vaccination will reduce transmission.

- A number of studies have provided results suggesting that vaccination also prevents infections of all severity, including asymptomatic [Amit, Bernal, Chodick, Dagan, Daniel, Menni]. Some specifically demonstrate reduction in asymptomatic infection [Angel, Haas, Jones, Lillie, Lumley, Milman, Pritchard, Sadoff, Shah, Tande, Weekes], in most cases by a large percentage. Others demonstrate that onward transmission is largely reduced, looking at data on transmission within families [Harris, Salo, Shah], within residential care communities [Cavanaugh, De Salazar, Monge] or amongst regularly screened employees [Keehner, Swift, Tang].

- An alternative approach is to model the predicted transmission from general efficacy trials [Lipsitch], also suggesting transmission is low in those vaccinated. Another is to look at viral load, which correlates with infectiousness [Marc, Marks]. There is animal evidence that vaccination leads to reduced viral load in the unvaccinated population, and human evidence that those who become infected post-vaccination have reduced viral load [Levine-Tiefenbrun, McEllistrem] . Note that immune response may vary with age [Moustsen-Helms, Müller, Yang HS]. Antibodies detected in the upper respiratory tracts of vaccinated people, both IgA and IgG [Becker, Mades, Sterlin] suggest a mechanism for reduced transmission.

- Taken together, these findings point to significant reduction in transmission by those who have been fully vaccinated [Richterman]. The question of duration of immunity and the effect of variants are both discussed below. Some vaccines may perform better than others, and this is likely to be a factor considered by countries in permitting international travel. One group that shows reduced immune response from vaccination is the immunosuppressed, particularly solid organ transplant recipients [Boyarsky].

- Most of these studies show that the vaccines prevent asymptomatic transmission somewhat less efficiently than symptomatic, therefore it is likely that a high proportion of those "breakthrough" cases occur in a vaccinated community will be asymptomatic [Gruskay, White]. This observation may prompt consideration of some surveillance testing of vaccinated travellers in communities with a low tolerance for introduced cases – even though they will have reduced chance of onward transmission.

Duration of immunity following vaccination or infection

- Studies point to immunity being established within two weeks after vaccination [Gupta] and retained beyond 6 months following vaccination [Doria-Rose, Hall, Pegu]. Immunity is complex, and laboratory studies looking only at antibody production do not tell the full story of immunity which involves cellular and local responses as well. Cell-mediated immunity may be maintained even with declining antibody levels [Geers, Tarke]. Studies have been conducted to evaluate booster doses [Wu], and delayed second dose [Abu-Raddad]. Using a different vaccine for the second dose from the first, known as "heterologous prime-boost," has shown strong or enhanced antibody response [Barros-Martins, Frias, Groß]. Immunity following vaccination has been demonstrated in pregnant and lactating women [Collier Y], with reduced infection in those vaccinated and pregnant [Goldshtein]. Memory B cell response in lymph nodes and peripheral blood show a robust germinal centre response after mRNA vaccination which suggests very long lasting immunity [Turner2].

- There are still questions about the strength and duration of immunity of those who have had documented infections with COVID-19, but evidence is accumulating to suggest good immunity for several months [Ahluwalia, Bilich, Cromer, Dan, Krutikov, Sokal, Turner1, Wajnberg, Zuo] and even beyond a year [Gaebler, Gallais, Radbruch, Wang&Muecksch]. (Additionally, serology studies have shown, in survivors of SARS in 2003, [Anderson] persistence of neutralising antibodies to the virus for 9-17 years afterwards, which is of interest because of the viral similarity. Likewise, T-cell cross-immunity from seasonal coronaviruses seems to suggest the possibility of long-lasting protective immunity [Sokal]). Immune protection appears to be less in older people [Collier DA, Hansen], and is less following milder [Caniels] or asymptomatic [Long] initial infections. However, seroprevalence studies show antibodies in significant numbers of those without a history of diagnosed COVID-19 [Vázquez Rivas], mild [Ogega] and even asymptomatic [Nielsen] infections are capable of generating adequate antibody response.

- There are cases of individuals with proven second infections (with genetically different virus) including some more severe cases in the second infection, but they remain rare [Piri, Tillett, Vitale] with a rate around 0.7% [Qureshi] and a tendency to less severe infections the second time. They are more common in older [Wall] and immunosuppressed [Agha, Borobia] people. It is yet to be established whether second infection is more common with some of the variants. Recovery from infection followed by a booster vaccination has been shown to produce strong antibody response [Anichini, Gallais, Ibarrondo]. Indeed, whether vaccination is required in those who have recovered from infection may be questionable [Shrestha].

