Editorial:

Air Travel and SARS-CoV-2: Many Remaining Knowledge Gaps

Running Title: Air Travel and SARS-CoV-2: Knowledge Gaps

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50-word teaser: *COVID-19 is with us indefinitely and air travel is a necessity. Needed research has lagged due to pandemic disruption but must not stall due to COVID indifference. A US government report proposes that national aviation authorities, not health agencies, take the lead. Research priorities and study designs are proposed.*

Air travel encompasses the movement of passengers and crew through airports, onto and off aircraft, and in flight. At airports at either end of the journey, many persons from geographically diverse regions with differing transmission levels and population immunity all interact with airline and airport operations staff and with each other. A holistic assessment of air travel risks should also include ground transportation to and from the airport as well as exposures occurring during post-flight assessment and quarantine where applicable. As timing of the actual transmission event is so critical to know yet so elusive, the threshold for absolute proof of an in-flight transmission is high even in the face of high circumstantial probability. In addition, few of the asymptomatic index cases and few of the asymptomatic secondary cases are ascertained unless systematic testing of all passengers is done on and subsequent to arrival. In the disruption of the pandemic, the opportunities and funding for rigorous prospective studies have been few. Of importance, real human behaviors during air travel are still largely unknown.

Due to the high burden of proof, many, yet surprisingly few, instances of air travel associated SARS-CoV-2 transmission have been published or documented during the pandemic. Large flight-associated case clusters (up to 59) that come to attention[1,2] are in reality dwarfed by the large steady totality of cases escaping the low intensity of post-travel surveillance practiced in most countries during the pandemic. Only a few low population countries (notably Hong Kong, Australia, New Zealand) quarantined and serially tested all arriving passengers over 2 weeks of observation; Chinese data in this regard are obscure. Several robust estimates indicate that during pandemic waves up to 2% of passengers on a typical flight (international or domestic) tested positive for SARS-Co2 within 7 days of arrival with the majority detected immediately upon arrival.[3] Indisputable genomic data prove that SARS-CoV-2 is transmitted

during air travel,[4,5] but the body of published data do not permit any conclusive assessment of likelihood and extent even if risk is low but not insignificant in usual scenarios.

Most studies to date are based on non-systematically selected retrospective observational events or on modelling based substantially on crude surrogate assumptions from the pre-COVID era. The variation in design and methodology restricts the comparison of findings across studies. Comprehensive prospective investigations of passenger risk behaviors, before, during and after the flight, remain almost non-existent 3 years into the pandemic. A robust systematic review and a Cochrane Library analysis provide comprehensive detail on the significant limitations of existing data on air travel related transmission and the effectiveness of current mitigation measures.[6,7]

GAO Report

A recent detailed report sent to the US Congress by a federal watchdog agency, the government General Accounting Office (GAO), synthesizes the status of research on communicable diseases in air travel through March 2022 (https://www.gao.gov/assets/gao-22-104579.pdf.) The report, prepared in consultation with 17 multidisciplinary experts (this author included) provides important, though potentially controversial, recommendations for a cohesive national strategy to advance and coordinate this critical area of research. Though national structures vary by country, conceptually some of the advice appears to be broadly applicable.

GAO stressed the need for more prospective research involving real-world situations and human behavior to inform evidence-based mitigation measures, policy, and regulations. Stakeholders and experts cited a lack of federal coordination of interdisciplinary research by relevant federal departments and agencies. An inability of public health, medical, and

engineering researchers to access aircraft, airports, passengers or data still poses large challenges. Aviation regulatory authorities (FAA in the US) generally have broad authority to conduct and sponsor research on communicable diseases in air travel, but these agencies have historically maintained that infectious diseases lie outside of the core responsibility for aviation safety.

Public health and travel medicine researchers face a broad complexity of jurisdictions in air travel including the competent national authorities for transportation, immigration, homeland security, health (local, state, CDC equivalent) as well as the local airport authority which may be public or private. Once at the gate, the traveler is mostly under control of the air carriers. Travel risk reflects the whole journey but as the traveler moves through airports and onto aircraft, they are passed from jurisdiction to jurisdiction while moving from departure curb to arrival curb. Obtaining permission from multiple appropriate authorities can present an obstacle to even something as simple as asking passengers to fill out a questionnaire or collecting a nasal swab. In addition, researchers may not always easily obtain technical data needed to improve their hypotheses and models, such as detailed information on cabin and ventilation characteristics from aircraft manufacturers (many models of airplane in use) or airline-boarding practices from airlines. Finally, not only do air travel industry stakeholders have a built-in bias to find good news, so do many authorities who rely on different kinds of user fees have a disincentive to fund or support overly detailed investigations.

To alleviate the above constraints, GAO recommended an unprecedented solution, that Congress should consider directing the national aviation regulatory authority which has jurisdiction over both airports and airlines, FAA, to be the lead agency in developing and advancing needed research on communicable diseases in air travel, in coordination with

appropriate federal agencies—such as national health authorities (CDC) and port of entry authorities (homeland security).

Research Priorities

Given the unknown role of so many internal and external variables in the 3rd pandemic year, standardized guidelines for conducting and reporting future studies of transmission on aircraft should be developed.

Generally, quantitation of transmission risk during air travel will not be optimally precise given the nature of these variables. Robust studies will require major targeted funding, be overseen by non-conflicted investigators, be close to real world experiences and closely document (continuous video monitoring) prospective cohorts through the air travel continuum during a period of ongoing SARS-CoV-2 transmission. Specially arranged flights will be necessary. To prove in-flight transmission, all passengers or volunteer subjects need to have PCR testing on departure, on arrival, quarantine 7-14d, and re-test several times during quarantine. Various scenarios including differing incidence rates of SARS-Co-V-2 at origin and destination, differences between sequential evolving variants, intensity of viral load in index cases correlated to location of secondary cases, and vaccination status of passengers will need to be investigated.

At the same time certain behaviors and logistical considerations for future mitigation measures can be studied in isolation in either real-world or artificial circumstances. Incompletely studied conditions or behaviors that may affect disease transmission on an airplane include masking/unmasking during long or short flights (including eating or drinking), use of adjustable over seat vents (gaspers), human interactions outside assigned seats (seats are

optimally ventilated in contrast to lavatories and galleys), boarding procedures, in-flight movement of flight crew, flight duration, passenger spacing, ventilation availability and intensity at gate and prior to power-up of all engines at takeoff.

Data on transmission to and from flight crew are mostly available only to the airline medical departments. Infection may have been acquired anywhere off or on-duty, but such data, which airlines currently regard as protected private health information should be anonymously made available for sophisticated scrutiny.

The effect of travel restrictions, pre- and post-flight testing, and differing infectious dose and transmission parameters for viral variants are areas of investigation of broader impact than the journey itself.

In summary, COVID-19 is with us indefinitely and air travel is a necessity. Needed research must not stall despite the perception that the pandemic is almost over just because case growth is no longer exponential.

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