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Public Health and Health Systems Impacts of SARS-CoV-2 Variants of Concern: A Rapid Scoping Review — Source link

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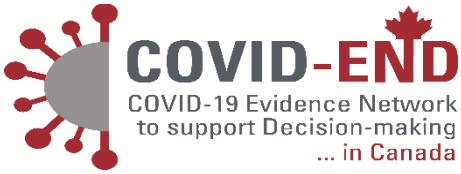

Public Health and Health Systems Impacts of SARS-CoV-2 Variants of Concern

Rapid Scoping Review

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Definitions & Abbreviations

ABM: Agent-based Model
AGREE II: Appraisal of Guidelines Research and Evaluation
aIRR: adjusted incidence rate ratios
B.1.1.7: variant of concern originating in the United Kingdom, also known as VUI 202012/01 and VOC 202012/01
B.1.351: variant of concern originating in South Africa, also known as 20H/501Y.V2
BMI: body mass index
CanCOGen: Canadian COVID Genomics Network
CENTRAL: Central Register of Controlled Trials
CFR: Case Fatality Rates
CI: confidence interval
CIDRAP: Center for Infectious Disease Research and Policy
Ct: cycle threshold, provides a relative measure of viral quantity
COG-UK: COVID-19 Genomics UK
CDSR: Cochrane Database of Systematic Reviews
dQALY: discounted quality-adjusted life years
E484K: escape mutation in the SARS-CoV-2 virus, present in B.1.1.7
ECDC: European Centres for Disease Control
FDA: Food and Drug Administration
HCW: healthcare workers
HR: Hazard Ratio
HVAC: heating, ventilation, and air conditioning
ICU: Intensive Care Unit
IQR: interquartile range
IR: incidence rate
LOS: length of stay
mRNA: messenger ribonucleic acid
NGS: next generation sequencing
NOS: Newcastle-Ottawa scale
NPI: Non-Pharmaceutical Interventions
NRW: North-Rhine Westphalia
OR: odds ratio
P.1: variant of concern originating in Brazil, also known as B.1.28.1
PCR: polymerase chain reaction, method for DNA replication and genome sequencing
PHU: Public Health Unit
PPE: personal protective equipment
PR: prevalence ratio
R: reproduction
R_0: basic reproduction number, expected number of cases generated by one case in a population when everyone is susceptible to infection
R_t: effective reproduction number

RR: risk ratio
RT-LAMP: reverse transcription loop-mediated and transcription-mediated amplification isothermal amplification
RTD: Rapid Antigen Test
SA: South Africa
SAPSII: severity score at admission
SIDARTHE: a type of model
SGTF: spike OR S gene target failure, correlates with the increase of confirmed, sequenced variants
SGTL: spike gene late detection
SD: standard deviation
UK: United Kingdom
US: United States
VE: vaccine efficiency
VOC: variant of concern
WHO: World Health Organization
WGS: whole genome sequencing

Abstract

Background: As of April 2021, three SARS-CoV-2 variants of concern (VOC: B.1.1.7, B.1.351 and P.1) have been detected in over 132 countries. Increased transmissibility of VOC has implications for public health measures and health system arrangements. This rapid scoping review aims to provide a synthesis of current evidence related to public health measures and health system arrangements associated with VOC.

Methods: Rapid scoping review. Seven databases were searched up to April 7, 2021 for terms related to VOC, transmission, public health and health systems. A grey literature search was conducted up to April 14, 2021. Title, 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 or health system outcomes.

Results: Of the 2487 articles and 59 grey literature sources retrieved, 37 studies and 21 guidance documents were included. Included studies used a wide range of designs and methods. Most of the studies and guidance documents reported on B.1.1.7, and 18 studies and 4 reports provided data for consideration in relation to public health measures. Public health measures, including lockdowns, physical distancing, testing and contact tracing, were identified as critical adjuncts to a comprehensive vaccination campaign. No studies reported on handwashing or masking procedures related to VOC. For health system arrangements, 17 studies were identified. Some studies found an increase in hospitalization due to B.1.1.7 but no difference in length of stay or ICU admission. Six studies found an increased risk of death ranging from 15-67% with B.1.1.7 compared non-B.1.1.7, but three studies reported no change. One study reported on the effectiveness of personal protective equipment in reducing VOC transmission in the hospital. No studies reported on screening staff and visitors, adjusting service provisions, or adjusting patient accommodations and shared spaces, which is a significant gap in the literature. Guidance documents did not tend to cite any evidence and were thus assumed to be based on expert opinion.

Conclusion: While the findings should be interpreted with caution as most of the sources identified were preprints, findings suggest a combination of non-pharmaceutical interventions (e.g., masking, physical distancing, lockdowns, testing) should be employed alongside a vaccine strategy to improve population and health system outcomes. While the findings are mixed on the impact of VOC on health system arrangements, the evidence is trending towards increased hospitalization and death.

Introduction

The SARS-CoV-2 virus, responsible for COVID-19, was declared a global pandemic by the World Health Organization (WHO) in March 2020.[1] By April 2021, over 143 million cases of COVID-19 had been reported worldwide according to Johns Hopkins University,[2] with 4.5 million new cases identified in the first week of April alone.[3] A further three million people have died as a result of COVID-19 since the start of the pandemic.[2] Increased numbers of COVID-19 cases is causing significant concerns around identifying and enforcing public health measures to control the spread of the virus and ensuring health systems can manage current and new admissions.

So far, three variants of the original SARS-CoV-2 lineage were declared variants of concern (VOC) by the WHO, with other variants under ongoing assessment.[4] 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.[5] In December 2020, the B.1.1.7 VOC (201/501.1.V1 or 2020/12/01) was first identified in the United Kingdom (UK)[6] and as of April 13, 2021, 132 countries had reported cases of the B.1.1.7 variant.[3] A second VOC was identified in South Africa (SA), known as B.1.351 (20H/501Y.V2) and has since been identified in 82 countries,[3] while the P.1 VOC (previously known as B.1.1.28.1) which originated in Brazil, has been identified in 52 countries.[3] While evidence is continuing to emerge on the impact of the circulating VOC on population health and health systems arrangements, early data suggests an increased risk of transmission associated with all three VOC.[3,7–9] Specifically, B.1.1.7 is estimated to be between 43-90% more transmissible than non-VOC,[3,7,8] while B.1.351 is between 1.5[3,10] and 2.5[7] times more transmissible than non-VOC. There is limited evidence on the transmissibility of P.1, but early trends suggest it also has transmission advantage over non-VOC.[3,7,9] Clearly, these circulating VOC present a risk to public health and safety.

The increased transmissibility of VOC has led to increase in surges in COVID-19 incidence and consequently, hospitalizations and mortality.[8] The first wave of the pandemic demonstrated the potential for even well-equipped health systems to experience overwhelmed intensive care units (ICUs) and system disruption with wide ranging health consequences.[11] For example, as of April 23, 2021, in Canada, cases of COVID-19 have been increasing and ICUs in some regions are at increasing risk of exceeding capacity to provide the usual calibre of critical care.[12] However, due to the emergent nature of SARS-CoV-2 and the VOC, health systems and public health must make pragmatic decisions before evidence is available. This leaves many public health officials and healthcare administrators with uncertainty about the priority actions to minimize increased risk of spread of VOC and particularly whether there needs to be any existing modification to public health recommendations.[13] There is also increasing pressure on the health system,[14] despite a lack of evidence to inform measures needed to minimize the burden on the healthcare system. Therefore, this rapid scoping review aims to provide a synthesis of current evidence related to VOC in the context of public health and health system impacts. This review is a follow-up to the rapid scoping review on transmission conducted by this team.[9]

Objective

To identify, appraise and summarize evidence related to the following questions about public health and health system impacts of the three major SARS-CoV-2 VOC as known in April 2021 (B.1.1.7, B.1.351, and P.1):

1. What is known about the implications of the three priority VOC for public-health measures on:
    a) Modifying approach to vaccination (e.g., using vaccines that offer greater protection against variants, using different vaccines for first and second doses and/or re-vaccinating those initially vaccinated with vaccines with limited efficacy for new strains)
    b) Modifying infection-prevention (i.e., public-health) measures in the community (e.g., changing duration of hand washing; changing mask type and characteristics, double masking, or other changes to masking; and changes to physical and temporal distancing)

c) Modifying infection-control procedures, such as:
   - Changing duration for quarantining of exposed or potentially exposed individuals
   - Changing duration for isolating suspected or confirmed cases (e.g., for exposed health workers)
   - Changing testing strategy, including approach to testing, frequency of testing, and turn-around time for test results
   - Changing approach to contact tracing
   - Changing approach to outbreak management

2. What is known about the implications of the three priority VOC for health system arrangement (particularly for hospitals) on:
   a) Adjusting capacity planning to accommodate changes in the risk of re-infection and the risk of severe disease (e.g., hospitalization, admission to ICU, and death)
   b) Adjusting personal protective equipment (PPE) procedures for health workers
   c) Adjusting restrictions and screening of staff and visitors (e.g., visitor policy changes, approach to and frequency of screening)
   d) Adjusting service provision (e.g., cohorting patients in hospitals based on the VOC they have)
   e) Adjusting patient accommodations, shared spaces, and common spaces (e.g., improvement to HVAC (heating, ventilation and air conditioning) systems)

Design

Rapid scoping review, following standardized rapid and scoping review guidelines.[15–17] This review will be updated in June 2021; the most up-to-date version will be listed on the COVID-END website.

Methods

A broad, comprehensive search was designed by an information specialist to retrieve all literature related to VOC. The electronic database search was executed on March 15, 2021 and again on April 7, 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 concurrently. The electronic database search was followed up by a grey literature search, executed on March 18-19, 2021 and again April 12-14, 2021, using a list[18] of specific COVID-19 resource websites in addition to broader searches of Google and Twitter. Only English language searches were conducted, but non-English results were considered for inclusion. Full search details are available at Appendix 1.

Evidence specific to public health and health system arrangement impacts were identified and tagged during the screening process related to any of the protocol questions. Studies that reported on immune escape (vaccine/prior infection protection), non-VOC impacts, testing approaches, transmission, case studies without public health or health system impacts, or animal studies were excluded. Reviews, overviews, and news articles that presented no original data were excluded but checked for references to primary studies.

Title/abstract and full-text screening was completed by two reviewers in Covidence. The data extraction form was designed in consultation with knowledge user partners; data were extracted by two reviewers and verified by a third. The final report was reviewed by health system and infectious disease experts engaged on our team.

Quality appraisal was conducted using the Newcastle-Ottawa scale (NOS)[18] and the AGREE II tool.[19] Case-control or cohort design studies were assessed using the NOS, cross-sectional studies were assessed using the adapted NOS,[20] and guidance documents were assessed using AGREE II. Two team members independently conducted quality appraisal for all eligible studies. Reviewers met to discuss scores and a third, independent team member was consulted to assist with resolving conflicts. Modeling studies, lab-based studies and other grey literature sources were not appraised.

Cohort studies were awarded a maximum of nine stars and cross-sectional studies awarded a maximum of 10 stars, based on three scoring categories: selection, comparability, and outcome. Two stars were subtracted from pre-print studies as an added layer of quality assessment due to the emerging nature of studies on this topic. Final scores for observational studies were presented as a percentage, based on an average between the two appraiser scores. An overall quality rating of low, medium or high was reported for each observational study, which correlated with a score of <50%, 50-80% or >80% respectively.

Guidance documents were awarded a maximum of 161 points on the AGREE II tool, by scoring quality on a scale of 1-7 across 23 separate items within six domains. Guidance documents were scored following the AGREE II formula for each domain: [(Obtained score - Minimum possible score)/(Maximum possible score - Minimum possible score)] x100%. This scaled domain score was presented for each of the six domains. The same formula was used to calculate the final overall assessment score, where each appraiser gave an overall rating from 1-7 and indicated whether they would recommend the guideline. An overall quality rating of low, medium, or high was given based on a function of the overall guidance score and decision to recommend the guidance document.

Results

The search retrieved 2487 electronic database records and 59 grey literature records, of which 37 studies and 21 guidance documents were included (see Appendix 2 for PRISMA Flow Diagram). Of the 37 studies identified, 25 were preprints, eight were published in peer-reviewed journals, and four were reported in grey literature sources (see Appendix 3 – Tables 1 and 2 for a summary table of included studies). Three sources reported solely on P.1, one source reported on B.1.351, 25 sources reported on B.1.1.7, six reported on all three, one on B.1.1.7 and B.1.351, and one reported on a non-specific VOC. There was a wide variation in countries, including the UK (n=12), the United States (US) (n=4), France (n=3), Brazil (n=3), Canada (n=2), Germany (n=2), Israel (n=2) and one each from Denmark, Italy, Lebanon, the Netherlands, Portugal, and South Africa. Three studies reported on multiple countries.

Of the 21 guidance documents, most discussed all VOC, except for one that focused solely on B.1.1.7 and two that focused on B.1.1.7 and B.1.351 (Appendix 3 – Table 3 summary of guidance documents). Most of the guidance documents originated from public health agencies or health authorities within Canada (n=14), with others from the UK (n=3), Ireland (n=1), the US (n=1), Europe (n=1) and international (n=1).

A note about the guidance documents included in this review

- The guidance documents included in this rapid scoping review are not the result of a comprehensive jurisdictional scan. They were retrieved via Google using a general search for keywords related to VOC. As a result, the guidance featured throughout this review is under-representative of Canadian provinces whose guidance was not specific to VOC at the time of the search (e.g., Atlantic provinces where VOC may not have been identified or prevalent at the time), or whose guidance was not optimally indexed for Google searching. A comprehensive jurisdictional scan, including hand-searching of provincial websites and consultation with personal contacts, will be produced in an upcoming separate report.

Critical Appraisal

Of the 33 included non-grey literature studies (preprints and peer-reviewed), 11 were cohort studies and five used a cross-sectional design, and thus subject to appraisal using the NOS. Cohort studies scored six to nine stars out of a possible nine, which is a 67-100% in overall quality. Cross-sectional studies scored one to eight stars out of a possible 10, with a range of 10-80% for overall quality. Four studies scored 80% or higher,[24–27] indicating high quality. The majority (n=8) scored 50-80%,[28–35] suggesting medium quality, while four studies were considered low quality, scoring 10-44%.[36–39] Twelve of the 33 studies were pre-prints, meaning they had not yet been peer reviewed. As the quality of preprints should be interpreted with caution, efforts were made to reflect this in the overall score through the removal of two points. A complete overview of NOS scores by study can be found in Appendix 4. Of note, four studies were laboratory-based and 13 were epidemiological modeling studies and were therefore not included in the quality assessment.

Of the 25 grey literature resources included in this review, 21 were guidance documents and appraised using AGREE II. The overall quality scores of included guidance documents ranged from 16.7% to 83.3%, indicating a range of low quality to high quality. However, it is important to note that no guidance documents included in this review were clinical practice guidelines, but rather public health directives presented in a variety of formats. A complete overview of guidance document scores based on the AGREE II tool can be found in Appendix 4.

Question 1: Public Health Measures

Question 1A: Modifying approach to vaccination (e.g., using vaccines that offer greater protection against variants, using different vaccines for first and second doses and/or re-vaccinating those initially vaccinated with vaccines with limited efficacy for new strains).