- There is evidence that recovery from COVID-19 infection is associated with good immunity against variants [Hall, Redd] as discussed below. Again, T-cell response is important, not only antibody response [Gangaev] – and there is even some early evidence of memory T-cell response without documented infection [Wang&Yang].

- Efficacy has been studied more extensively with some vaccines (particularly the mRNA vaccines from Pfizer and Moderna, and also the Astra-Zeneca vaccine), than others. There are differences in the efficacy of different vaccines. Studies of the Sinopharm [Al Kaabi] and Coronavac [Jara] vaccines also show good efficacy after two doses at preventing death and hospitalisation, with lesser effectiveness at preventing total cases.

Vaccine safety concerns

- Early in 2021, cases were observed of a rare type of blood clotting disorder (under various names including thrombosis and thrombocytopaenia syndrome TTS), some severe or fatal, in the days after receiving the AstraZeneca vaccine [Greinacher, Schultz]. Initially these were considered not elevated above population rates, but subsequently they were classified as rare side effects of vaccination for the AstraZeneca vaccine [See, Schultz]. The benefit was assessed as outweighing risk in the older age groups, but many countries suspended use of some vaccines in younger age groups (using a variety of age cut-offs) and some suspended use altogether [Karron]. Investigations continue into whether there is a causal relationship with vaccination, such as by induction of antibodies to clotting pathway mediators [Cines]. Although some cases were also reported in association with the Johnson & Johnson vaccine, they were at lower rates [Sadoff] and this vaccine was later cleared by major regulators for resumption of use. A meta-analysis [Chan] of data from 10 countries points out the low incidence in the elderly, with a clear overall benefit of vaccine, with a higher risk in the younger adults where the risk-benefit ratio may depend on local COVID prevalence. A South African study [Takuva] showed low rates of these complications.

- A separate concern was identified regarding myocarditis following second doses of the Pfizer vaccine, particularly in younger males [O'Leary]. Studies indicate that this is a rare event and usually self-limiting, but it is under continued investigation [Shay]. A separate concern is under investigation relating to Guillain-Barre syndrome following (Johnson&Johnson) vaccination.

Part 3: Virus variants – effect on risk

Impact on transmission

- The appearance and proliferation of more transmissible variants of the SARS-CoV2 virus since late 2020 have changed the risk equations somewhat. A higher R_0 (reproduction number) is how this is considered in risk modelling. Currently the Alpha/B1.1.7 (first identified in UK), Beta/B1.351 (South Africa) Gamma/P1 (Brazil) and Delta/B.1.617.2 (India) are the dominant variants, and there is well-established evidence of greater transmissibility in all [Dagpunar, Faria, Faria, Horby, Mascola, Munitz, Tegally, Wall]. In Israel the Alpha/B.1.1.7 variant became the dominant strain in under a month, being significantly more transmissible [Munitz]. The more the SARS-CoV-2 virus continues to proliferate, the more likely it is that more transmissible variants will appear and eventually predominate.

Impact on severity

- There has been preliminary evidence that variants have slightly greater propensity to cause severe illness than the original "wild" virus – in particular, in the case of the Beta/B.1.351 and possibly the Gamma/P1. Although there were preliminary indications of greater mortality for the Alpha/B.1.1.7 variant [Davies], other studies have not borne this out [Frampton, Graham]. The Alpha variant appears to lead to a longer period of infectiousness [Kissler], which may contribute to its increased transmissibility. In some studies there are indications that the Delta/B.1.617.2 variant leads to significantly greater risk of hospitalisation [Bager, Ong, Sheikh] especially in those with multiple co-morbidities.

Impact on testing effectiveness

- Studies to date seem to agree that PCR tests remain sensitive to the currently circulating variants of concern, but some antigen tests which target single spike protein sites could be of reduced efficacy against some or all of those variants with spike protein differences. Some caution should be applied

before implementing any antigen tests at scale, to verify their effectiveness with variants of concern in circulation.

