Vaccination and its Effect on SARS-CoV2 Onward Transmission: A Narrative Review

(version 2.1)

CAPSCA – COVID-19 Aviation Scientific Advisory Group (CASAG)

1. Introduction:

1.1. International air travel has been drastically reduced in the face of the COVID-19 pandemic. Aviation organizations are concerned to understand when re-opening of quarantine-free travel may be safely achieved for vaccinated travellers. With over 1.5 billion vaccines now having been administered worldwide, there is a need to understand to what extent vaccination can prevent transmission. This could inform guidance on how to introduce vaccination as an extra layer of the multi-layered strategy, with a view to safely avoiding or reducing quarantine requirements. The pre-requisite question is: how effective is vaccination in preventing SARS-CoV2 transmission – with the subsidiary question, different but related: how effective is vaccination in preventing asymptomatic infection?

2. Methods:

2.1. CASAG performed a search of scientific literature and technical reports regarding the efficacy of COVID-19 vaccines. The literature included Google Scholar, PubMed, and Cochrane Library databases. Numerous studies and relevant papers included in the IATA Document *COVID-19: Air Travel, Public Health Measures and Risk: A Brief Summary of Current Medical Evidence* were also included. The group performed further filtering aiming to include only papers related to virus transmission after vaccinations, immunogenicity assessment, or viral load counts of fully vaccinated individuals.

2.2. Once the list of relevant studies was established, CASAG proceeded to assess each paper using the GRADE handbook concepts (The Grading of Recommendations Assessment, Development, and Evaluation). This approach is a systematic analytical tool, used and endorsed by WHO, BMJ, NHS, CDC, IDSA, European Commission, American Red Cross, Chest, among others, to produce evidence summaries and graded recommendations. The GRADE structured process analyzes different metrics of each scientific paper such as size effect, main outcomes, secondary outcomes, study methods, discussion, and conclusions in order to establish quality and strength of certainty of the selected evidence body. GRADE process output provides the basis for panel consensus and informed support for guideline panels in developing public health policies.

2.3. CASAG gathered via online meetings to discuss roles, assignments, and methods in general, also set up progress meetings and deliverable due dates. During virtual work sessions, group members discussed literature relevance, quality, caveats, and limitations as the evidence assessment process advanced. Discussions led to panel consensus and formulation of conclusions.

3. Results:

3.1. An initial search of the databases using relevant keywords retrieved a total of 24 peer-reviewed articles and 13 pre-print articles as of 25 May 2021. After filtering out articles non-relevant to the main research question, 14 peer-reviewed articles and 9 pre-prints were selected for analysis.

3.2. The literature review focused on articles relevant to WHO emergency use listed vaccines. Almost all studies (22/23) were specific to mRNA vaccines. Also, most studies addressed vaccine effectiveness as main outcome (20/23), others addressed viral loads (2/23), and immunogenicity (1/23), and two were technical reports. Among the group of selected studies, 1 consisted of a phase III clinical trial, 2 were case-control studies, 11 were cohort studies, 4 were correspondence, 2 were narrative reviews, and 3 were modeling studies.

3.3. After independent review, discussion, and analysis of the selection of papers by CASAG members, the evidence grading process retrieved 1 "high quality of evidence" study, 4 "moderate quality of evidence" studies, and 19 "low quality of evidence" studies. Due to the rapid pace of vaccination rollout at the moment of the literature review, most papers were, inevitably, observational rather than experimental in nature, which the GRADE process defines as "low quality" but the included studies were generally well-designed methodologies in very large cohorts.