Seven studies contributed data which may be relevant to modifying the current approach to vaccine scheduling and delivery (see Table 1). Of the seven studies, 5 were modeling[40–42] or lab-based studies[43,44] which were not critically appraised. The two studies that were critically apprised were of low quality.[36,37]

Key findings for consideration include:

- **Age appears to be a factor in immune response after the first dose of mRNA-based vaccines**
- **Optimal vaccine schedules combined with non-pharmaceutical interventions (i.e., restrictions, masks, physical distancing) is expected to limit the number of COVID-19 related deaths and preserve ICU capacity**
- **Age and gender may influence response to public health messages regarding vaccine uptake**

Four guidance documents (two low-quality,[45,46] one medium-quality,[47] and one high-quality[48]) contained information related to vaccination approaches, but none explicitly recommended changing to vaccines or vaccination schedules that offer greater protection, using different vaccines for first and second doses, or re-vaccinating. It is acknowledged that current guidance is predicated on a rapidly changing evidence base.

Table 1. *Study summary on findings related to modifying approach to vaccination, categorized by study topic*

Author, year (country)	Study Objective	Data Collection	Sample	Outcome Measures	Key Findings	Quality Appraisal
Use of vaccines or vaccine schedules that offer greater protection						
Exploring vaccine protection using a correlate of laboratory neutralization in consideration of variants						
Collier et al., 2021 (UK)	Assess age related immune response following 1st and 2nd dose BNT162b2 vaccination	Dec 9, 2020- Feb 3, 2021	51 adults (n=24, <80 years; n=26, > 80 years)	Serum antibody neutralization 3 weeks after 1st dose	Age was significantly correlated with serum neutralization in both wild type and B.1.1.7 after 1st dose of BNT162b2 vaccine. OR 9.5 (2.3-40.2 ,p=0.002) for participants > 80 years achieving inadequate neutralization against wild type and OR 12.2 (3.1-48.9, p<0.001) for B.1.1.7. No age-related difference in neutralization following 2nd dose.	N/A
Jangra et al., 2021 (USA)	Assess impact of E484K mutation in neutralizing activity of specific antisera	Not reported	34 sera from SARS-CoV-2 positive individuals & 5 from individuals fully vaccinated with Pfizer	Serum neutralization efficiency	In an *in vitro* microneutralization assay comparing serum neutralization of vaccinated and convalescent individuals against E484K and the USA-WA1/2020 virus, the neutralizing activity was lower against E484K for both human convalescent (low IgG:2.4 fold, moderate IgG: 4.2 fold, high IgG: 2.6 fold in geometric mean) and post-vaccinated (3.4 fold) individuals	N/A
Exploring different vaccination schedules						
Pageaud et al., 2021 (France)	Model expected dynamics of COVID-19 with variant strains applying protective measures and several vaccine strategies	N/A	Santé publique France data from January 8, 2021, January 27, 2021 and February 18, 2021	# of individuals removed, # of in hospital deaths, ICU resource use	While rapid vaccination of the whole population within 6 months provides the best outcome, a one-year vaccination campaign with extended non-pharmaceutical interventions (I.e. public health measures) would limit the number of deaths and avoid ICU resource saturation	N/A
Giordano et al., 2021 (Italy)	Model to compare different vaccines campaign scenarios, varying SARS-CoV-2 profiles and restrictions	Hypotheti-cal 110-day window ending on Feb 7, 2021	Data on new positive case provided by SIDARTHE	Health care costs, death	Non-pharmaceutical interventions have a higher impact on epidemic evolution than vaccinations and should remain in place throughout the vaccine campaign	N/A
Munitz, 2021 (Israel)	Explore transmission dynamics of B.1.1.7 to estimate effectiveness of public health measures on elderly and general population	Dec 6, 2020-Feb 10, 2021	>300,000 RT-PCR samples	SGTF data, reproduction number Rt and cycle threshold	Significant decrease in B.1.1.7 cases reported after Jan 14, 2021 among 60+ age group is likely attributed to rollout of Israeli vaccination program (i.e., 60+ eligible for vaccines) as B.1.1.7 increase among 0-59 age group and no other public health measures implemented during same time frame	N/A
Attitudes towards vaccines related to VOC						
Bachtiger et al., 2021 (UK)	Assess impact of new variants on COVID-19 vaccine hesitancy and attitude	Nov 13 & Dec 31, 2020	9617 respondents from Imperial College	2 questionnaires completed within participants' personal	Intention to vaccinate increased from 71.5% (6521/9122) in the first questionnaire to 85% (8,187/9617) in second questionnaire after B.1.1.7 emergence. Age and gender influence vaccine behaviours	10% (low quality)

Author, year (country)	Study Objective	Data Collection	Sample	Outcome Measures	Key Findings	Quality Appraisal
			Healthcare NHS Foundation Trust	electronic health record		
Comparing natural or vaccine protection against COVID-19						
Lumley et al., 2021 (UK)	Compare protection conferred by vaccine and B.1.1.7	Apr 2020-Feb 28, 2021	HCW in Oxford University Hospitals	PCR-positive test, antibody status	Natural immunity with detectable anti-spike antibodies & two doses of vaccine (Pfizer or Oxford-AstraZeneca) provides similar protection against SARS-CoV-2 infection and the B.1.1.7 variant	44% (low quality)

Use of vaccines or vaccine schedules that offer greater protection

A total of five studies provide data which may be useful to consider when designing how vaccines are rolled out with the emergence of the variant strains. All five studies were modeling or lab-based studies and thus were not critically appraised.

Exploring vaccine protection using a correlate of laboratory neutralization in consideration of variants

Two small studies provided data related to serum neutralization protection against VOC. Collier et al. conducted a prospective cohort study in the UK including 51 participants (median age 81 years; n=24, <80 years; n=27 > 80 years), to assess immune response following the first and second dose of mRNA-based vaccines. Vaccine elicited serum antibody neutralization was measured as a dilution of serum required to inhibit infection by 50% in an *in vitro* neutralization assay at least 3 weeks after the first dose of vaccine. Age was found to be statistically correlated with serum neutralization in both the wild type and B.1.1.7 after the first dose. The adjusted odds ratio (OR) for participants 80 years and older versus younger than 80 for achieving inadequate neutralization against wild type was 9.5 (2.3-40.2, p=0.002) and against the B.1.1.7 variant was 12.2 (3.1 – 48.9, p<0.001). Re-testing 3 weeks after the second dose showed no age-related differences in neutralization activity.

Jangra et al. examined the impact of the E484K mutation on the neutralization activity of SARS-CoV-2 specific antisera using a sample of 34 sera from SARS-CoV-2 positive individuals and sera from 5 individuals who were fully vaccinated with the Pfizer vaccine.[44] *In vitro* microneutralization were performed in a blinded manner with both the USA-WA1-2020 virus (similar to strains in the early phase of the COVID-19 pandemic) and an identical recombinant SARS-CoV-2 except for the E484K mutation on the spike receptor binding domain. Serum neutralizing activity of human convalescent and post-vaccinated donors was significantly lower against E484K (convalescent low IgG: 2.4-fold, moderate IgG: 4.2-fold, high IgG: 2.6-fold; vaccinated samples: 3.4-fold based on geometric means) when compared with USA-WA1-2020.

Exploring different vaccination schedules

Two studies modeled the impact that changes in the vaccine scheduling would have on VOC. Pageaud et al. used a stochastic agent-based model (ABM), stratified by age, which considered the influence of the variant strains, three different non-pharmaceutical intervention (NPI) protocols (relaxed, intensive, extended), and four different vaccine schedules (6,12, 18, 24 months) to examine impact on number of cases, deaths, hospitalizations and ICU resource use.[41] A 6-month vaccination campaign with an intensive-NPI resulted in the least number of deaths (~18000) and avoided ICU resource saturation. With a 12-month vaccine schedule, the number of deaths were 3 times higher and extended-NPI was needed to avoid ICU resource saturation. Vaccine campaigns up to 18 and 24 months would lead to 81 and 93 thousand deaths respectively and saturation of the ICU resources, even with intensive-NPI. In all models with vaccine schedules longer than 6 months, extended-NPI was needed to avoid ICU resource saturation.

Giordano et al. employed a SIDARTHE compartmental model using Italian field data to predict the impact of VOC based on various vaccination campaigns in Italy.[42] Authors reported 20 unique scenarios associated with differing speeds of vaccine rollout, transmissibility profiles and public health measure strategies. Containment strategies (i.e., lockdowns, physical distancing) had a 5-fold impact on reducing human losses in the period of February 2021 to January 2022 in slow, medium and fast vaccine schedules indicating NPIs have a larger effect than vaccination speed. The model demonstrates that in consideration of the highly transmissible VOC, NPIs are crucial for controlling the epidemic. Preemptive strategies (first close when case numbers start to rise and then open at low case numbers) will reduce hospitalizations and deaths when compared with delayed interventions (keep open then close when case numbers start to rise to prevent ICU saturation). Early closures drastically reduce death and healthcare system costs compared with delayed closures.

One study, Munitz et al., provided real-world evidence of the effectiveness of a vaccine roll-out through reporting a correlation of Israel's vaccination campaign with rates of variant B.1.1.7 using data from >300,000 RT-PCR samples collected between December 6, 2020, and February 10, 2021. [49] B.1.1.7 had become the dominant variant (92%) up to January 14, 2021

among all age groups (r>0.99). After January 14 (with 50% of 60+ age group receiving first dose of vaccine), there was a decline in the 60+ age group compared with individuals 0-19 years old (r=0.35) and 20-59 years old (r=0.28). A national lockdown implemented in January 2021 and a surveillance testing program in nursing homes and the community enabled early detection and helped to contain viral spread in at risk populations.

Different vaccines for first and second dose

No studies to date have reported on this outcome.

Attitudes towards vaccine related to VOC

Changes in COVID-19 vaccine hesitancy related to VOC emergence were assessed in the UK by Bachtiger et al. as part of an ongoing cross-sectional/longitudinal study involving 18581 participants examining the effects on well-being of the COVID-19 pandemic.[37] Study participants were invited to complete weekly surveys through their personal electronic health record, Care Information Exchange. Questionnaires related to vaccine behaviour were sent on November 13, 2020 (following Pfizer vaccine reported efficacy of >90%) and on December 31, 2020 (after first reports of B.1.1.7). Intention to receive the vaccine increased from 71.5% (n=6521 of 9122 participants) in the first questionnaire to 85.1% (n= 8187 of 9617 participants) in the second questionnaire. Three hundred seventy-five participants in the second questionnaire indicated they changed their minds to wanting vaccination considering news of the new VOC B.1.1.7. Yearly increase in age (adjusted-OR: 1.045 [95% confidence interval (CI):1.039-1.050]) and female gender (adjusted-OR: 0.540 [95%CI:0.461-0.632]) increased and decreased vaccine acceptance, respectively. This study was critically appraised as low quality, so these findings should be interpreted with caution.

Comparing natural and vaccine protection against COVID-19

Lumley et al. followed a sample of 13109 health care workers (HCW) from Oxford University Hospitals to determine the protection conferred following infection from B.1.1.7 and one and two doses of vaccines.[36] HCW were offered asymptomatic nasal and oropharyngeal swab PCR testing every two weeks and serological testing every two months from April 2020 and the staff vaccination program began December 8, 2020. Data is reported up to February 28, 2021. Anti-timeric spike IgG ELISA was used to determine antibody status. The rates of PCR-positive tests were highest in the unvaccinated seronegative HCWs and 85% lower in unvaccinated seropositive HCWs (aIRR=0.10 [0.08-0.26, p<0.001]). The incidence of any PCR-positive result was reduced by 64% in seronegative HCWs following first vaccination (aIRR=0.36 [0.26-0.50; p<0.001]) and 90% following second vaccination (aIRR=0.10 [0.02-0.38; p<0.001]). B.1.1.7 did not significantly alter the extent of protection for PCR positive infection in those who were seropositive (aIRR =0.40 [95%CI 0.10-1.64; p=0.20]) or following a first vaccine dose (aIRR=1.84 [0.75-4.49; p=0.18]). Overall, findings suggest immunity induced by natural infection with detectable anti-spike antibodies, including B.1.1.7, and vaccine is robust. This study was critically appraised as low quality, so these findings should be interpreted with caution.

Guidance documents related to vaccination approach

- As the influence of VOC on vaccine effectiveness remains under investigation and vaccines against VOC-specific mutations are in development but not yet available, no guidelines or guidance documents are able to explicitly recommend changing to vaccines that offer greater protection. Likewise, there was no guidance related to using different vaccines for first and second doses, or to re-vaccinating due to evolving studies in these areas.
- Instead, guidelines focused on vaccine approaches in general, offering scenario-based recommendations. If whole genome sequencing reveals that the effectiveness of vaccines against VOC is deteriorating,[48] Health Canada suggests vaccines and vaccination approaches should be modified as quickly as possible.[45] In countries in which the spread of the virus remains slow, jurisdictions may decide to begin by targeting at-risk groups, or by targeting "key transmitters"; however, in places where spread of VOC is rapid, targeting key transmitters becomes less feasible and less effective.[47]

- At the end of February 2021, the Center for Infectious Disease Research and Policy (CIDRAP) at the University of Minnesota offered the following suggestions to strategically deploy the vaccine supply in the US:[46]
  - Allocating vaccine with people ≥65 years given highest priority;
  - Deferring second doses of mRNA vaccines until after the surge;
  - Deferring the second dose of mRNA vaccines in people with confirmed COVID-19 infections;
  - Authorization and use of half-dose regimen for Moderna vaccine.
- Health Canada recognizes that to react quickly to changes in vaccine effectiveness against VOC, especially when little is known about a new variant, "harmonising all the vaccines on one or a few sequences may not be straight forward, and vaccines with a variety of sequences, developed as quickly as possible by the manufacturers, may be a pragmatic and rapid means of introducing updated vaccines at this stage in the pandemic. More sophisticated regulatory control could be introduced once the virus is better understood."[45]

Question 1B: Modifying infection-prevention (i.e., public-health) measures in the community (e.g., changing duration of hand washing; changing mask type and characteristics, double masking or other changes to masking; and changes to physical and temporal distancing)

Six sources reported on identifying infection-prevention measures in the community, particularly around physical distancing (see Table 2). Four sources were modeling studies[40,42,50,51] and the other two were grey literature,[52,53] thus no quality appraisal was completed.

Key findings for consideration include:

- **Evidence supporting modification to infection-prevention measures related to VOC is sparse, particularly related to hand washing and masking protocols**
- **Physical distancing and other non-pharmaceutical interventions are important in reducing the spread of VOC in the community**
- **Opportunities exist to expand evidence related to infection-prevention measures in the workplace, particularly in the presence of more highly transmissible VOC**

Five guidance documents (low to medium quality) offer recommendations on infection prevention measures in the community, encompassing general community settings, personal services such as hair salons, and the retail sector.[54–57] None of these guidance documents cited supporting evidence, suggesting expert consensus was used to derive recommendations.