Impact on vaccine effectiveness

- The evidence suggests that there may be some decline in effectiveness of some vaccines against currently circulating variants of concern [Emary, Ho, Ikegame, Kustin, Mascola, Wang&Nair], and studies point to the greatest impact so far being in the case of the AstraZeneca vaccine having limited effectiveness against the Beta/B.1.351 variant [Madhi, Wang&Nair]. Most approved vaccines appear effective in preventing severe disease, hospitalisation and death [Hall, Redd, Rubin]. Furthermore, available evidence suggests that the mRNA vaccines in wide distribution (Pfizer-BioNTech and Moderna) appear to retain reasonably strong effectiveness overall against the current variants [Abu-Raddad, Benenson, Keehner, Kustin, Liu, Tarke, Thompson MG, Wu]. Neutralizing antibodies appear have been shown to be produced against a range of variants [Caniels, Edara] but at reduced levels [Caniels, Wall] but with evidence of preserved T-cell response [Geers]. Another study showed efficacy in pregnant and lactating women [Collier]. New vaccine formulations are being tested to improve efficacy against variants.

- A South African study [Shinde] confirmed around 60% efficacy of the Novavax vaccine against the Beta/B.1.351 variant (but 49% in the HIV positive participants). The Pfizer vaccine demonstrated in vitro activity against the Beta and Alpha variants as well as the variants identified in New York (Iota/B.1.526) and California (Epsilon/B.1.429) classified in USA as variants of concern [Liu], and activity of the vaccine was confirmed beyond 6 months [Pegu]. A study from Public Health England showed effectiveness after two doses of either AstraZeneca (60%) or Pfizer (88%) [Bernal2], against Delta/B.1.617.2, similar to Alpha although reduced compared with the wild-type virus; similar results were found in Scotland [Davis]. These findings followed indications of likely activity of vaccine-induced antibodies against the B.1.617 subgroups and B.1.618 [Tada], and studies pointing to more "breakthrough" infection by Delta in those vaccinated [Micochova]. There are indications of reduced activity of the Pfizer vaccine against the B.1.617 variants [Hoffman, Vaidyanathan], and of reduced activity specifically against Delta [Wall] particularly after only one dose, but in general after two doses the response is retained. Moderna was similarly shown to have good, but reduced, efficacy against Delta [Choi A], and Johnson&Johnson associated with reduced neutralising antibodies against Delta [Jongeneelen]. Other studies show, in spite of a reduced overall efficacy, high effectiveness at preventing hospitalisation [Stowe] or at preventing infection in the vulnerable [Hyams, Shrotri]. Some studies [Micochova, Sheikh] also indicate less efficacy of AstraZeneca than Pfizer against the Delta variant, and similarly reduced efficacy of Coronavac against Gamma [Souza].

Part 4: Reducing the risk with international travel

Quarantine of travellers

- Quarantine is applied differently in different locations. It ranges from total confinement in a locked guarded hotel room through to instruction to remain home but relying on an "honesty system" – the latter having been shown to have non-compliance rates up to 80% in studies. At the stringent end of the spectrum it is substantially (but not completely) effective at preventing importation of cases, whereas at the lax end of the spectrum it may provide only modest reduction of risk [Oxera]. As discussed above, testing programmes can enhance quarantine and may be able to allow reduction of the duration or stringency of quarantine measures, without significantly increasing importation risk [Johansson, Russell]. IATA has determined from repeated customer surveys, and observed travel patterns that quarantine requirements are a major disincentive to travel [IATA internal].

Testing technologies and strategies

- While PCR has remained the primary diagnostic test throughout the pandemic, there has been increasing development of rapid antigen tests (RAT). Initially these were of much lower cost and higher speed than PCR testing, but of reduced sensitivity and specificity. Progressively through the pandemic these differences have reduced, with the cost and time of PCR testing reducing, and the sensitivity (and specificity) of RAT improving. Now there are some extremely rapid PCR tests and some studies show RAT tests with very good sensitivity and specificity [Pickering, Pilarowski, Pekosz] although this is not a consistent finding [Dinnes]. In some situations, RAT testing may have an advantage over PCR in detecting only the cases most likely to be infectious [Norizuki, Pekosz], whereas PCR also detects virus well beyond the infectious period [Mina]. However, the sensitivity of RAT testing is less when used in asymptomatic people [Dinnes, Fernandez-Monteroa, Nkemakonam, Pollock, Wagenhauser], or when viral load is low [Muhi, Oh]. This is important in the context of testing travellers, since asymptomatic cases are a large contributor to transmission [Johansson, Letizia, Oran, Ren]. This area continues to evolve rapidly [Humphries] and a further Cochrane review of RAT performance is awaited [Dinnes].

