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Public Health Implications of SARS-CoV-2 VOC

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Evidence up to July 14, 2021

Introduction

The SARS-CoV-2 virus, responsible for COVID-19, was declared a global pandemic by the World Health Organization (WHO) in Mar 2020.[1] As of July 18, 2021, over 190 million cases of COVID-19 had been reported worldwide and over 4 million people have died as a result of COVID-19 since the start of the pandemic.[2] Increased numbers of COVID-19 cases are causing significant concerns around identifying optimal vaccination strategies and enforcing appropriate public health measures to manage the spread of the SARS-CoV-2 virus.

As of July 29, 2021, four variants of the original SARS-CoV-2 lineage have been declared variants of concern (VOC) by the WHO, with other variants under ongoing assessment (see Table 1).[3] VOC are defined by their increased potential for transmission, presence of genomic mutations, and rapid spread across countries or regions leading to possible decreased effectiveness of public health measures.[4] The increased transmissibility of VOC has led to surges in COVID-19 incidence and consequently, hospitalizations and mortality.[5] Therefore, this living systematic review aims to provide a synthesis of current evidence related to VOC in the context of public health measures. This living synthesis builds on a previous rapid scoping review examining the impacts of VOC on public health and health systems conducted by this team.[6]

Table 1. Current variants of concern (VOC)[3 7]

WHO Name	PANGO LINEAGE	Alternate name	Country first detected in	Earliest samples
Alpha	B.1.1.7	VOC 202012/01	United Kingdom	September 2020
Beta	B.1.351	VOC 202012/02	South Africa	August 2020
Gamma	P.1	VOC 202101/02	Brazil	December 2020
Delta	B.1.617.2	N/A	India	October 2020

Key Points of Interest

- The majority of available evidence is related to the Alpha variant; very little published about the Delta variant
- Speed of vaccine rollout is a key factor in reducing transmission rate and disease burden
- Non-pharmaceutical interventions (NPIs) (e.g., social distancing, masking) alongside vaccine rollout is an essential component of an overall disease management plan
- There is evolving evidence regarding changes in vaccine scheduling related to inter-dose timing and need for third dose of vaccine
- Strict NPIs may lead to overdispersion of highly transmissible variants, leading to their eventual dominance
- Lockdowns should be strict when imposed, yet the most effective length is undetermined
- Adherence to strict NPIs and lockdowns wanes over time, which may impact effectiveness

Categories of evidence included in this report are as follows:

Modifying approach to vaccines: Any studies that reported on changing approaches to vaccinations such as modelling the rollout schedules or impact of NPIs in relation to vaccine schedules. Four sub-categories fell under this category:

a) Modelling potential vaccination rollout schedules
b) Evaluating past vaccination rollout schedules
c) Modelling potential vaccination rollout schedules in the presence of NPIs
d) Evaluating past vaccination rollout schedules in the presence of NPIs

Infection prevention measures: Any studies that reported on public health measures aimed at preventing the spread of VOC such as mask wearing, hand washing or physical distancing.

Infection control measures: Any studies that reported on public health measures aimed at controlling the spread of VOC such as quarantines, lockdowns, screening or testing strategies.

Results Tables

The following tables present a summary of evidence in relation to each of the categories described above.

Table 2. Evidence related to modifying approach to vaccination, divided by VOC

*Note: only observational studies were appraised for quality

Category	Alpha (B.1.1.7)	Beta (B.1.351)	Gamma (P.1)	Delta (B.1.617.2)
Modifying approach to vaccination				
Modelling potential vaccination rollout schedules	• Accelerated vaccine rollout (60doses/day/10,000 pop) would reduce severe health outcomes [8] • Estimated current vaccine schedule of 1/1000 doses/person/day would need to be quadrupled to control the spread of VOC [9] • Speed of vaccine rollout is key factor in achieving low IAR and burden of disease [10–14] • Change in inter-dose vaccine period from 21 to 42 days is preferrable for vaccine mode of action at the end of infection course, severe epidemic and low vaccine supply rate [15] • Third dose of vaccine is required to eliminate developing mutations are reduce transmission rates [16] • Proactive surveillance and prioritized vaccination can reduce severe illness and mortality in vulnerable groups [17]	• Speed of vaccine rollout is key factor in achieving low IAR and disease burden [11] • Third dose of vaccine is required to eliminate developing mutations and reduce transmission rates [16]	• Speed of vaccine rollout is key factor in achieving low IAR and disease burden [14] • Third dose of vaccine is required to eliminate developing mutations and reduce transmission rates [16]	• Speed of vaccine rollout is key factor in achieving low IAR and disease burden [14] • Third dose of vaccine is required to eliminate developing mutations and reduce transmission rates [16]