Table 2. *Study summary on public health infection-prevention measures in the community*

Author, year (country)	**Objective**	**Data collection period**	**Sample**	**Outcome measures**	**Relevant key findings**	**Quality appraisal**
Borges et al., 2021 (Portugal)	Investigate the proportion of SGTF cases to gain insight on B.1.1.7 frequency and spread in Portugal	Week 49, 2020 to week 3, 2021	Data set from Portuguese National Institute of Health Dr. Ricardo Jorge Dec 2020 to Feb 5, 2021	SGTF & SGTL test	Physical distancing measures (general lockdown) implemented in weeks 2 & 3 of 2021 decelerated the growth rate of SGTF positive cases	N/A
Domenico et al., 2021 (France)	Assess the impact of social distancing on historical and variant strain through modeling	N/A	Flash1 survey data from Santé publique France on Jan 28, 2021	B.1.1.7 prevalence	Strong social distancing measures (e.g., curfews, lockdowns, work from home) including mild lockdown are needed to decelerate the surge of B.1.1.7 in the third wave	N/A
Vazquez et al., 2021 (Germany)	Estimate SARS-CoV-2 rate of transmission per proximity contact and generate a model to simulate infectious disease outbreaks in workplaces	Not reported	605 individuals from one workplace	Proximity data between two coworkers tracked for 44 days through Bluetooth wearable devices	Using single case workplace proximity data and reproductive numbers for SARS-CoV-2 and B.1.1.7, the transmission rate per contact was determined to be 3 times higher for B.1.1.7 (0.041) vs SARS-CoV-2 (0.014). Workplaces can use proximity data to simulate disease outbreaks and management strategies	N/A

Hand washing and mask protocols

We did not identify any published or preprint studies relevant to modifying hand washing or mask protocols related to the variants of concern. However, a Public Health Ontario Environmental Scan identified 3 out of 14 jurisdictions reviewed had changed the type of mask recommended in public in response to the VOC (from cloth masks to medical masks or respirators).[53] No evidence was identified or cited from these jurisdictions to support the recommended change. A Centers for Disease Control and Prevention communication from the Epidemiology Taskforce on the VOC indicates that current mitigation strategies including masking and hand washing work.[52]

Physical distancing

Three studies contributed data related to physical distancing in consideration of the VOC (Table 2). In a surveillance study evaluating the spread of B.1.1.7 in Portugal between December 20, 2020 and January 20, 2021, Borges et al. concluded that the physical distancing measures implemented in weeks 2 and 3 of 2021 strongly decelerated the growth of B.1.1.7.[50] While models had forecasted the proportion of SGTF/SGTL cases to reach up to 68% (95% CI:65-71), the proportion of SGTF and SGTL positive cases remained below 50% until week 7 of 2021.

Domenico et al. used a discrete, stochastic model integrating demography, age profile, social contacts, and mobility data over time to model the impact of social distancing measures on two strains of SARS-CoV-2 (historical, B.1.1.7).[40] Strain circulation dynamics for France, Ile-de-France regions and Nouvelle Aquitaine were secured through Santé Publique France on January 28, 2021. The model estimated that the progressive social distancing implemented in January 2021 brought the reproductive number of the historical strain below 1 but the B.1.1.7 cases increased exponentially with the estimated reproduction (R) about 1 in all three regions. The authors suggest that strengthening social distancing measures with the addition of restrictive measures such as weekend lockdown will be needed to decelerate the resurgence of B.1.1.7 in a third wave.

Vazquez et al. conducted a novel modelling study at the level of a workplace using co-worker proximity data gathered through Bluetooth technology.[51] Proximity data, collected from button devices worn by 605 workers for a period of 44 days, provided a temporal network to model the spread of airborne viruses. This data is combined with an infection transmission model developed by the team to estimate the SARS-CoV-2 transmission rate per proximity contact. Social distancing is modelled by removing different fractions of the proximity contacts. Based on the proximity data from the sample workplace, the model estimated the transmission rate per proximity contact for SARS-CoV-2 cases as 0.014 and B.1.1.7 as 0.041 per proximity contact, approximately 3 times higher. While the introduction of infection-prevention measures such as social distancing and mask wearing reduces the infection rate, B.1.1.7 transmissibility remained 2 times larger than the wild-type.

Guidance documents related to infection control in the community

- Hand washing guidelines remain relatively unchanged considering VOC. Mask use in all public places remains important. Multi-layer masks are recommended. Eye protection is now recommended in some circumstances in the community. Physical distancing remains important, especially in cases of VOC with higher viral load. In Ontario, infection control measures remain generally unchanged because of VOC. Cleaning of surfaces is still recommended by some guidelines. None of the guidelines cited in Table 3 cite any evidence. **Please note that this table is not representative of all provinces (see note about guidance documents included in this review, page 4).**

Table 3. *Summary of guidance documents from select jurisdictions on hand washing, masking, and physical distancing guidelines in community settings*

	Hand washing	Mask protocols	Physical distancing	Other
In the community (general)	Hand washing remains important.[54]	Multi-layer masks are better than single-layer masks. Masks should snugly fit the face with both nose and mouth covered. It may be necessary to extend masking requirements to places not currently mandated as of Dec 23, 2020 (e.g., workplaces, schools).[54] Masks (medical or non-medical) should continue to be worn in all public spaces and washed daily.[57]	If B.1.1.7 is associated with a higher viral load (speculated at the time of writing - Dec 23, 2020, later proven),[9] that would increase the amount of virus generated by respiratory activities, making physical distancing and ventilation very important. Reconsider 2m as the default distance (rather than 1m+) to reduce the risk of close-range transmission, however there is little benefit to increasing distancing beyond 2m.[54] Work from home if possible. If not possible, follow all physical distancing guidelines in the workplace. Avoid unnecessary travel, even within the province.[57]	At this time, there is no change to infection prevention and control measures recommended for COVID-19 based on the identification of a VOC as part of the outbreak. Health units should continue to follow setting-specific outbreak guidance.[58] Frequent, focused, cleaning of high hand-touch surfaces is likely to be more effective than cleaning surfaces where contact with hands is rare.[54]
Personal services (e.g., hair salons, spas, tattoo parlors)	For direct client services requiring gloves, it is important to properly remove gloves safely, and to wash hands thoroughly afterwards.[56]	It is recommended that service providers wear eye protection, such as a face shield or goggles, in addition to a non-medical mask when providing direct client services.[56]	NR*	NR
Retail sector	Handwashing supplies should be provided for workers and customers in the retail sector.[55]	Wear masks over nose and mouth at work, and eye protection - the latter especially when physical distancing cannot be maintained.[55]	Physical distancing remains the most effective way to reduce the risk of spreading COVID-19.[55]	Surfaces should be cleaned frequently, and retail areas should be well-ventilated.[55]

*NR: Not Reported

Question 1C: Modifying infection-control procedures, such as, changing duration for quarantining of exposed or potentially exposed individuals, changing duration for isolating suspected or confirmed cases (e.g., for exposed health workers), changing testing strategy, including approach to testing, frequency of testing, and turnaround time for test results, changing approach to contact tracing, changing approach to outbreak management.

We identified 10 studies which contributed data relevant to modifying infection-control procedures which are summarized in Table 4. Of these 10 studies, 8 were modeling,[50,59–62] lab-based[63,64] or grey literature[65] and thus not critically appraised. Of the two that were appraised, one was high quality[29] and the other was medium quality.[30]

Key findings for consideration include:

- **The U.S. Food and Drug Administration (FDA) issued a statement of concern on January 28, 2021 related to three tests: Accula SARS-CoV-2 test, TaqPath COVID-19 Combo Kit, Linea COVID-19 Assay Kit. Jurisdictions should ensure local testing is adequate to detect VOC**
- **Non-pharmaceutical interventions (e.g., lockdowns) appear to be important to limit transmission during vaccine rollout particularly if rapid mass vaccination is not feasible**
- **High VOC transmission among individuals living in the same household, particularly among pre-symptomatic and asymptomatic cases, is concerning and warrants aggressive public measures (rapid testing, contact tracing, masking, quarantining and support for out of household quarantine)**

We identified six guidance documents (low to high quality) related to quarantine/isolation (terminology often used interchangeably), testing, and contact tracing from five jurisdictions (Alberta,[66] Ontario,[58] Manitoba,[67] UK,[68,69] and Ireland[70]) and one encompassing all of Canada. Guidance around these infection-control procedures varied across jurisdictions, but typically included a quarantine or isolation period of 10 to 14 days, mandatory testing at two points during quarantine/isolation, and enhanced contact tracing for suspected VOC cases.

Additionally, there were seven guidance documents related to outbreak management, including three that focused on recommendations for genomic surveillance methods, appropriate tests, and sampling approaches.[46,47,54,58,65,71,72]

Table 4. *Summary of studies presenting findings on testing, public health measures, and infection-control procedures related to VOC*

Author, year (country)	Objective	Data Collection Period	Sample	Outcome measure	Relevant key finding	Quality appraisal
Testing						
Abdel Sater et al., 2021 (Lebanon)	Evaluate a primer to confirm deletion mutations Δ69/ Δ70 and Δ106/ Δ107	Dec 9, 2020-Jan 10, 2021	20 samples from SARS-CoV-2-positive patients confirmed through TaqPath kit	SYBR Green-Based RT-PCR	This primer could be used as a second step test in RT-PCR to confirm B.1.1.7 in COVID positive S-Gene negative patients.	N/A
Akingba, 2021 (South Africa)	Evaluate the field performance of the PanBio assay to detect B.1.351	Nov 17-20, 2020	677 patients from 6 mobile clinics	N/A	The assay reliably detected B.1.351 virus infection in ambulatory ill patients. Sensitivity was >90% in patients with high viral loads CTs<30.	N/A
Outbreak management through lockdowns						
Graham, 2021 (Scotland, Wales & England)	Examine the association between regional proportion of B.1.1.7 and reported symptoms, disease course, rates of infection and transmissibility	Sep 8-Dec 31, 2020	Data from 36920 participants in the COVID Symptom Study who tested positive for COVID-19	Self-reported symptom data	Regional and then national lockdown Dec 19 – Jan 5 led to reduced Rt: 0.8 among regions with high proportion of B.1.1.7 cases	80% (high quality)
Scherbina, 2021 (US)	Estimate the benefits of a lockdown in the US similar to those imposed in Europe	N/A	N/A	Estimated future monetary cost of the pandemic	Modeling suggests strict lockdown could reduce R by 76%, or R_0: 0.933. A less restrictive lockdown would lead to R_0:1.66. Optimal lockdown time of 6-7 weeks is needed to achieve high-dQALY outcomes, or 4-5 weeks to meet low-dQALY outcomes	N/A
Outbreak management with general public health guidelines						
Borges, 2021 (Portugal)	Investigate the proportion of SGTF cases to gain insight on B.1.1.7 frequency and spread in Portugal	Dec 2020-Feb 5, 2021	3367 positive SGTF tests (proxy for B.1.1.7) from Portuguese National Institute of Health	SGTF & SGTL test	After implementing public health measures, a decelerating trend was observed in proportion of SGTF/SGTL remaining below 50% in week 7 of 2021	N/A

Author, year (country)	Objective	Data Collection Period	Sample	Outcome measure	Relevant key finding	Quality appraisal
Buchan, 2021 (Canada)	Compare household secondary attack rates in those with VOC versus non-VOC index cases in Ontario	Feb 7-27, 2021	5617 index cases and 3397 secondary cases	Household secondary attack rate 1-14 days after index case	Secondary attack rate 1.31 higher in VOC vs non-VOC in same household, further accentuated in asymptomatic (RR=1.91) and pre-symptomatic (RR=3.41) cases. Findings suggest need for aggressive public health measures physical distancing, masking, testing and contact tracing	67% (medium quality)
Piantham and Ito, 2021 (UK)	Propose a method to estimate selective advantage of mutant strain over previous strains	Sep 1, 2020-Feb 19, 2021	71692 B.1.1.7 strains and 65850 non-B.1.1.7 strains	Time from illness onset in a primary case to illness onset in secondary case	B.1.1.7 has an estimated reproduction advantage of 33.7% over non-VOC, suggesting control measures need to be strengthened by 33.7%	N/A
Public Health Ontario, 2021 (Canada)	Communicate the current actions in mitigating VOC in the province of Ontario	N/A	N/A	N/A	Regardless of the variant, following public health measures is the best way to stop transmission	N/A
Smith, 2021 (UK)	Assess the impact of environment on VOC transmission	Oct 19-Dec 7, 2020	N/A	Global population density, temperature and reproduction number (R)	Warmer temperatures are associated with decreased VOC transmission. However, impact of temperature is only secondary to public health measures, with UK observing effect of temperature on VOC only after lockdown measures lifted	N/A
Zimerman, 2021 (Brazil)	Assess whether social isolation into small families or groups is associated with the emergence of new variants	Jun 1, 2020-Jan 10, 2021	773 genomic sequence samples	Social isolation index (SII), which is based on percentage of individuals who stayed within 450m of their home	In the state of Amazonas, where household sizes are large, there was a positive correlation between SII and the prevalence of P.1 when SII was above 40%. Authors hypothesize that forced prolonged cohabitation may boost viral mutation and increased infectivity.	N/A

**high-dQALY: discounted quality-adjusted life years based on $431,000 being the higher end; low-dQALY: discounted quality-adjusted life years based on $150,000 being the lower end; NA = not appraised

Duration of quarantine and/or isolation

No studies were found relevant to the impact of VOC on duration of quarantine or isolation. However, according to a Centers for Disease Control and Prevention report, the increased transmissibility of VOC demonstrates the need for higher adherence to current mitigation strategies, including quarantine.[52]

Frequency or change of testing

We identified a wide range of studies evaluating different genome sequencing strategies, antigen tests or assays and primers for use in rapid PCR tests in our search. However, studies regarding testing were only included in this report if they explicitly identified implications for potentially modifying existing public health testing measures. Two studies and one report identified through the grey literature were deemed relevant for this sub-question.

Abdel Sater et al. designed and evaluated a primer set that could be used in a rapid, low-cost screening protocol to confirm deletion of mutations Δ69/ Δ70 in the spike gene and Δ106/ Δ107 in the NSP6 gene.[63] The method was tested using 20 clinical samples from previously tested SARS-CoV-2 positive patients, 16 of which were S-negative and 4 were S-positive. The primer set successfully identified the presence and absence of S deletions Δ69/ Δ70 in 100% of both the S-negative and S-positive profiles. This protocol may be of particular benefit in areas where access to laboratories to conduct genome sequencing is limited.

Between November 17 and 20, 2020, Akingba et al. tested the field performance of the PanBio SARS-CoV-2 Rapid Antigen Test (RTD) with 677 patients attending one of 6 mobile clinics in Nelson Mandela Bay, South Africa.[64] This rapid test is available and validated for use in Canada. At this time, South Africa was experiencing their second wave of the pandemic and B.1.351 was responsible for 84% of infections in Nelson Mandela Bay. The same nasopharyngeal swab used in the RTD was also sent for PCR for direct comparison. The antigen test had an overall sensitivity of 69.17% (95%CI:61.44,75.80) and specificity of 99.02% (95%CI:98.78,99.26). However, sensitivity improved in clinical samples with a high viral load (CT), with 100% detection when CT was <20, 95.5% when CT was 20-25 and 89.3% when CT was between 26-30.

On January 8, 2021, the FDA issued an emergency use authorization (EUA) statement containing caveats about the following three tests: 1) the Accula SARS-CoV-2 test performance might be impacted if the patient sample contains genetic variant at position 28881; 2) the TaqPath COVID-19 Combo Kit has significantly reduced sensitivity to certain mutations including B.1.1.7; and 3) the Linea COVID-19 Assay Kit has significant reduced sensitivity to certain mutations including B.1.1.7.[73] Notably, the report did not include primary evidence to support these statements.

Contact tracing

No studies were identified related to impact of VOC on contact tracing.

Changing approach to outbreak management

Eight studies reported on outbreak management across a range of outcomes. Two studies discussed managing outbreaks by stricter NPIs. Graham et al. conducted an ecological study to explore the rate of infection and transmissibility of B.1.1.7 in the UK.[27] Between September 28 and December 27 2020, B.1.1.7 was found to increase R_t (effective reproduction number) to 1.35 compared with historical SARS-CoV-2 variants. However, following a strict lockdown between December 19, 2020 and January 5, 2021 the estimated R_t of B.1.1.7 had decreased to 0.8 in three regions in England where 80% of infections were related to the variant. A modeling study conducted by Scherbina et al. identified the impact of different lockdown measures on community infection rates of B.1.1.7 with assessment of future monetary costs, in the form of missed work days, direct medical costs and the value of lost lives.[60] The authors suggested that a strict lockdown could reduce the transmission rate to below one (R_0=0.933), while a less strict lockdown would see the reproductive number exceed one (R_0=1.66) and worsen the impact across all measures.