- A further relevant consideration is acceptability. Importantly saliva-based testing which has been validated extensively for PCR but not for RAT, can be applied frequently with high effectiveness [Babady, Norizuki, Tan, Wyllie] and much less drop-out than nasopharyngeal or oronasal swabbing [Ehrenberg]. Although reported results have been varied, the effectiveness depends on having clarity of the method used; salivary PCR has the potential to become the gold standard [Tan]. A further development is the use of anterior nasal self-sampling, shown to be sensitive to medium to high viral loads [Osmanodja], and such a method is now accepted by US CDC if done with an approved test, in conjunction with a telehealth provider affiliated with the test manufacturer, and with identity verified and documented.

- Effectiveness needs to be considered in the real world, which means consideration of implementation, delivery, reliability (across different users), acceptability and scalability. Turnaround time is also important – if a more accurate test takes 1-2 days to get a result, this may be less effective than a less sensitive test with an immediate result (to allow earlier intervention such as isolation) [Pickering]. It is more appropriate to consider not just a test, but the effectiveness of a test strategy (for example, weekly PCR testing for a group of workers, vs RAT every day or every second day) [Holmdahl, Larremore, Mina, Mina]. Conversely, routine one-off testing of low prevalence populations does have a high risk of missed cases (due to reduced sensitivity in asymptomatic people) as well as false positives (due to the Bayesian effect of amplifying their likelihood in a low prevalence group). Routine RAT testing would need to have a means of conducting confirmatory (probably PCR) testing as rapidly as possible. Such a system was examined in Japanese travellers, using salivary antigen tests as the primary with PCR confirmation when required [Yokota] but limited sensitivity may still be a concern and further analysis is awaited. In a different setting, a randomised controlled trial of attending an indoor event included demonstration of the possible utility of an antigen test pre-entry [Revollo].

- There are other molecular tests as alternatives to PCR, including isothermal PCR or "LAMP" which use alternative amplification methods, usually achieving greater speed of testing. There are also quantitative antigen tests which may have improved acceptability in certain domains. This is a rapidly changing field. Other novel technologies such as breath spectroscopy [Rusciewizc] and detector dogs [Grandjean, Hag-Ali] show potential. These should be considered, although both efficacy and scalability are yet to be established.

Reduction in importation risk from testing

- The first requirement may be for the country of destination to set the level of risk of importation that it can accept, taking into account the epidemiological situation, the capacity of the health system to manage cases, and the capacity and reliability of the contract tracing system locally [Steyn].

- A number of studies have modelled the possible reduction in importation risk from testing in association with international travel [Clifford, Dickens, Goel, Johansson, Kiang, Russell, Smith, Steyn, Wells]. A Cochrane review of 62 studies [Burns] noted that most of the studies are from modelling only, with few real-word examples, but it only covered publications up to November 2020 and a further review is awaited. WHO [personal communication] also undertook a detailed analysis but only of papers up to November 2020. Several further papers have subsequently been published [Dickens, Johansson].

- In situations where travel is from low prevalence to high prevalence, the importation risk is low with a negligible incremental case likelihood. Modelling has indicated that destinations already with a high new case rate receive minimal impact from imported cases [Russell].

- With travel between countries of similar new case rates at the time of travel (provided that the rate data is reliable, with adequate testing programmes in place) then testing around the time of travel will reduce importation by a significant proportion [Clifford, Johansson, Oxera]. This should ensure that the travellers entering are of lower risk than the community at the destination and protect significantly against introducing a variant not already present.

- Efficacy of testing to reduce importation is better if closer to the time of travel; testing on arrival is still more effective. However in-airport testing creates logistical challenges at large scale.