Evaluating vaccination rollout schedules		N/A	• Targeted vaccination of 80+ age group associated with decreased mortality compared with younger group [18] *Medium quality evidence*	N/A
Modelling different vaccine schedules in relation to NPIs	• Advocate for NPIs to remain in place during vaccine roll out until sufficient population immunity [19–25] • NPI alongside accelerated vaccine roll out is needed to control outbreak [23,26–28] • In OECD, countries fully vaccinating 40% of the population would allow for easing of containment policies [29]	• Advocate for NPIs to remain in place during vaccine roll out until sufficient population immunity [19,20]		Combination vaccine (accelerated) and NPIs are required to reduce transmission rate [25,26,30]
Evaluating different vaccine schedules in relation to NPIs	N/A	N/A	N/A	N/A

Table 3. Evidence related to infection prevention measures, divided by VOC

Category	**Alpha (B.1.1.7)**	**Beta (B.1.351)**	**Gamma (P.1)**	**Delta (B.1.617.2)**
Infection prevention measures				
Hand washing	• VOC responds similarly to ethanol and soap as non-VOC [31]	• VOC responds similarly to ethanol and soap as non-VOC [31]	N/A	N/A

Masking	• Moderately effective masks, when worn consistently correctly by a large portion of the population, are effective at preventing transmission [32]	N/A	N/A	N/A
Physical distancing	• Settings where physical distancing is unlikely (e.g., hair salons; visiting with friends inside the home) present the highest risk of transmission [33] • Strong physical distancing measures are critical[34] and may need to be strengthened by 33.7% [35] • In daycares, strict contact restrictions like group assignments among children and staff assignments to groups prevent infections [36] *Appraised studies were of medium to high quality*	• Strong physical distancing measures are critical even with a mass vaccination campaign [19]	N/A	N/A

Table 4. Evidence related to infection control measures, divided by VOC

Category	Alpha (B.1.1.7)	Beta (B.1.351)	Gamma (P.1)	Delta (B.1.617.2)
Infection control measures				
Testing	• Testing and routine surveillance of populations at risk are critical [37 38] • Self-collection and pooling approaches to testing of travellers allows large-scale screening using less human,	• Testing and routine surveillance of populations at risk are critical even with a mass vaccination campaign [19]	• Mass saliva analysis is a cheap, easy to collect, and feasible asymptomatic testing strategy to potentially slow variant outbreaks [41]	• The optimal testing strategy is weekly testing of the entire unvaccinated population, plus a 10-day isolation requirement for

	material and financial resources [39]; surveillance of travellers remains important [21] • Daily testing for 5 days could circumvent the need for quarantine of travellers[40] • Pre-flight tests may prevent the majority of transmission from travellers [40] *Appraised study of high quality*			positive cases and their households [42]
Quarantine (close contacts and travellers)	• Alpha cases almost twice as likely to give rise to household clusters compared with wild type cases, highlighting importance of quarantining household contacts [43,44] • Mandatory quarantine and contact tracing are required[37,40,45–47] • A 10-day quarantine period may be as effective as a 14-day quarantine period [40] *Appraised studies of medium quality*	• Mandatory quarantine and contact tracing are required [46,47] • Beta may require more extreme quarantine and testing measures [45] than other variants including Alpha	• Mandatory quarantine may be an effective way to contain Gamma [47] • Forced prolonged cohabiting may boost viral ability to generate Gamma mutation [48]	
Isolation (confirmed COVID-19/VOC cases)	• Complete isolation of Alpha cases is required to prevent outbreaks; even a small number of infected people dramatically increases the probability of sustained community transmission [10]	N/A	N/A	• To control outbreaks, the optimal testing strategy is weekly testing of the entire unvaccinated population, plus a 10-day isolation requirement for positive cases and their households [42]