Five research articles and one grey literature source reported on managing outbreaks through the implementation of general public health measures. Borges et al. associated the implementation of public health measures, namely physical distancing, in Portugal with a decrease in proportion of SGTF/SGTL (i.e. an indicator of B.1.1.7).[50]

Another study by Buchan et al. conducted in Ontario, Canada compared the number of secondary attack rates among households with reported VOC cases versus households with non-VOC index cases.[29] VOC secondary attack rates were 1.28 times higher for VOC versus non-VOC. Further, the secondary attack rates were observed to be higher for asymptomatic index cases (RR=1.91, 95%CI:0.96,3.80) and pre-symptomatic cases (RR=3.41, 95%CI:1.13,10.26). This significant increase transmission of VOC in households particularly for asymptomatic and pre-symptomatic cases suggests a need to support strict household quarantine guidance and provision of outside the home quarantine support and monitoring of cases.

Somewhat supporting that household transmission may be a key feature to monitor in VOC outbreaks, a study conducted by Zimerman et al. in Brazil reported contrasting findings in terms of outbreak management.[30] In the study comparing the prevalence of the P.1 variant with social isolation data, authors found that prevalence of P.1 actually increased when individuals remained within 450m of their home. This study therefore highlights the need to tailor public health measures to specific populations and that vigilance regarding household transmission is warranted.

In a modeling study conducted by Piantham and Ito, it was estimated that B.1.1.7 has a reproductive advantage of 33.7% over non-VOC.[59] Authors reported that public health measures should therefore be strengthened by 33.7% to account for the increased transmissibility of B.1.1.7.

Smith et al. assessed the impact of temperature on VOC prevalence in the UK.[61] Warmer temperatures were found to be associated with lower VOC transmission, but this was only secondary to the impact of public health measures.

In addition to these four articles, a guidance document from Public Health Ontario broadly suggested that despite the VOC in circulation, following all existing public health measures would be the best way to stop transmission.[65]

Guidance documents related to quarantine/isolation, testing, and contact tracing

- Quarantine and/or isolation requirements vary across Canada and in other countries. Both 10-day (Alberta, Manitoba, UK) and 14-day (Ontario, Ireland) isolation periods are in effect in various jurisdictions; it is unclear whether these isolation periods were enacted in response to VOC, or if they pre-dated VOC. Testing is commonly required on day 0 and on or after day 10 of isolation (Alberta, Ontario, Manitoba, Ireland); UK requires testing on day 2 and day 8. Contact tracing approaches are variable but appear generally enhanced in response to VOC. In the UK and Ireland, more emphasis is placed on requiring a recent travel history from anyone presenting for care. The recommendations across jurisdictions are summarized in Table 5. **Please note that this table is not representative of all provinces (see note about guidance documents included in this review, page 4).**

Table 5. *Guidance related to quarantine/isolation, testing, and contact tracing requirements in a selection of provinces and countries*

Jurisdiction / Setting	**Quarantine / Isolation**	**Travel**	**Testing**	**Contact Tracing**
Canada – Schools	NR	NR	Where diagnostic test capacity is constrained, screening tests can be used for lower-risk contacts. If a VOC is in the community, then it may be appropriate to implement more screening tests if community prevalence suggests this would be beneficial.[74]	When at least one positive case in the school is linked to a VOC, Canada's COVID-19 Testing and Screening Expert Advisory Panel recommends both diagnostic testing of contacts and broad-based screening testing to break the chains of transmission.[74]
Alberta	People who have tested positive for P.1 or B.1.351 are legally required to self-isolate for 10 days from onset of symptoms or date of test. Household contacts, if isolating with the infected person, must quarantine/self-isolate for the 10 days plus 14 additional days after the initial person has completed their isolation. Close contacts (outside the household) of people infected with P.1 or B.1.351 must self-isolate for 14 days after exposure.[66]	NR	Everyone with symptoms is encouraged to get tested immediately. Close contacts of those infected with P.1 or B.1.351 are required to get tested immediately, and then again between day 10 and day 14.[66]	NR
Ontario	Quarantine remains 14 days for anyone with a high-risk exposure. While contacts should be encouraged to seek testing for COVID-19, completion of the test is not required prior to exit from quarantine. All household members of symptomatic individuals are required to quarantine until the symptomatic individual receives a negative COVID-19 test result or is provided an alternative diagnosis by a healthcare professional.[58]	NR	High-risk contacts recommended to get tested immediately. For contacts that test negative initially, they are recommended to test again on or after day 10 of quarantine. If the initial test was collected on or after day 7 of quarantine, repeat testing on or after day 10 is not necessary. If there has been a discrete exposure to a case (i.e., when the contact was exposed at a specific time(s), such as a visit), the contact should be advised	Have a lower threshold for classifying contacts as high risk of exposure and requiring quarantine, based on the risk assessment of exposure that considers duration, mask use, ventilation, etc. Health units are generally not required to ensure contacts are tested or follow up on results of testing with contacts (unless necessary for outbreak management). While contacts should be encouraged to seek testing for COVID-19, completion of

Jurisdiction / Setting	Quarantine / Isolation	Travel	Testing	Contact Tracing
			to test on or after day 7 of quarantine. Repeat testing is not required if the specimen was collected on or after day 7. However, repeat testing on or after day 10 of quarantine is recommended if the initial specimen was collected on day 0-6 of quarantine.[58]	the test is not required prior to exit from quarantine. As part of routine contact follow up, public health units should counsel contacts to tell their household members that they are required to stay home except for essential reasons for the duration of the contact's quarantine period. Essential reasons include: attending work/school/childcare and essential errands such as groceries or picking up prescriptions.[58]
Manitoba	An individual who has tested positive for COVID-19 due to a VOC must isolate for a minimum of 10 days, and if symptomatic, has been symptom free for 24 hours. If the positive individual isolates at home, all members of that individual's household must also self-isolate (quarantine) for the same 10 days as the positive case and must self-isolate (quarantine) for a further 14 days following to ensure the virus was not transmitted in the final days of the case's isolation, for a total of 24 days of self-isolation (quarantine).[67]	NR	Any close contacts without symptoms will be advised to get tested on notification and at day 10 after their last exposure to a positive case. The first testing of asymptomatic contacts in the self-isolation period is optional to allow earlier identification of asymptomatic cases, and initiation of contact tracing and isolation if positive. For those who test positive, testing is recommended again at day 10. Close contacts must be asymptomatic and are required to have a negative test to remove from self-isolation at day 14. If not tested, self-isolation is extended for 14 days after the case finishes their isolation period.[67]	Manitoba has lowered the threshold of what's considered "prolonged contact" with a COVID-positive case to identify close contacts. This will help identify more close contacts and reduce the spread of the virus. If someone tests positive for COVID-19, all household members will be considered close contacts and will have to self-isolate. If someone is a close contact of a case who lives in a different household, all members of the close contact's household must also stay home until the close contact has been tested and they have a negative result.[67]
UK	Anyone who has been tested must isolate with their household and follow the guidance for households with possible or confirmed coronavirus infections until they get their result.[68]	Travellers who are permitted to enter the UK from countries listed within the travel ban to the UK are currently required to self-isolate for 10 days on arrival along with their household. Any contacts identified in the UK should also self-	From Feb 15, 2021, travellers to the UK will be PCR tested for SARS-CoV-2 at Day 2 and Day 8.[69] The UK began implementing surge testing on Feb 1, 2021. Surge testing is	NR

Jurisdiction / Setting	Quarantine / Isolation	Travel	Testing	Contact Tracing
		isolate for 10 days from the last date of contact after the traveller returns to the UK.[69]	increased testing (including door-to-door testing in some areas) and enhanced contact tracing in specific locations.[68]	
Ireland	10 days of self-isolation is required for any cases of COVID-19 in the community. Unaccompanied minors (i.e., those under 18 years of age) can quarantine at home if their guardian (parent or approved representative e.g. school) can supervise their quarantine.[70]	People traveling into Ireland who are at risk of having a VOC are required to stay in mandatory hotel quarantine (MHQ) for a period of 14 days. People can leave quarantine on day 10 if their day 10 test is negative and no symptoms are detected. For those who test positive for COVID-19, the period of self-isolation required is 14 days from the date of onset of symptoms, or the date of the test, if asymptomatic, the last 5 of which must be fever-free. This is different to the requirement for 10 days self-isolation for other community cases of COVID-19.[70]	People in MHQ are administered a test on day 0 and day 10. The aim of the public health response is to delay the importation and spread of VOC in an area where they are not widely circulating. This is achieved by a combination of testing before arrival in Ireland, and quarantine and testing of incoming travellers from states where there is a risk of importation of VOC, due either to high levels of virus in the community and/or known circulation of VOC. The testing requirements apply to all children over three years of age.[70]	Enhanced contact tracing for cases suspected to be infected with VOC should be undertaken.[70]

Guidance documents related to outbreak management and prevention

- Engineering, procedural, and personal controls are essential for reducing transmission when interactions between people are unavoidable. This means people need to reassess their environments to ensure all precautions have been taken considering emerging VOC. Additionally, an indoor humidity of 40-60% is recommended.[54]
- Callan et al. defined Canada as a "Category G" country, in which COVID-19 was controlled or kept out until recently, but the future is uncertain as cases are currently increasing or peaking. In Category G countries, the authors recommend keeping all current disease control measures in place until vaccines become widely available and strengthened to compensate for new virus variants.[47]
- In Ireland, single VOC cases are managed as outbreaks by the Department of Public Health, triggering a full epidemiological investigation. This investigation focuses on whether the person has a history of travel in the preceding month; if not linked to travel, extensive efforts are required to identify any epidemiological links with other cases.[70]
- In Ontario, although no environmental cleaning protocols have been adapted in response to VOC, all VOC infections identified within the health system trigger immediate testing of all associated patients and staff, and sample sequencing of 1-3 cases to check for VOC is required with every COVID-19 outbreak. If a VOC outbreak is confirmed, all associated patients and staff should be tested every 3-5 days.[72] When considering reopening or loosening of restrictions, Public Health Ontario recommends that “re-opening in a green-level public health unit (PHU) adjacent to a PHU with higher COVID-19 incidence may yield higher risks of COVID-19 than opting for a larger geographic region where all included PHUs have achieved similar COVID-19 control” and that, generally, gradual re-opening is more successful at controlling COVID-19 than rapid re-opening.[65]

Genomic surveillance guidelines

- The Canadian COVID Genomics Network (CanCOGen) recommends targeted genomic surveillance in the following scenarios, using multi-target COVID-19 RT-PCR tests with S-gene target dropouts (TaqPath three-target assay):[71]
    - All international travellers and their close contacts, prospectively
    - All international travellers and their close contacts, retrospectively
    - Cases of suspected reinfection
    - Severe acute COVID-19 cases in individuals younger than 50 years old without significant comorbidities
    - Cases in vaccinated individuals with subsequent laboratory-confirmed SARS-CoV-2 infection
    - Cases linked to known or suspected super spreading events
    - Geographic sampling in sub-regions with a pronounced increase in the case notification rate
    - Random sampling for routine national genomic surveillance
- Public Health Ontario is now using a VOC PCR test on eligible SARS-CoV-2 positive samples to detect both N501Y and E484K mutations at the same time; this will identify B.1.1.7, B.1.351, and P.1 and mitigates the need for whole genome sequencing (WGS) of all samples. WGS is best suited to population surveillance and not individual identification of VOC cases, as it is complex and takes 4-5 days.[75]
- The European Centres for Disease Control (ECDC) and WHO have co-produced a comprehensive guidance document outlining recommended approaches to screening and sequencing for VOC. The organizations recommend WGS to confirm VOC infection, and also support Sanger or partial next generation sequencing (NGS) amplicon-based sequencing, with which targeted whole or partial S-gene sequencing can be performed using a genetic analyzer. For the early detection and prevalence calculation of VOC, the organizations support several approaches to diagnostic screening assays, including S-gene drop out or target failure (SGTF), multiplex RT-PCR (including SGTF), screening SNP assays, screening SNP by specific real time RT-PCR melting curve analysis, and reverse transcription loop-mediated and transcription-mediated amplification isothermal

amplification (RT-LAMP). Sequencing should be performed on at least a subset of these assays to confirm VOC identification. While the document acknowledges that rapid antigen detection tests appear to be as effective at identifying VOC as they are at previous variants, they do not differentiate between variants. The document includes several recommendations for VOC screening, including timely testing of people with symptoms, targeted or convenience sampling to aid early detection, and regular representative sampling to assess the level of VOC circulating in the community (and therefore reducing risk of bias in VOC screening results). The document ends with recommendations for assessing the quality of new testing methods or assays.[48]

- Ireland is developing a WGS program with plans to sequence up to 1500 samples per week. The samples will be collected both reactively (e.g., targeting travellers, clusters) and proactively (e.g., random representative sampling).[70]

Question 2: Health System Arrangements

Health system impacts due to VOC were reported in 17 original studies. The sections below are divided by sub-objectives and are discussed in relation to the relevant objective. Overall, 13 studies related to health system impacts were eligible for critical appraisal. Two were appraised as low quality,[38,39] seven as medium,[28,30–35] and four as high.[24–27]

Question 2A: Adjusting capacity planning to accommodate changes in the risk of re-infection and the risk of severe disease (e.g., hospitalization, admission to ICU, and death).

Key findings for consideration include:

- **NPI (e.g., curfew, lockdown) may minimize risk of reaching hospital capacity due to VOC infections**
- **Emerging data is somewhat conflicting but overall suggests there is an increase in hospitalization due to B.1.1.7 but no difference in length of stay**
- **Findings are mixed on the impact of B.1.1.7 on intensive care unit admissions**
- **While there are mixed findings on impact of VOC (B.1.1.7 and P.1) on death, there were more studies (n=6) that found an increased risk compared to no change (n=3). In studies that reported an increase in death, B.1.1.7 was found to increase the risk between 15% to 67% compared to non-VOC. The impact of rationed critical care and health system capacity strain on mortality may be difficult to separate in some of these studies**
- **Two guidance documents from Ontario refer to health facility capacity planning; neither refer specifically to increased hospitalization as a result of VOC, but rather communicate general guidance for moving COVID-19 patients between units**

While most studies related to this sub-question reported on the impact of VOC on hospitalization, admission to ICU and death (see Table 6), Haas et al. also discussed impact of vaccine efficiency (VE).[32] Haas et al. conducted the first nationwide estimates on the effectiveness of two doses of the Pfizer vaccine against a range of SARS-CoV-2 outcomes, including hospitalization and deaths, in Israel. Haas was appraised as medium quality in the critical appraisal. Between December 2020 and March 2021, there were 202,684 COVID-19 infections, 139,835 (69.0%) in people over 15 years. There were 6,040 hospitalizations, of which 3,470 were severe and critical, and 754 deaths in people over 15 years. The prevalence of B.1.1.7 of tested cases was 93.9%. During the study period, over half (51.5%) of people over 15 years and 82.8% of people over 65 years received two doses of Pfizer. Among COVID-19 related hospitalizations, most were in people unvaccinated (4,382, 72.5%) with a small number of admissions who had received two doses in the prior 7 days (421, 7.0%). The incidence rate (IR) (per 100 000 person-days) of COVID-19 among people over 15 years was 116.2 in unvaccinated and 5.3 in vaccinated at least 7 days after the second dose. The adjusted VE was 94.1% (95% CI 93.4–94.7) against COVID-19 infection. Adjusted VE against COVID-19 hospitalization was 96.0% (95% CI 95.2–96.6) and VE against severe and critical hospitalization was 96.2% (95% CI 95.5–96.8). In relation to deaths, 457 (60.6%) were in unvaccinated individuals and 99 (13.1%) in individuals who had received the second dose at least 7 days ago. Adjusted VE against death was 93.3% (95% CI 91.5–94.8). VE estimates against all outcomes were slightly higher when measured 14 days after the second dose than VE estimates that were done after 7 days; however, overall, this study suggested there is high VE 7 days after the second doses of Pfizer against hospitalizations, severe and critical hospitalizations, and deaths.