- Travel from high prevalence to low prevalence locations presents more challenges, and in most cases, such travel currently requires some form of quarantine. There is consensus from modelling studies that a programme of testing in association of travel can be applied which will reduce the required quarantine, if not eliminating it entirely [Goel, Johansson, Kiang, Quilty, Russell, Smith, Wells]. Many seem to converge on a short period of quarantine (3-7 days) with testing at the start and end [Humphries, Johansson]

- As noted above, no pre-flight testing system can fully prevent travellers from having already been infected, and incubating at the time of travel. The timing of testing in relation to travel has been studied, and many countries have introduced a requirement for testing in the 72 hours prior to travel. This strikes a compromise between the risk of becoming infected in the time between the test and the travel, and the difficulties of reliably obtaining and confirming a result prior to travel. Testing 48-72 hours prior to travel has been assessed by different studies as reducing the importation risk but to varying degrees [Clifford, Johannson, Oxera].

- Testing in association with quarantine has been studied, and many indicate that a quarantine period of around 7 days, with 2 or 3 occasions of PCR testing (or in some cases RAT testing) can be as effective as a 14 day quarantine period, at reducing importation risk [Dickens, Johansson].

- If the destination is prepared to accept a higher risk of imported cases, based on its public health systems (including contact tracing), then even shorter periods, supported by testing programmes, could be acceptable. [Clifford, Goel, Johansson, Kiang, Russell, Smith, Wells]. If the risk is further reduced by travellers being vaccinated, along with validated testing programmes, the need for quarantine may be able to be removed, if based on sound studies.

Contact tracing

- Regardless of the state of vaccination, the systems and processes of contact tracing remain vital in blocking chains of transmission and preventing spread. As countries begin to achieve control of the epidemic, contact tracing becomes even more vital for maintaining that control [Lash]. Systems which facilitate tracking and tracing (such as applications which record places visited, with or without GPS tracking assistance or detection of other visitors in the vicinity) are part of the risk management

process. For example, some countries allow exit from quarantine on condition of using a GPS tracking device for a period of days. Applications that release location data have obstacles to widespread acceptance by users although some have addressed this by ensuring users retain control over the release of information [O'Connell]. For both public health authorities and airlines, an important element of managing the risks of air travel is the use of a passenger locator form, ideally an electronic one, to assist with follow-up of any passengers later found to be a positive case, and potentially infectious during travel. The ability of a destination to carry out contact tracing on arriving travellers is an important component of assessing travel-related risk.

Part 5: Differing national approaches

- Current approaches of countries are highly divergent. At mid-April 2021, around half of countries required tests for arriving travellers, and around 80 countries required quarantine. Of those requiring tests, two-thirds required PCR testing, and a third required more than one test for each traveller. About 15 countries allow quarantine to be shortened on the basis of tests. Eight countries were exempting vaccinated travellers from quarantine [WHO, personal communication], most requiring the travel to be at least 2 weeks following vaccination.

- Any of these approaches depend on being able to verify that the required testing or vaccination has been carried out, and verify the identity of the traveller as matching the person whose result is presented. IATA has developed its travel pass for exactly this purpose, and there are also some other applications which fulfil similar functions; such electronic solutions will be necessary to support scaled-up numbers of travellers and many countries are already using them on a preliminary basis.

- As at July 2021, EASA/ECDC and also the US CDC have recommended or instituted removal of quarantine requirements for the fully vaccinated and a number of EU countries are supporting, or have introduced such a relaxation. Similarly, many countries are modifying testing requirements for the fully vaccinated travellers.

Part 6: Other relevant considerations

Therapeutics

- Little of the focus of this document has been on therapeutics. But if treatments become available which reliably and affordably prevent infection from progressing to becoming severe and fatal, the risk equations will be dramatically altered. This aspect needs to be considered, but at this stage, whilst there have been many gains from various therapies (including steroids, anti-thrombotics, antivirals, anti-inflammatories, interferon, various monoclonal antibodies, etc) the available therapeutics appear so far to have made relatively little global impact on the infection fatality ratio. A meta-analysis of the monoclonal antibody agent tocilizumab [Avni] looking at eight randomised controlled trials showed reduction in 28-day mortality, requirement for ventilation and ICU admission.

- There also needs to be consideration of the more severe and prolonged complications of mild to moderate cases [Nasserie], increasingly referred to as "long COVID" and carrying significant health, social and economic effects [Mallapaty]. If therapies were developed and broadly available that reduced mortality and morbidity to a level commensurate with influenza, travel restrictions would likely not be justified.

- There will also be other advances; for example, a sulfate polysaccharide nasal spray was shown in an initial randomised controlled trial in Argentina to prevent a high proportion of cases in health care workers [Figueroa], and a further nasal spray of nitric oxide being explored.

Part 7: References

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