Study	Author	N	Relevant Outcome	Reference
Ad26.COV2.S Phase III Trial	Jerald Sadoff et al	19,630	Efficacy of at least 66% for preventing asymptomatic infection.	NEJM. April 21, 2021 DOI: 10.1056/NEJMoa2101544
BNT162b2. Israel cohort	Eric Haas et al.	111,518	Vaccine effectiveness 7 days after the second dose was 91·5% against asymptomatic infection.	Lancet. May 5, 2021 DOI: 10.1016/S0140-6736(21)00947-8
UK COVID Symptom Study App	Cristina Menni et al.	627,383	Infection rates after a single vaccine dose decreased by 72% after 45–59 days following BNT162b2, and 60% at 21–44 days following ChAdOx1 nCoV-19.	Lancet. April 27,2021 DOI: 10.1016/S1473-3099(21)00224-3
Clalit Health Services cohort (Israel)	Noa Dagan et al.	596,618	Vaccine effectiveness for asymptomatic infection was 90%, 7 or more days after the second dose.	NEJM. April 15, 2021 DOI: 10.1056/NEJMoa2101765
UK's COVID-19 Infection Survey	Emma Pritchard et al.	373,402	Reduction in odds of new infection episodes with no self-reported symptoms was 49% post second dose	MedRxiv. April 23, 2021 DOI: 10.1101/2021.04.22.21255913
Long-term care facilities cohort (Spain).	Susana Monge et al.	299,209	Indirect protection in the non-vaccinated estimated for naïve individuals was 81.4%	MedRxiv. May 25, 2021 DOI: 10.1101/2021.04.08.21255135

Households of healthcare workers (Public Health England)	Anoop Shah et el.	144,525 HCW	Household members of vaccinated healthcare workers had a lower risk of COVID-19 case compared to household members of unvaccinated healthcare worker (hazard ratio 0·70)	MedRxiv. Mar 21, 2021 DOI: https://doi.org/10.1101/2021.03.11.21253275
Patients screened prior to procedures (Mayo Clinic)	Aaron Tande et al	39,156	Compared to unvaccinated patients, the risk of asymptomatic SARS-CoV-2 infection was lower among those >10 days after 1st dose (RR=0.21) and >0 days after 2nd dose (RR=0.20)	Clinical Infectious Diseases, 10 Mar 2021, https://doi.org/10.1093/cid/ciab229

Table1. (Partial) Summary of relevant papers.

4. Discussion:

4.1. The main conclusions from the scientific literature reviewed so far are:

a) Several studies show that SARS-CoV-2 vaccination substantially reduces asymptomatic infections as well as symptomatic cases of COVID-19.
b) Some human studies show that viral load is reduced in fully vaccinated people who subsequently test positive for SARS-CoV-2.
c) Some human studies looking at defined populations including families of healthcare workers, care home residents, or workplaces, have demonstrated reduced transmission by those few who have been vaccinated and subsequently become infected.
d) Of the few infections which occur in vaccinated persons, most are likely to be asymptomatic. If there is a need to reliably detect those infections, symptoms will not be a reliable way to do so.

4.2. The limitations or caveats on these findings include:

a) Many of the reports are from pre-print rather than peer-reviewed papers.
b) Many of the studies are necessarily observational in nature. However, a few controlled trials are also included.
c) Not all vaccines currently in use have been represented in the body of evidence. The greatest number of studies looked at Pfizer-BioNTech, Moderna and Astra-Zeneca vaccines. Further data may be required for others (in particular, the other WHO EUL listed vaccines).
d) Further study is required regarding mixed vaccine approaches ("heterologous prime-boost," where the second dose is different from the first) or non-standard intervals between vaccine doses.
e) Not all studies have taken into account currently emerging variants. Variants of Concern (VoC) will continue to appear and need to be considered in applying these conclusions.
f) The length of immunity is currently unknown. Vaccine induced protection from COVID is well established at 2 weeks after the final dose and appears to last for at least 6 months thereafter. Further data may mean this time could be extended, or that booster doses may be required.

g) Finally, there are studies showing that vaccine effectiveness is likely reduced amongst those with suppressed immune responses.

5. Summary:

5.1. The numerous pre-print and peer-reviewed studies included in the CASAG review consistently indicated that vaccination against COVID-19 substantially reduces mild/asymptomatic infections, (as well as preventing most severe/fatal infections).

5.2. The evidence supports that vaccination substantially reduces transmission of SARS-CoV-2. This indicates that on a travel setting, fully vaccinated travelers might not be drivers of onward transmission of SARS-CoV-2.

5.3. Some limitations that should be considered include vaccine types, variant emergence, non-standard intervals/combinations, certain medical conditions, and possible decline in immunity over time.

6. References:

Note: Preprints have not been peer-reviewed. They should not be regarded as conclusive, guide clinical practice/health-related behavior, or be reported in news media as established information.

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