Domenico et al. provided a unique mathematical model to estimate the role that curfew measures could have on hospitalization in France.[40] They found that if the epidemic progressed under curfew conditions (6pm nightly, implemented nationwide January 16th) before school holidays and vaccination is accelerated, hospital capacity would be reached around week 13 in France (which had 2.2% B.1.1.7 penetration), week 12 in Île-de-France (which had the highest B.1.1.7 penetration, 6.9%), and week 14 in Nouvelle Aquitaine (which had the lowest B.1.1.7 penetration 1.7%). The partial relaxation of social distancing (estimated at 15% increase in effective reproduction number) would shorten these estimates by at least 1

week. Stronger social distancing, equivalent to the efficacy measured during the second lockdown (estimated 15% reduction in effective reproduction number), would maintain hospitalizations below the peak of the second wave in Île-de-France and Nouvelle Aquitaine but would not be enough to avoid a third wave in France, even under accelerated vaccination (100k-200k doses/day). Accelerated (200,000 first doses/day) and optimistic vaccination rollouts (300,000 first doses/day) would reduce weekly hospitalizations by about 20% and 35% in week 16 (i.e., April 19-25, 2021) compared to a stable vaccination campaign without acceleration (100,000 first doses/day).

Table 6. *Summary of findings for capacity planning and health systems arrangements*

	Hospitalization/Severity	Admission to ICU	Death
Increased due to VOC	• After adjusting for sex, age, region and comorbidities, individuals with B.1.1.7 were 1.6x more likely to be hospitalized vs wild type (adjusted OR of 1.64, 95%CI, 1.32-2.04). Individuals with B.1.1.7 had a 64% increased risk of hospitalization. (Bager, Denmark, Jan-Feb 2021, medium quality)[28] • There was a statistically significant increase in the hospitalization rate for regions in the top 10% percentile of reported VOC cases. Regarding time dynamic effects, the hospitalization rate was ~38% higher in high VOC regions (9+ VOC cases) compared to their pre-VOC observation (Mitze and Rode, Germany, Jan-Feb 2021, no appraisal)[76] • In wave two (high B.1.1.7 prevalence), the number of admissions increased (35.1% v 54.8%) vs. with wave one (non-B.1.1.7). Patients with non-B.1.1.7 and B.1.1.7 were not significantly different in terms of age or ethnicity, but where more likely to be female, obese but less frail. On admission, B.1.1.7 patients were more likely to be hypoxic. (Snell, UK, March 2020-Feb 2021, medium quality)[35] • There was a significant association between infection with B.1.1.7 and hospitalization in UK within 14 days of positive test (OR: 1.39, 95%CI 0.98-1.98, p=0.07), however, the length of hospital stay was similar. After adjusting for sex, age, ethnicity, residential property classification and week of specimen date, the risk of hospitalization was higher in B.1.1.7 cases compared to wild type cases (HR 1.34, 95% CI:1.07-1.66, p=0.01). (Dabrera, UK, Oct-Dec 2020, medium quality)[31]	• There was an estimated increase of 1.29 [CI: 0.5, 2.1] additional COVID-19 patients in intensive care per 100,000 population, which is a 42% increase compared to the hospitalization rate pre-VOC (combined). (Mitze and Rode, Germany, Jan-Feb 2021, no appraisal)[76] • In both the adjusted and unadjusted analysis, the primary care group had a higher risk of admission to critical care for B.1.1.7 patients compared with the non-B.1.1.7 patients (adjusted HR: 1.99; 95% CI: 1.59 - 2.49). In the critical care cohort, a lower risk of admission for critical care in the B.1.1.7 group was mainly accounted for after adjustment for date of admission to critical care (HR: 0.84, 95% CI: 0.64 - 0.99). (Patone, England, Nov 2020-Jan 2021, medium quality)[34]	• An increase of 0.1 in the proportion of B.1.1.7 was related with a 15.3% increase in the total number of deaths (Jablońska, Europe, Jan-Feb 2021, medium quality)[33] • The mortality hazard ratio for people with B.1.1.7 compared to those with previous variants was 1.64 (95% CI 1.32 to 2.04). In this community-based, relatively low-risk group, there was a 32% to 104% increased risk of death. (Challen, UK, Oct 2020-Feb 2021, high quality)[24] • The estimated hazard ratio for B.1.1.7 was 1.55 (95% CI 1.39– 1.72), indicating that the hazard of death in the 28 days following a positive test was 55% (39– 72%) higher for B.1.1.7 than non-B.1.1.7. Correcting for misclassification and missing SGTF status, this increased to 61% (42–82%). (Davies, UK, Nov 2020-Feb 2021, no apprisal)[77] • B.1.1.7 was associated with 67% increased risk of death at 28 days after a positive COVID-19 test (HR: 1.67, 95%CI, 1.34-2.09). (Grint, England, Nov 2020-Jan 2021, high quality)[26] • While there were no changes in Case Fatality Rates (CFR) in children or adolescent, all other groups above 20 years of age had statistically significant increases in CFR when diagnosed in February 2021 (P.1) as opposed to January 2021 (non-P.1) (De Oliveira, Brazil, Jan-Feb 2021, low quality)[39] • Each geographical region of Brazil varied in terms of their mortality over the three periods, with the North region being the hardest hit, experiencing a collapse in the provision of healthcare in the first wave and last

	Hospitalization/Severity	Admission to ICU	Death
			periods (P.1) with high mortality in all age groups (De Andrade, Brazil, Feb 2020-Feb 2021, low quality)[38]
No change between VOC and wild-type	• After correcting for mean age, sex, ambient temperature, and humidity, there was no association between B.1.1.7 and the number of symptoms reported over a 4-week period after a positive test, the number of hospitalizations, long symptom duration or proportion of asymptomatic cases (Graham, Scotland, Wales and England, Sept-Dec 2020, high quality)[27] • There was no significant difference in length of stay or time to hospital admission from symptom onset for patients with B.1.1.7 than for patients without B.1.1.7. (Frampton, UK, Nov-Dec 2020, high quality)[25] • Pairing 29 B.1.1.7 cases to 58 controls (non-B.1.1.7) on age and gender, there was no significant difference on time from first symptoms to ED admission or severity or need for immediately ICU management. (Courjon, France, Dec 2020-Feb 2021, medium quality)[30]	• In terms of intensive care, the numbers were too small to be conclusive on the association with B.1.1.7 (13 ICU among 128 B.1.1.7 admissions (10.2%) versus 115 ICU among 1090 admissions (10.6%) after infection with other lineages. (Bager, Denmark, Jan-Feb 2021, medium quality)[28] • There was no significant difference between those admitted to the ICU before B.1.1.7 was dominate (23%) compared to after, (26% and 35%), p=0.374. For ICU patients, neither the severity score at admission (SAPSII) nor the depth of the respiratory distress seemed to increase by the variant (Courjon, France, Dec 2020-Feb 2021, medium quality)[30] • While there was variation in the age profile of hospitalized patients between Feb 2020-Feb 2021, but there was no evidence of an increase in hospitalization in the last period (related to high P.1) for adults between 18 and 50 years (De Andrade, Brazil, Feb 2020-Feb 2021, low quality)[38]	• There was no difference in the percentage of patients with and without B.1.1.7 who died within 28 days (16% B.1.1.7 vs. 17% non-B.1.1.7, p=0·74). There was no excess mortality risk associated with B.1.1.7 compared with non-B.1.1.7 in unadjusted analyses (PR 0·85 [95% CI 0·52–1.41] for B.1.1.7 vs non-B.1.1.7), or adjusted analysis (PR 1·12 [95% CI 0·71–1·78]). (Frampton, UK, Nov-Dec 2020, high quality)[25] • In the unadjusted analysis, there was no difference in 28-day mortality risk for B.1.1.7 compared to non-B.1.1.7 patients, but after adjusting for confounders, there was a higher risk of 28-day mortality in B.1.1.7 patients (adjusted HR: 1.59; 95% CI: 1.25- 2.03), mainly explained by age (HR: 1.53, 95% CI: 1.28-1.82 with adjustment for age alone). In the critical care cohort, after adjusting for confounders, critical care mortality did not differ significantly between B.1.1.7 and non-VOC B.1.1.7 groups (adjusted HR: 0.93, 95% CI 0.76-1.15). (Patone, England, Nov 2020-Jan 2021, medium quality)[34] • In a matched cohort analysis, there was no evidence of an association between B.1.1.7 and non-B.1.1.7 on death within 28 days of COVID-19 positive test (OR: 0.90, 95%CI 0.57-1.41, p=0.64), with similar median time between positive test and death (8 days for B.1.1.7 and 9 days for non-B.1.1.7 (Dabrera, UK, Oct-Dec 2020, medium quality)[31]

Hospitalization/Severity

Seven studies reported on health system impacts related to hospitalization and severity of illness. Four studies in Europe reported increases in hospitalization and/or severity of illness associated with B.1.1.7 compared to the wild type; however, another three studies found no difference. Among the seven studies that reported on hospitalization, four were appraisal as medium quality studies and two as high-quality studies (one not appropriate for appraisal). Table 6 below provides a summary of findings with additional detail provided in text below.

Increases in risk of hospitalization/severity

Bager et al. conducted an observational cohort study of 35,887 SARS-CoV-2 positive individuals in Denmark between January 1st to February 9th, 2021.[28] While Denmark was in a lockdown after December 16th and it was effective ~~as~~ in reducing case numbers and hospital burden, B.1.1.7 increased during this time and was found to have a reproduction number of 1.25 on February 16th. 11.6% of their sample had B.1.1.7 and the proportion of individuals with B.1.1.7 increased from 1.9% to 45.1% during their data collection period. They found no significant difference in hospitalization between B.1.1.7 vs non-B.1.1.7 in their crude analysis (OR 0.87; 95%CI, 0.72-1.05), but after adjusting for sex, age, region and comorbidities, B.1.1.7 was 1.6 times more likely to be associated with hospitalized than wild type (adjusted OR of 1.64, 95%CI, 1.32-2.04). They concluded that individuals infected with B.1.1.7 had a 64% increased risk of hospitalization~~s~~ compared to individuals infected with other lineages.

An epidemiological and modeling study was conducted in Germany on the 7-day incidence rate (per 100,000 population), and the hospitalization rate (per 100,000 population).[76] All three VOC were combined for power due to the low spread in Germany at the time of the study – by February 4th, 2021, 204 out of 401 (50.1%) of the HUT-3 regions had at least one VOC case. Hard-hit cities included Flensburg where the 7-day incidence rate drastically increased in January 2021 relative to the average development in Germany due to illegal parties and NRW cities (Cologne, Leverkusen and Duren). The hospitalization rate for Flensburg shows a significant increase ~16 days after treatment start (considered one week before the first VOC case). However, this should be interpreted with caution as it was calculated on a relatively small number of hospitalized patients per 100,000 population at the local area level (i.e., 2 patients before VOC vs. 8 cases after VOC). Interestingly, treatment effects estimate, for the NRW cluster, an increase in the 7-day incidence rate by ~40% but no significant increase in hospitalization rates. Difference-in-difference analysis point to positive but insignificant correlations for all regions but in regions with an early VOC reporting before January 22nd, they found a statistically significant increase in the hospitalization rate for regions in the top 10% percentile of reported VOC cases. Regarding time dynamic effects for the hospitalization rate, significant effects were found ~15 days after treatment start for regions with 9+ VOC cases. After 20 days, the hospitalization rate was ~38% higher in high VOC regions compared to their pre-VOC observation. This corresponds with two additional patients in intensive care per 100,000 in high VOC regions, suggesting that hospitalization tends to grow over time with B.1.1.7 cases.

Snell et al. conducted a retrospective cohort study in the United Kingdom on 2,341 individuals admitted to the Guy's Hospital and St. Thomas Hospital within 14 days following a positive test during first wave (March 13, 2020-May 12, 2020, n=838, considered non-B1.1.17) and second wave (October 2020-Feb 2021, n=1503, predominantly B.1.1.7).[35] In wave two, the number of admissions increased compared with wave one (54.8% vs. 35.1%). In the second wave, B.1.1.7 made up 83% of all sequenced isolates and 85% of sequenced isolates from admitted cases. Snell et al. examined differences between the two waves in terms of patient composition. While the general statistics were similar, they found that wave two hospitalized patients (regardless of VOC status) were slightly younger (60 vs. 62 years, p=0.019) and more likely to be female (47.3% vs. 41.8%, p=0.011). Considering comorbidities, individuals in wave two were less likely to have a diagnosis of frailty (11.5% v 22.8%, p<0.001), have a history of stroke (4.3% v 8.6%, p<0.001) or cancer (4.8% v 7.2%, p=0.022) but were more likely to be obese (29.1% v 24.6%, p=0.02). There was no significant difference on other comorbidities of diabetes, kidney disease, hypertension, cardiovascular disease, or respiratory disease. Shifting to comparing admitted patients with B.1.1.7 (n=400) or non-B.11.7 VOC (n=910), the groups were not significantly different in age (62 years vs 64 years, p=0.22) or ethnicity. However, patients with B.1.1.7 were more likely to be female (48.0% vs 41.8%, p=0.01), less likely to be frail (14.5% vs 22.4% p=0.001), more likely to be obese (30.2% v 24.8%, p=0.048), and more likely to be hypoxic on admission (70.0% vs 62.5%, p=0.029), the main indicator of severe disease, than non-B.1.1.7 patients.

Dabrera et al. conducted a matched cohort study in the UK to explore whether B.1.1.7 was associated with more severe clinical outcomes compared to wild type COVID-19.[31] In 5,642 cases, 131 individuals had a hospital admission within 14 days of their positive test: 76 (2.7%) VOC and 55 (1.9%) wild-type cases (p=0.006). There was a significant association between infection with B.1.1.7 and hospitalization within 14 days of positive test (OR: 1.39, 95%CI 0.98-1.98, p=0.07); however, the length of hospital stay was comparable (B.1.1.7 median length of stay (LOS) 5 days (IQR 3-10, range 0-37) vs wild type LOS 8 days (IQR 4-13.5 days, range 0-31), p=0.07). In univariable analysis, B.1.1.7 infection and risk of hospitalization within 14 days were not associated (HR: 1.07, 95%CI: 0.89-1.29, p=0.48); however, adjusting for potential confounders (sex, age, ethnicity, residential property classification and week of specimen date) resulted in the risk of hospitalization being higher for B.1.1.7 cases compared to wild type cases (HR 1.34, 95% CI:1.07-1.66, p=0.01).

No changes in risk to hospitalization/severity

Graham et al. conducted a longitudinal cohort study on 36,920 users of the COVID symptom study mobile app in Scotland, Wales and seven regions in England who tested positive for COVID-19 between September 28th and December 27th, 2020 while the proportion of B.1.1.7 was exploding, along with surveillance data from 98,170 sequences from the COVID-19 UK Genetics Consortium (COG-UK), 16% of which were B.1.1.7.[27] Therefore this study took place before health system strain was excessive. They compared the proportion of B.1.1.7 in each region and the proportion of reports per week for each symptom, disease burden and self-reported hospitalization. After

adjusting for mean age, sex, ambient temperature, and humidity, there was no association between B.1.1.7 and the number of symptoms reported over a 4-week period after a positive test, the number of hospitalizations, long symptom duration or proportion of asymptomatic cases.