Lockdowns	• Alpha requires stronger lockdown measures than wild type [28,49,50] including increased length [51] and stricter regional travel restrictions [38] • Shorter, stricter lockdowns may be more effective than longer, moderate lockdowns due to waning adherence[28]	N/A	N/A	N/A
Other/combined NPIs	• Strong test-trace-isolate programs could be enough to contain Alpha [26] • In day-cares, NPIs like closures in the event of an outbreak can help contain Alpha [52] • Strict NPIs may lead to overdispersion of highly transmissible variants, leading to their eventual dominance [53]	N/A	• Strict NPIs are required to contain Gamma [30]	• Even modest improvements in a find, test, trace, isolate and support program would control transmission[54]

Overview of the Evidence

As of July 14, 2021, 47 studies have reported on VOC and public health measures. We include 18 studies from an earlier rapid review and 29 from our updated search on July 14th 2021. The key findings of included studies can be found in tables 2-4 below, while a more detailed summary of each study can be found in the supplementary material tables. The majority of reported evidence was related to Alpha (n=26) with fewer studies reporting on Beta (n=6 studies), Gamma (n=7 studies) and Delta (n=10 studies).

Modifying Approach to Vaccines delivery

- 23[8–30] studies reported on vaccine delivery. The majority of modelling studies exploring potential vaccine rollout schedules made recommendations for accelerated vaccination campaigns. This included studies that modelled vaccine rollout in both the presence and absence of NPIs, such as lockdown measures
- NPIs are recommended to continue in tandem with a vaccine rollout schedule

Infection Prevention Measures

- The one[31] study that reported on hand washing and VOC, reported that Alpha and Beta respond similarly to ethanol and soap as wildtype SARS-CoV-2
- The one[32] study that reported on mask wearing and VOC, reported that when worn correctly, masks are effective against Alpha
- Five[19,33–36] studies reported on VOC and physical distancing measures. All studies recommended imposing strong physical distancing measures in the presence of Alpha or Beta

Infection Control Measures

- Eight[19,21,37–42] studies reported on testing strategies related to VOC. Testing and routine surveillance of populations are critical to containing Alpha and Beta, even in the presence of mass vaccination campaigns. Cheaper approaches to testing are possible for detecting Alpha and Gamma
- Eight[37,40,43–48] studies reported on quarantine and VOC. Mandatory quarantine were reported as necessary to contain Alpha and Beta. Alpha and Gamma were identified as giving rise to more household clusters than wildtype, suggesting a need for adequate household quarantine measures.
- Two[10,42] studies reported on isolation and VOC to contain transmission of the virus. One study was related to Alpha and Gamma respectively. Isolation duration varied across studies.
- Five[28,38,49–51] studies reported on lockdowns and VOC. All studies reported needing strict lockdown measures to contain Alpha. Some studies recommended longer lockdowns and more restrictive travel restrictions, while one study recommended short, strict lockdowns to mitigate the waning adherence to longer lockdowns.
- Five[26,30,52–54] studies reported on other NPI infection control measures and VOC. Two studies recommended modest to strong test, trace and isolate strategies as necessary to

control the spread of Alpha and Delta. Three studies recommended employing NPIs in conjunction with vaccine rollout to mitigate the spread of Alpha.

Methods

This living synthesis is building on previous evidence gathered up to May 11, 2021. Searches for this update were run on July 14, 2021 in MEDLINE (Ovid MEDLINE All), Embase (Elsevier Embase.com), the Cochrane Database of Systematic Reviews (CDSR) and Central Register of Controlled Trials (CENTRAL) (Cochrane Library, Wiley), Epistemonikos' L·OVE on COVID-19, and medRxiv and bioRxiv. Titles/abstracts and full text were screened independently by two reviewers. Data were double extracted using a standardized form. Studies were included if they reported on at least one of the VOC and public health measures. Critical appraisal was conducted for case-control, cohort, and cross-sectional studies using the Newcastle-Ottawa Scale (for studies included in previous versions of this report) and the appropriate Joanna Briggs critical appraisal tools for studies newly included in this update. Critical appraisal was not conducted for modelling studies.

List of Abbreviations

COVID-19: coronavirus disease 2019
IAR: Infection attack rate
NPI: non-pharmaceutical intervention/s
VOC: variant/s of concern
WHO: World Health Organization

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