Frampton et al. conducted a cohort study in the UK to describe emergence of B.1.1.7 in two North Central London hospitals including clinical outcomes in patients with and without the VOC.[25] Of the 341 samples sequenced and positive for SARS-CoV-2, 198 (58%) were B.1.1.7 and 143 (42%) were non-B.1.1.7. Eighty-eight (44%) of B.1.1.7 patients received oxygen by mask or nasal prongs compared with 42 (30%) of non-B.1.1.7 patients. While length of stay, risk of hospitalization within 14 days of a test, and time to hospital admission from symptom onset were similar, B.1.1.7 patients were younger, had fewer comorbidities and more likely to be from an ethnic minority compared to non-B.1.1.7 patients.

Courjon et al. conducted an observational study in France (Nice) with 1,247 patients admitted to the emergency department to analyze changes in clinical profile and outcomes.[30] Of those admitted by February 22nd, 29 had B.1.1.7 (12.5%). This reflects the prevalence of B.1.1.7 in the area, which increased from 2.6% in December 2020 to 79.1% in February. In hospitalized patients, the mean age of admission was significantly lower in the period between Feb 8th-22nd (considered high B.1.1.7) at 59.2 years (SD=14.0) compared to December 7th-21st (no/low B.1.1.7) at 70.7 years (SD=13.6), $p < 0.001$. Patients were also more likely to have no comorbidity (42% vs. 16%, $p = 0.04$). When pairing 29 cases to 58 controls on age and gender, there was no significant difference between B.1.1.7 patients and non-B.1.1.7 on time from first symptoms to emergency department admission or severity or need for immediate ICU management.

Admission to ICU

Five studies reported on health system impacts related to admission to ICU. Two studies in Europe reported increases in admission to ICU with B.1.1.7 compared to the wild type; however, another three studies found no difference. Among the five studies that reported on admission to ICU, three were apprised as medium quality and one as low quality (one not appropriate for appraisal). Table 6 provides a summary of findings with additional detail provided in text below.

Increases in ICU Admission

Mitze and Rode conducted an epidemiological and modeling study in Germany on the hospitalization rate per 100,000 population.[76] All three VOC were combined for power due to the low spread in Germany at the time of the study. Mitze and Rode found that an increase of 1.29 [CI: 0.5, 2.1, $p<0.05$] additional COVID-19 patients in intensive care per 100,000 population, which is a 42% rise in hospitalization in VOC regions compared to pre-VOC regions (3.08 patients in intensive care per 100,000 population).

Patone et al. conducted a retrospective cohort study in England to explore the risk of critical care admission for patients with B.1.1.7 compared with wild type.[34] They compared two cohorts: a ‘primary care cohort’ which was patients in primary care with a positive community COVID-19 test reported between November 1st, 2020 and January

26th, 2021 (n=381,887, 52.0% B.1.1.7, and 712 were admitted to critical care, 63.1% B.1.1.7). The 'critical care cohort' were patients admitted for critical care with a positive community COVID-19 test reported with an identified SGTF status between November 1st, 2020 and January 27th, 2021 (n=3432, 58.8% B.1.1.7). In both the adjusted and unadjusted analysis, the primary care group had a higher risk of admission to critical care for B.1.1.7 patients compared with the non-B.1.1.7 patients (adjusted HR: 1.99; 95% CI: 1.59 - 2.49). Considering time varying HR, it increased from 1.20 (95% CI: 0.58 - 2.48) at one day to 3.29 (95% CI: 1.17 - 6.29) at fifteen days after a positive test. There was no significant interaction between B.1.1.7 and sex, ethnic group, or age group. When adjusting only for the date of positive test, it did not account for the increased risk of admission for critical care (adjusted HR 1.28 95% CI: 1.05 - 1.56). In the critical care cohort, B.1.1.7 ICU patients tended to be younger (means 57.8 versus 59.3 years) and less obese than non-B.1.1.7 patients. Acute severity of illness, as measured by the APACHE II score, tended to be lower in B.1.1.7 patients, but the proportion receiving invasive mechanical ventilation within the first 24 hours of critical care and organ support was similar between the two groups. After adjusting for date of admission to critical care, the lower risk of admission for critical care in the B.1.1.7 group was accounted for (adjusted HR: 0.84, 95% CI: 0.64 - 0.99).

No Changes in ICU Admission

Bager et al. conducted an observational cohort study in 35,887 SARS-CoV-2 positive individuals in Denmark between January 1st to February 9th, 2021.[28] While Bager et al. was able to find an increased risk of general hospitalization due to B.1.1.7, the numbers were inconclusive on the impact of B.1.1.7 on intensive care admission due to small sample sizes. They reported only 13/128 ICU among B.1.1.7 admissions (10.2%) compared to 115/1090 ICU admissions after infection with wild type (10.6%).

Courjon et al. conducted an observational study in France (Nice) with 232 patients hospitalized in the infectious disease ward and ICU to analyze modification in clinical profile and outcome traits.[30] They found no significant difference between percentage of COVID-19 hospitalized patients admitted to the ICU before B.1.1.7 was dominate (23% [December 7-21, 2021]) compared to after (26% [January 24-February 7, 2021] and 35% [February 8-22, 2021]), p=0.374. For ICU patients, neither the severity score at admission (SAPSII) nor the depth of the respiratory distress seemed to increase with B.1.1.7.

De Andrade et al. conducted an epidemiological study during the first year of the pandemic to compare the age profile of patients hospitalized with COVID-19 as well as hospital mortality and ICU use by age group in large geographic regions of Brazil.[38] They compared across three time periods: (1) February 16th- June 20th 2020; (2)June 21- October 24th 2020; (3) October 25th, 2020 and February 20th, 2021. The third timepoint corresponds with the increasing prevalence of P.1 in Brazil. Of the 620,363 completed records of patients hospitalized, 244,611 (34.0%) had indication for use of ICU. While there was variation in the age profile of hospitalized patients between the three periods, there was no evidence of an increase in hospitalization the last period for adults between 18 and 50 years. Geographically, they report that in the North and Northeast regions, the proportion of 18–50-year-olds in the last period was similar to the

first period during which they were also substantially affected by the pandemic. In the Southeast and South, there was a consistent reduction in these age groups over the periods. In the Central West region, which experienced the pandemic more during the second period, hospitalization with adults between 18 and 50 years old was higher in the first period, decreasing and maintain during the second and third period. They conclude that the rise in the North aligns with a collapse of the health care system in some areas, which was likely associated with disease severity due to P.1.

Death

Nine studies reported on health system impacts related to risk of death. Four studies in Europe and two in Brazil reported increased risk of death for individuals with B.1.1.7 compared to the wild type; however, another three studies found no difference. Among the nine studies, three were apprised as high quality, three were medium quality, and two were low quality (one not appropriate for appraisal). Table 6 provides a summary of findings with additional detail provided in text below.

Increases in Death

Jabłońska et al. conducted a correlational study across 38 European countries to detect the association between COVID-19 mortality and proportion of VOC through the second wave in Europe using multivariate regression models.[33] A higher proportion of B.1.1.7 across countries was associated with higher COVID-19 mortality peak and total mortality during the second wave of the pandemic in Europe. Between January 1st to February 25th, 2021, "an increase of 0.1 in the proportion of B.1.1.7 was related ~~with~~ to a 15.3% increase in the cumulative number of deaths during that period" (p.5).

Challen et al. conducted a matched cohort study in the UK to explore whether there is change in mortality at 28 days from infection with B.1.1.7 compared with wild type.[24] The study consisted of 54,906 matched pairs who tested positive for COVID-19 between October 1, 2020 and January 29, 2021 (followed until February 12, 2021). In 54,902 matched cohort pairs, there were 227 deaths in B.1.1.7 individuals vs. 141 non-B.1.1.7 individuals. The mortality hazard ratio for people with B.1.1.7 compared to those with non-B.1.1.7 was 1.64 (95% CI 1.32 to 2.04). As a community-based study, this suggests that even in a relatively low-risk group, there was an increased risk of death from 32% to 104%.

Davies et al. conducted an epidemiological modeling study to describe the association between B.1.1.7 and hazard of death and disease severity within 28 days of positive test in the UK.[77] Of the 2,245,263 individuals with a positive community test between November 1, 2020 and February 2021, half (51.1%) had a conclusive SGTF reading and, of these, 58.8% had SGTF, indicative of B.1.1.7. Among those with known SGTF status, the crude COVID-19 death rate was 1.86 deaths per 10,000 person-days of follow-up in the B.1.1.7 group versus 1.42 deaths in the non-B.1.1.7 group. The hazard ratio for B.1.1.7 was 1.55 (95% CI 1.39– 1.72), meaning that the risk of mortality in the 28 days following a positive test was 55% higher for B.1.1.7 than for non-B.1.1.7 cases. After correcting for misclassification of SGTF and missing SGTF status, there was a 61% (95% CI: 42–82%) higher hazard of death associated with B.1.1.7; however, this was not consistent across age groups. In females aged 70–84, the estimated risk of

death within 28 days of a positive SARS-CoV-2 test increased from 2.9% without B.1.1.7 to 4.4% with B.1.1.7 (95% CI 4.0–4.9%) and for males 70-84, it increased from 4.7% to 7.2% (95% CI: 6.4–7.9%). Similarly, in females 85 or older, the estimated risk increased from 13% to 19% (95% CI: 17–21%) and for males 85 or older, it increased from 17% to 25% (95% CI: 23-27%). These estimates reflect a substantial increase in absolute risk in older age groups, but the risk of COVID-19 death following a positive test in the community remains below 1% in most individuals younger than 70 years old.

Grint et al. conducted a cohort study to estimate the risk of death following COVID-19 infection in England by comparing B.1.1.7 to non-B.1.1.7.[26] They found that B.1.1.7 was consistently associated with increased risk of death within 28 days compared to non-B.1.1.7 cases with the hazard ratio at 1.67 (95%CI, 1.34-2.09, p<0.0001). The risk of death was low for those under 65 years of age without comorbidities, though higher for males than females (B.1.1.7: Males 0.14%; Females: 0.07% vs. non-B.1.1.7: Males: 0.09%; Females: 0.05%). The risk of death was consistently higher for males and increased with age and with comorbidities. The highest risk was seen among those aged 85 years or older with 2+ comorbidities (B.1.1.7: Males 24.3%; Females: 14.7% vs. non-B.1.1.7: Males: 16.7%; Females: 9.7%).

De Oliveira et al. conducted an epidemiology study to explore data from the state of Parana, in the south of Brazil, where the P.1 variant was identified on February 16th, 2021, to assess trends in mortality data as reported CFRs among different age-groups.[39] Prior to the introduction of P.1, all age groups had either a decline or stable CFR, however, in February 2021, an increase in CFR for almost all age groups was observed. While there were no changes in CFR in children or adolescent, all other groups above 20 years of age had statistically significant increases in CFR when diagnosed in February 2021 as opposed to January 2021. For individuals between 20 and 29 years of age, there was a 3-fold higher risk of death when diagnosed in February 2021 compared to January (RR: 3.15 [95%CI: 1.52-6.53], p<0.01). This risk of death was also higher in other age groups, although to a lesser extent – 93% for 30–39-year-old (1.93 [95%CI:1.31-2.85], p<0.01), 11-% for 40-49-year-old (RR: 2.10 [95%CI:1.62-2.72], p<0.01), and 80% for 50-59-year-old (RR: 1.80 [95%CI:1.50-2.16], p<0.01).

De Andrade et al. conducted an epidemiological study during the first year of the pandemic to compare the age profile of patients hospitalized by COVID-19 as well as hospital mortality and use of ICUs by age group in large geographic regions of Brazil.[38] They compared across three time periods: (1) February 16th and June 20th 2020; (2) June 21st and October 24th 2020; (3) October 25th, 2020 and February 20th, 2021. The third timepoint corresponds with the increasing prevalence of P.1 in Brazil. Each region varied in terms of their mortality over the three periods, with the North region being the hardest hit, experiencing a collapse in the provision of healthcare in the first and last periods with high mortality in all age groups, with a rise in hospital deaths among adults aged 18-60 years. The high mortality in the third wave was among adults aged 18-70 years, reflecting the severity of the pandemic in the region and the impact of P.1.

No Changes in Death

Frampton et al. conducted a cohort study in the UK to describe emergence of B.1.1.7 in two North Central London hospitals including clinical outcomes in patients with and without the VOC.[25] Of the included 399 patients, the proportion of patients who had severe~~ity~~ disease (i.e., WHO level of ≥6) or death were similar: 28% in the non-B.1.1.7 group vs. 36% in the B.1.1.7. The proportion of patients at level 6 or levels 7–9 on the WHO ordinal scale or who died were not statistically different: 18% in the non-B.1.1.7 group were at level 6 and 2% were at levels 7–9; 15% in the B.1.1.7 group were at level 6 and 6% were at levels 7–9. Similar rates of mortality were found, with 16% patients with B.1.1.7 dying within 28 days versus 17% with non-B.1.1.7. In both the unadjusted and adjusted analysis (controlling for hospital, sex, age, comorbidities, and ethnicity), there was no increased risk of mortality or severe disease with B.1.1.7 compared to non-B.1.1.7.

Patone et al. conducted a retrospective cohort study in England to explore the risk of critical care admission for patients with B.1.1.7 compared with the wild type.[34] They compared two cohorts: a 'primary care cohort' and 'critical care cohort' described above. There was no difference in death within 28 days between the B.1.1.7 group and non-B.1.1.7 group (0.3% both). In the unadjusted analysis, there was no difference in 28-day mortality risk for B.1.1.7 compared to non-B.1.1.7 patients, but after adjusting for confounders, there was a higher risk of 28-day mortality in B.1.1.7 patients, (adjusted HR: 1.59; 95% CI: 1.25- 2.03), mainly explained by age (HR: 1.53, 95% CI: 1.28-1.82 with adjustment for age alone). In the critical care cohort, after adjusting for confounders, critical care mortality did not differ significantly between B.1.1.7 and non-VOC B.1.1.7 groups (adjusted HR: 0.93, 95% CI 0.76-1.15). Both cohorts had no evidence of an interaction between B.1.1.7 and ethnic group, age group, or sex.

Dabrera et al. conducted a matched cohort study in the UK to explore whether B.1.1.7 was associated with more severe clinical outcomes compared to wild type.[31] In the matched cohort study of 5,642 individuals, 76 died within 28 days of a positive test; of which, 36 (1.3%) were infected with B.1.1.7 and 40 (1.4%) were infected with wild-type SARS-CoV-2. There was no association between B.1.1.7 and non-B.1.1.7 groups and death within 28 days of COVID-19 positive test (OR: 0.90, 95%CI 0.57-1.41, p=0.64), with similar median time between positive test and death (8 days for B.1.1.7 and 9 days for non-B.1.1.7 (Kruskal Wallis p=0.79). In the unadjusted analysis, there was a negative relationship between risk of death and B.1.1.7 infection (HR: 0.54, 95%CI:0.42-0.69, p=0.00); however, after adjusting for confounders (sex, age, ethnicity, residential property classification, week of specimen date and testing Pillar), there was no difference in risk of death among B.1.1.7 cases compared to non-B.1.1.7 (HR: 1.06, 95%CI:0.82-1.38, p=0.65).

Question 2B: Adjusting personal protective equipment (PPE) procedures for health workers

One modeling study, which was not critically appraised, reported on this outcome. Pham et al. evaluated the impact of different interventions on transmission, HCW absenteeism and test positivity as a marker of intervention efficiency against B.1.1.7 transmission through modeling.[78] In the baseline scenario, it was assumed that HCWs were using PPE while in COVID wards when seeing patients but not during breaks or when in other parts of the hospital, assuming 95% of HCW worked in same wards over time. While specific PPE was not defined, PPE efficiency was defined as percentage reduction of droplet transfer. Assuming 90% effective PPE use in COVID wards, they found that extending PPE use to non-COVID wards (all HCW used PPE with 90% effectiveness when on ward) would prevent 93.7% of all transmissions and would also prevent outbreaks among patients and HCWs. Even if PPE effectiveness was reduced to 70%, findings did not change significantly, however, if was reduced to 50% or below, screening HCW every 3 days was more effective than PPE use in all wards. Overall, PPE use in all wards was model to be more effective than all other interventions.

Guidance documents related to PPE procedures

- Four guidance documents (one low-quality,[79] two medium-quality,[69,70] and one high-quality[75]) located from the UK, Ontario, and Saskatchewan report on PPE procedures. If stringent procedures were already in place prior to the emergence of VOC, PPE procedures in healthcare settings remain relatively unchanged in response to VOC.[68,69] Saskatchewan has added eye protection to its list of required PPE for healthcare staff, physicians, and visitors unless physical distancing can be maintained,[79,80] as this was not already a requirement. **Please note that this guidance is not representative of all provinces (see note about guidance documents included in this review, page 4).**

Question 2C: Adjusting restrictions to and screening staff and visitors (e.g., visitor policy changes, approach to and frequency of screening)

No studies to date have reported on this outcome, but guidance documents (without citation of evidence) were located from Ontario, Saskatchewan, the UK, and Ireland. In Canada, where visitor restrictions have already been in place for some time, there were few changes in response to VOC. In the UK and Ireland, greater emphasis was placed on obtaining patients' travel history.

Guidance documents related to staff and visitor screening/restrictions

- Public Health Ontario guidelines (high quality) recommend reduction of visitors to healthcare facilities in response to increased VOC cases.[72] Similarly, in Saskatchewan (low quality), only one designated family member or support person can travel to support residents/patients in end-of-life situations or with essential care needs. Any visitor restrictions should not be based solely on the VOC situation in the visitor's geography of origin, but rather continue to be informed by an array of vigilant screening measures.[79] In the UK and Ireland (medium quality), more emphasis is placed on requiring a recent travel history from anyone presenting for care.[69,70]
- In Ontario, any VOC cases originating in a healthcare facility should trigger immediate testing of all patients and staff in the affected areas.[72]
- **Please note that this guidance is not representative of all provinces (see note about guidance documents included in this review, page 4).**

Question 2D: Adjusting service provision based on VOC status (e.g., cohorting patients in hospitals based on the SARS-CoV-2 variants they have)

No studies to date have reported on this outcome, but guidance documents (without citation of evidence) were located from Ontario, Saskatchewan, and the UK. Notably, Ontario does not recommend cohorting B.1.1.7 patients but does recommend the use of private rooms for B.1.351 and P.1 patients, despite evidence that B.1.1.7 is the most transmissible VOC of the three.[9]

Guidance documents related to adjusting service provision

- In Saskatchewan, guidelines (low quality) do not recommend cohorting based on VOC diagnosis.[79] In Ontario (high quality), cohorting is not recommended for B.1.1.7 patients, but those with B.1.351 or P.1 should be housed in private rooms where possible.[72]
- In emergency departments in the UK, it is recommended that any patients at risk of being SARS-CoV-2 positive (VOC or not) should be accommodated in a single room with ensuite bathroom facilities, regardless of their reason for presentation (medium quality).[69]
- **Please note that this guidance is not representative of all provinces (see note about guidance documents included in this review, page 4).**

Question 2E: Adjusting patient accommodations, shared spaces and common spaces (e.g., improvement to HVAC systems)

No studies to date have reported on this outcome, but two guidance documents recommend improving building ventilation whenever possible.

Guidance documents related to adjusting patient accommodations

- Public Health Ontario requires that all healthcare facilities review their HVAC systems in accordance with CSA Z317.2:19, a standard for special requirements for HVAC systems in health facilities by the Canadian Standards Association.[81] Guidelines for the community from the UK (medium quality) also recommend improving building ventilation whenever possible, or using air-cleaning alternatives.[54] **Please note that this guidance is not representative of all provinces (see note about guidance documents included in this review, page 4).**

Discussion

This rapid scoping review sought to identify, appraise, and summarize evidence related to the impact of VOC known in April 2021 (B.1.1.7, B.1.351, and P.1) on public health measures and health system arrangements. Our search identified 22 articles on public health measures and 17 articles related to health system arrangements. We also identified 21 guidance documents that provided information on public health and/or health systems arrangements.

Critical Appraisal

A total of 16 original research studies were assessed for quality (excluding 17 lab or modeling studies and 4 grey literature sources), indicating a strength of this review. While observational studies ranged in quality from low to high, the majority are preprints that have not yet been peer reviewed. Therefore, findings should be interpreted with caution to inform health system and public health recommendations. The studies which scored higher on the NOS were those which selected participants from large, representative samples and controlled for most confounders. Studies which tended to score lower on the NOS were those where self-reported data were used or when limited description of the non-respondent group was provided for cross-sectional studies. It is important to note that the NOS was originally developed for cohort and case-control studies, rather than studies of cross-sectional design. Although an adapted version of NOS was used to score cross-sectional studies,[20] there may be some limitations in applying this adapted version. We applied an additional quality control measure to observational studies by decreasing preprint study scores by two points. While this approach of downgrading preprints provides further appraisal of study quality, it is not considered in the standard NOS scoring instructions. For the purpose of presenting the most recent evidence on this topic, it was important to include preprint studies, which are typically excluded from systematic reviews, but are an essential consideration in COVID-19 reviews.

Twenty-one guidance documents were appraised, highlighting the breadth of grey literature included in this review. No guidance documents were classified as clinical practice guidelines, but the AGREE II tool was applied to all guidance documents as it is recognised as the gold standard for quality assessment of guidelines.[19] While we acknowledge the AGREE II tool was designed for clinical practice guidelines, due to a lack of alternative standard critical appraisal options, it was the best choice for this review. Guidance documents ranged from low to high quality, with sources consistently scoring low in Domain 3: Rigour of Development. This was largely due to the limited inclusion of methodological consideration and the heterogeneity across sources. It is important to note that within Domain 3, one item assessed whether a link between references and recommendations were made. Few sources cited original research, highlighting a gap in evidence-informed public health guidance across organizations and countries. The accuracy of quality appraisal of guidance documents could have been enhanced by including additional appraisers, however, the research team agreed that the overall scores are generally reflective of the quality of papers. Although certain

guidance documents were considered low quality based on AGREE II, they may be useful when considering changes specific to settings for which the document was intended (e.g., salons, schools).

Interestingly, the majority of observational studies were related to health systems, while the majority of guidance documents were related to public health measures. Of the four observational studies which reported on public health measures, only one was considered to be high quality. This further highlights the finding that public health guidance documents tended to be based on limited evidence, or on low quality evidence at best.

Guidance Documents

In almost all cases, guidance documents included in this review did not cite published evidence. Of note, guidance documents included in this review were found in topic areas where published evidence was scarce or not available, whereas topics with available published research were not reflected in guidance documents. Guidance included in this review may be based on evidence generated prior to the emergence of VOC, or on expert opinion.

Public Health Measures

Eighteen studies and 4 reports contributed data relevant to modifying existing public health measures. Modeling studies were the most common design (10/18) followed by observational studies (4/18) and laboratory studies (3/18). Of note, most studies (16/18) are preprints and have not undergone peer-review. In general, although available evidence is varied and scarce, findings from the included studies overwhelmingly support the implementation of strong public health measures (i.e., lockdowns, distancing, testing, contact tracing), running in parallel with a timely vaccine schedule. The increased transmissibility of the VOC signals the need for more pre-emptive (close and then open) versus reactive (open and then close) strategies. Most studies relevant to this question focused broadly on social distancing as a strategy, with no recommendation regarding objective metrics such as time or distance or type of social distancing strategy. No studies were found that focused on modification to handwashing or masking related to the emergence of variant strains. Age and gender may be an important target to consider when developing a population vaccine promotion campaign.

Health Systems Arrangements

Overall, there were 17 studies that reported on health system impacts, with most reporting on impact on hospitalization, ICU admissions and deaths. Among the studies that reported on the impact of VOC on hospitalization, trends suggest there is an increase in hospitalization due to B.1.1.7 but no difference in length of stay. There seems to be less agreement on the impact of B.1.1.7 on intensive care admissions, with two studies reporting increased admission to ICU with B.1.1.7 compared to the wild type, and three studies reporting no difference. While there are mixed findings on

impact of VOC (B.1.1.7 and P.1) on death, six studies found an increased risk compared to three studies that reported no change. For studies that reported an increase in death, B.1.1.7 was found to increase the risk 15% to 67% compared to non-VOC, suggesting that B.1.1.7 could be linked with higher mortality than non-B.1.1.7 strains. One study reported on the effectiveness of PPE in reducing VOC transmission in the hospital. No studies reported on screening staff and visitors, adjusting service provisions (e.g., cohorting), or adjusting patient accommodations and shared spaces, which is a significant gap in the literature.

Limitations

While this rapid scoping review has several strengths, there are limitations that must be acknowledged. First, due to the rapid production of the literature on COVID-19 and VOC, most of the studies included in this review were preprints, and have thus not yet undergone peer review. As mentioned above, this must be considered when interpreting the findings.

Additionally, our search strategy was limited to articles that specified reporting on one of the recognized VOC (B.1.1.7, P.1, or B.1.351). Given the growing trend that VOC are replacing the wild type as the dominant strain as well as the continued emergence of other variants of interest, future consideration of expanding the search strategy may be warranted. For example, this review did not consider the variant of interest that is emerging in India (B.1.617) or other variants of interest which may warrant future evaluation as these situations evolve.[82]

A third limitation is that our review is limited to studies that reported specifically on VOC, which makes it difficult to interpret some of the findings without taking into consideration the wider literature on SARS-CoV-2. For example, we report on attitudes towards vaccines only in context of VOC, without wider acknowledgement of the extensive body of literature on vaccine hesitancy. Canadian provincial and national guidance documents were also excluded if they did not specify recommendations for VOC.

Finally, the identification of guidance documents through the grey literature search may have been limited by different jurisdictional guidance document indexing protocols and practices. As such, the relevance of guidance documents included in this review may vary depending on different contexts across jurisdictions and do not necessarily reflect the breadth and scope of available guidance from across Canada. A comprehensive jurisdictional scan of provincial guidance documents is needed to address this gap.

Research Gaps

As evident in this rapid review, the nature of and findings on the impact of VOC on public health measures and health systems arrangements are quickly changing and emerging. We have identified several specific research gaps that need to be addressed to provide more robust evidence around public health measures and health system arrangement decisions.

1. Evidence is needed related to best practices for screening staff and visitors in health service organizations and adjusting service provisions
2. Evidence is needed to support/refute adjusting patient accommodations and shared spaces in a hospital setting with the presence of different strains
3. Standardized approaches and tools are needed to track adherence to different public health measures
4. Methods for appraising modeling studies need to be developed
5. Novel methods to collect and analyze data are needed to inform infection-prevention strategies for safer workplace environments with the emergence of highly transmissible strains
6. Standards for sharing surveillance data nationally to rapidly inform health policy and health system guidance documents are recommended worldwide
7. Information to support changes in guidance related to masking in light of more transmissible strains is needed
8. Evidence to guide best practice standards for screening and testing for variants of concern under different conditions is needed
9. Need for comprehensive jurisdictional scan to identify, compare, and contrast provincial strategies and guidelines

Conclusion

This rapid scoping review provides synthesized evidence related to the public health and health system impacts of the three major SARS-CoV-2 VOC (B.1.1.7, B.1.351, and P.1). While the findings should be interpreted with caution as most of the sources identified were preprints, findings suggest a combination of non-pharmaceutical interventions (e.g., masking, physical distancing, lockdowns, testing, contact tracing) should be employed alongside a vaccine strategy to improve population and health system outcomes. Additionally, while the findings are mixed on the impact of VOC on health systems arrangements, the evidence is trending towards increased hospitalization and death.

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Appendix 1: *Literature Search Strategy*

MEDLINE

COVID-19 search filter: CADTH https://covid.cadth.ca/literature-searching-tools/cadth-covid-19-search-strings/

1	(coronavirus/ or betacoronavirus/ or coronavirus infections/) and (disease outbreaks/ or epidemics/ or pandemics/)
2	(ncov* or 2019ncov or 19ncov or covid19* or covid or sars-cov-2 or sarscov-2 or sarscov2 or severe acute respiratory syndrome coronavirus 2 or severe acute respiratory syndrome corona virus 2).ti,ab,kf,nm,ot,ox,rx,px.
3	((new or novel or "19" or "2019" or wuhan or hubei or china or chinese) adj3 (coronavirus* or corona virus* or betacoronavirus* or CoV or HCoV)).ti,ab,kf,ot.
4	((coronavirus* or corona virus* or betacoronavirus*) adj3 (pandemic* or epidemic* or outbreak* or crisis)).ti,ab,kf,ot.
5	((wuhan or hubei) adj5 pneumonia).ti,ab,kf,ot.
6	or/1-5 [CADTH COVID-19 filter, no date limit]
7	(((uk or united kingdom or england or english or britain or british or kent) adj3 (variant* or voc or vui)) or "b117" or "20i 501yv1" or "variant of concern 202012 01" or "voc 202012 01" or "variant under investigation in december 2020" or "variant under investigation 202012 01" or "vui 202012 01").ti,ab,kw,kf.
8	(((south africa* or sa) adj3 (variant* or voc or vui)) or "b1351" or "501v2" or "501yv2" or "20h 501yv2" or "20c 501yv2").ti,ab,kw,kf.
9	((brazil* adj3 (variant* or voc or vui)) or "p1" or "b11281" or ((mutation* or spike*) adj3 (k417t or e484k or n501y))).ti,ab,kw,kf.
10	((mutation* or spike*) adj3 d614g).ti,ab,kw,kf.
11	or/7-10
12	6 and 11
	315 results 2021-03-15
	403 results 2021-04-07 (cumulative from last search)

Embase

COVID-19 search filter: CADTH adapted to Embase.com format; line 1 exploded

1	'SARS-related coronavirus'/exp
2	('coronavirinae'/de OR 'betacoronavirus'/de OR 'coronavirus infection'/de) AND ('epidemic'/de OR 'pandemic'/de)
3	(ncov* OR 2019ncov OR 19ncov OR covid19* OR covid OR 'sars-cov-2' OR 'sarscov-2' OR 'sars-cov2' OR sarscov2 OR 'severe acute respiratory syndrome coronavirus 2' OR 'severe acute respiratory syndrome corona virus 2'):ti,ab,kw,de,tt,oa,ok
4	((new OR novel OR '19' OR '2019' OR wuhan OR hubei OR china OR chinese) NEAR/3 (coronavirus* OR 'corona virus*' OR betacoronavirus* OR cov OR hcov)):ti,ab,kw,de,tt,oa,ok
5	((coronavirus* OR 'corona virus*' OR betacoronavirus*) NEAR/3 (pandemic* OR epidemic* OR outbreak* OR crisis)):ti,ab,kw,tt,oa,ok

6	((wuhan OR hubei) NEAR/5 pneumonia):ti,ab,kw,tt,oa,ok
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6
8	(((uk OR 'united kingdom' OR england OR english OR britain OR british OR kent) NEAR/3 (variant* OR voc OR vui)) OR 'b.1.1.7' OR '20i 501y.v1' OR 'variant of concern 202012 01' OR 'voc 202012 01' OR 'variant under investigation in december 2020' OR 'variant under investigation 202012 01' OR 'vui 202012 01'):ti,ab,kw
9	((('south africa*' OR sa) NEAR/3 (variant* OR voc OR vui)) OR 'b.1.351' OR '501.v2' OR '501y.v2' OR '20h 501y.v2' OR '20c 501y.v2'):ti,ab,kw
10	((brazil* NEAR/3 (variant* OR voc OR vui)) OR 'p.1' OR 'b.1.1.28.1' OR ((mutation* OR spike*) NEAR/3 (k417t OR e484k OR n501y))):ti,ab,kw
11	((mutation* OR spike*) NEAR/3 d614g):ti,ab,kw
12	#8 OR #9 OR #10 OR #11
13	#7 AND #12
	247 results 2021-03-15
	319 results 2021-04-07 (cumulative from last search)

Cochrane

1	MeSH descriptor: [Coronavirus] this term only
2	MeSH descriptor: [Betacoronavirus] this term only
3	MeSH descriptor: [Coronavirus Infections] this term only
4	{or #1-#3}
5	MeSH descriptor: [Disease Outbreaks] this term only
6	MeSH descriptor: [Epidemics] this term only
7	MeSH descriptor: [Pandemics] this term only
8	{or #5-#7}
9	#4 and #8
10	(ncov* or 2019ncov or 19ncov or covid19* or covid or "sars-cov-2" or "sarscov-2" or sarscov2 or "severe acute respiratory syndrome coronavirus 2" or "severe acute respiratory syndrome corona virus 2"):ti,ab,kw
11	((new or novel or "19" or "2019" or wuhan or hubei or china or chinese) near/3 (coronavirus* or "corona virus*" or betacoronavirus* or cov or hcov)):ti,ab,kw
12	((coronavirus* or "corona virus*" or betacoronavirus*) near/3 (pandemic* or epidemic* or outbreak* or crisis)):ti,ab,kw
13	((wuhan or hubei) near/5 pneumonia):ti,ab,kw
14	{or #9-#13}
15	(variant* or voc or vui or mutation* or spike):ti,ab
16	#14 and #15
	98 results in CENTRAL 2021-03-15 **2 results in CDSR 2021-03-15**
	118 results in CENTRAL 2021-04-07 (cumulative from last search) **2 results in CDSR 2021-04-07 (cumulative from last search)**

Epistemonikos

Basic search of the following terms within the LOVE:

variant* OR voc OR vui OR "B.1.1.7" OR "20I/501Y.V1" OR "202012/01" OR "B.1.351" OR "501.V2" OR "501Y.V2" OR "20H/501Y.V2" OR "20C/501Y.V2" OR "P.1" OR "B.1.1.28.1" OR "K417T" OR "E484K" OR "N501Y" OR "D614G"

1102 results 2021-03-15

1330 results 2021-04-07 (cumulative from last search)

medRxiv / bioRxiv

medRxiv and bioRxiv simultaneous search; Date limit: October 1 2020 – present; Title and Abstract search; All words (unless otherwise specified); 50 per page; Best Match; **round 2, update date limit February 1 2021 – present; round 3, update date limit March 1 2021 – present**

315 unique results total (all searches) up to and including 2021-04-07

Searches:

uk variant
united kingdom variant
england variant
english variant
britain variant
british variant
kent variant
south africa variant
brazil variant
variant of concern *(phrase search)*
variants of concern *(phrase search)*
B.1.1.7
20I/501Y.V1
202012/01
B.1.351
501.V2
501Y.V2
20H/501Y.V2
20C/501Y.V2
P.1
B.1.1.28.1
K417T
E484K
N501Y
D614G

Google

Google screening inclusion/exclusion criteria:

1. Exclude results from academic journals (e.g. JAMA)
2. Exclude results from PubMed

3. Exclude news articles, but check to see if they link to studies, preprints, or public health guidance
4. Include results from preprint servers (e.g. medRxiv; Research Square)

At time of record capture, indicate the **specific variant** (or combination), and whether it is related to any combination of the following using the grey lit tracking form:

- Transmission
- Public health measures
- Health systems arrangements

uk variant | united kingdom variant | british variant | kent variant | uk voc | united kingdom voc | british voc | kent voc | B117 | B.1.1.7 | 20I/501Y.V1 | 202012/01 | 501Y.V1
south africa variant | south africa voc | B1351 | B.1.351 | 501.V2 | 501Y.V2 | 20H/501Y.V2 | 20C/501Y.V2
brazil variant | brazil voc | P1 variant | P1 voc | P.1 variant | P.1 voc | B11281 | B.1.1.28.1
K417T | E484K | N501Y | D614G
variants of concern | COVID-19 variants | SARS-CoV-2 variants

Twitter

Basic search; Top results

uk variant
uk voc
B.1.1.7
B117
south africa variant
south african variant
sa variant
south africa voc
south african voc
sa voc
B.1.351
B1351
brazil variant
brazilian variant
brazil voc
brazilian voc
P.1
variants of concern
covid-19 voc
covid19 voc
covid voc
sars-cov-2 voc

Other websites

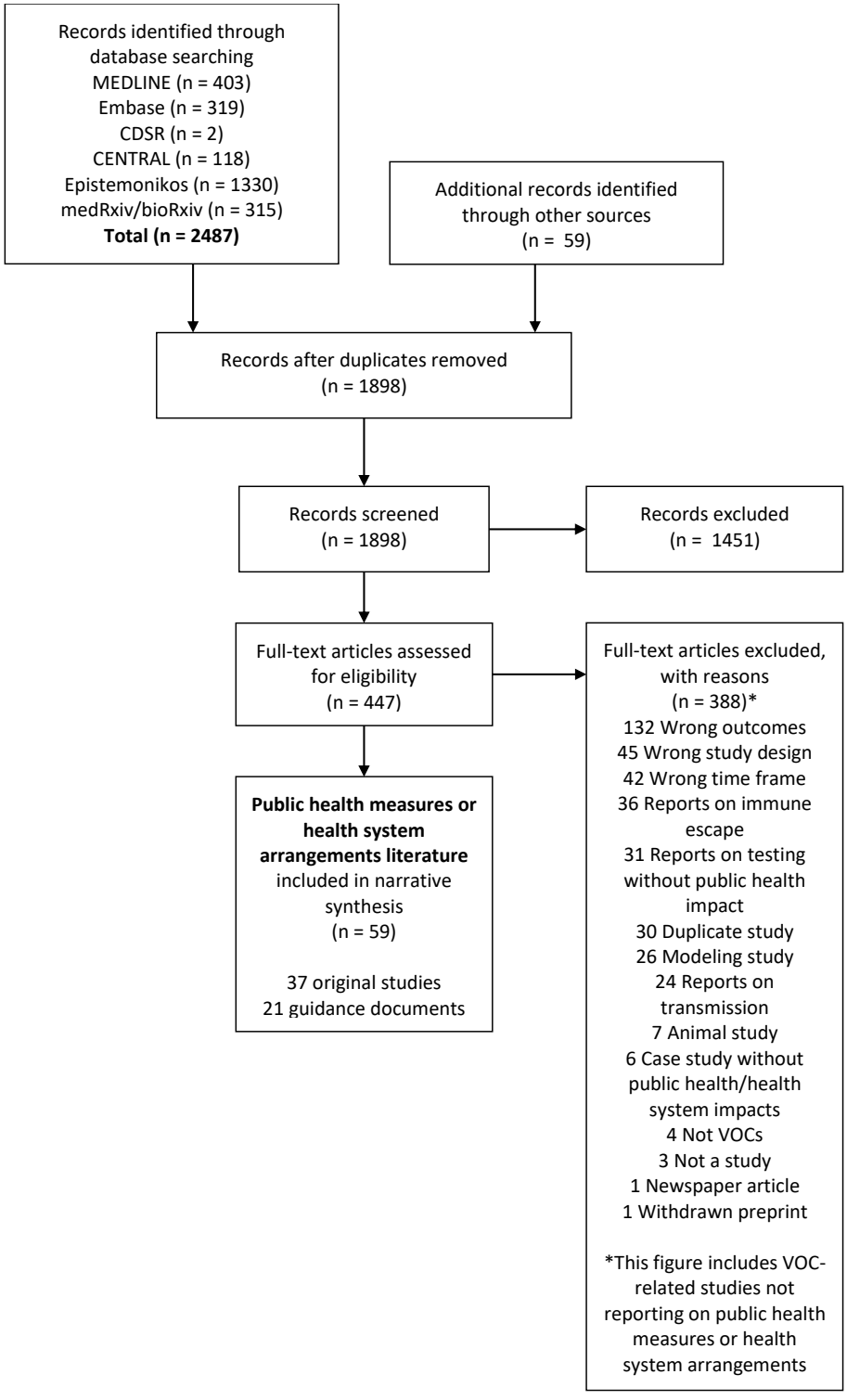
Manual searches of the following websites for terms like:

- variants

- surveillance data

WHO	https://www.who.int/
Canadian government websites (all) – includes Health Canada and PHAC	https://www.canada.ca/en.html
CDC	https://www.cdc.gov/
CADTH COVID-19 Evidence Portal	https://covid.cadth.ca/
Public Health England	https://www.gov.uk/government/organisations/public-health-england
South Africa Dept of Health	http://www.health.gov.za/
Brazil – Ministério da Saúde *search "variante" and check the box that says "Apenas em Ministério da Saúde"	https://www.gov.br/saude/pt-br
NZ Ministry of Health	https://www.health.govt.nz/
Australian Dept of Health	https://www.health.gov.au/
Italy - Dipartimento della Protezione Civile *Italian: "variante"	http://www.protezionecivile.gov.it/

Appendix 2: *PRISMA Diagram*



Appendix 3: *Summary of Findings Tables for Public Health Sources*

Legend:

Study Design	Low Quality	Medium Quality	High Quality
Observational study			
Guidance documents			
Laboratory study			
Modelling study			
Grey literature			

Table 1: *Summary of Public Health Sources*

Author, date	**Date of data collection**	**Source**	**Objective**	**Study design**	**Setting**	**Sample size**	**Outcome measures**	**Variant**	**Country**	**Main finding**
Graham, 2021	Sep 8th-Dec 31st	medRxiv	To examine the association between the regional proportion of B.1.1.7 and reported symptoms, disease course, rates of reinfection, and transmissibility.	Cross-sectional study	Community	36,920 COVID-19 positive users of the COVID symptom app. Surveillance data from the (COG-UK) and a SGTF correlate in community testing data.	Regional proportion of B.1.1.7 and symptoms, disease course, rates of reinfection and transmissibility. Disease burden was also examined by assessing self-reported hospital visits and reported long symptom duration	B.1.1.7	UK	No evidence of changes in reported symptoms, disease severity and disease duration associated with B.1.1.7.
Buchan, 2021	Feb 7th-27th, 2021	medRxiv	To compare secondary attack rates in households with VOC versus	Retrospective cohort study	Community	We identified 5,617 index cases and 3,397 secondary	Household secondary attack rate, defined as the number of household secondary cases that occurred 1-	B.1.1.7	Canada	This study provides strong evidence of increased transmissibility in households due to VOC and suggests that asymptomatic and pre-symptomatic

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			non-VOC index cases in Ontario			cases across the study period. Amongst index cases, 1,318 were classified as VOC (151 B.1.1.7 and 1,167 N501Y) and 4,299 were classified as non-VOC	14 days after the index case divided by the total number of household secondary contacts.			transmission may be of particular importance for VOC. Our study suggests that more aggressive public health measures will be needed to control VOC and that ongoing research is needed to understand mechanisms of VOC transmissibility to curb their associated morbidity and mortality.
Lumley 2021	From 01-September- 2020, data up to 28-February-2021	MedRxiv	1) Investigate & compare protection from SARS-CoV-2 infection through vaccination and prior infection (using anti-spike antibody status). 2) Estimate the protection from different vaccines, after one versus two doses and from infections with the B.1.1.7 variant	Observational cohort	Oxford University Hospitals (OUH)	13, 109 individual HCWs contributed 2,835,260 person-days follow-up. 74% female, 27% nurses, 14% physicians, median age 39(30-50)	PCR-confirmed symptomatic SARS-CoV-2 infection. Also considered any PCR-positive result (i.e., either symptomatic or asymptomatic) Antibody status was determined using an anti-trimeric spike IgG ELISA using an 8 million units threshold to determine antibody-positivity. To assess the impact of the B.1.1.7 variant on (re)infection risk, PCR-positive results with and without SGTF,	B.1.1.7	Oxfordshire, UK	In summary, pooling data from unvaccinated and Pfizer-BioNTech and AstraZeneca vaccinated HCWs, we show that natural infection resulting in detectable anti-spike antibodies and two doses of vaccine both provide robust protection against SARS-CoV-2 infection, including against the B.1.1.7 variant of concern.

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
							and those confirmed as B.1.1.7 on sequencing.			
Bachtiger, 2021	Nov 13th and Dec 31st, 2020	medRxiv	To inform public health messaging by determining how changes in COVID-19 vaccine hesitancy, attitudes towards administration, emergence of new variants & vaccine availability may affect herd immunity	Cross-sectional	Community	9617 (2nd questionnaire relevant to outcome measures)	Willingness to receive COVID-19 vaccine, attitudes towards prioritisation, plans to change behaviour following vaccination	B.1.1.7	UK	Slight increase in vaccine acceptance after learning of circulating VOC but vaccine acceptance is still below levels that would enable progress towards herd immunity. Overall majority (85.1%) of people want vaccine, and few people (12.5%) plan on drastically changing behavior following vaccination. Participatory community engagement should be part of a strategy to improve uptake by considering the public's preferences, such as those expressed here that teachers and BAME groups should be prioritized.
Abdel-Sater, 2021	Dec 9th, 2020-Jan 10th, 2021	medRxiv	To evaluate a Primer for use with SYBR RT-PCR test as a second step means for confirming B.1.1.7 or similar variant in COVID positive patients	laboratory study	N/A	20 samples from COVID positive patients with Ct<30	Quantitative SYBR Green Based RT-PCR	B.1.1.7	Lebanon	The SYBR RT-PCR test could be used as a second step test for early confirmation of VOC B.1.1.7 in COVID Positive S-Gene negative patients in case of shortage in sequencing tests. Our efforts will be helpful and can contribute to the early detection of the new variant (VUI 202012/01), for the prevention of transmission and early intervention

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
Akingba, 2021	Nov 17th-20th, 2020	medRxiv	Evaluate the field performance of the PanBio assay and provide evidence of performance on patients infected with 501Y.V2	Laboratory study	Community Testing, Mobile Clinics	A total of 677 patients from 6 mobile clinics were tested by both antigen and PCR	Used nasopharyngeal swabs to determine the accuracy of Abbott PanBio COVID-19 antigen RTD. RT-PCR was done using the Seegene nCoV assay with amplification on BioRad CFX realTime PCR machine	B.1.351	South Africa	The assay had an overall sensitivity of 69.2% and specificity of 99% in this clinical context. However, sensitivity was highly dependent on viral load. The assay reliably detected 501Y.v2 virus infection in ambulatory ill patients in this high prevalence community setting. Sensitivity was >90% in patients with high viral loads CTs<30. To optimize the use of antigen RDTs in different and changing circumstances, clinical predictors and the epidemiological context should be considered when deciding how to deploy these assays.
Collier and Ferreira, 2021	Dec 9th, 2020-Feb 3rd, 2021	medRxiv	Assess age correlated immune response following 1st & 2nd dose with mRNA-based vaccine in unselected elderly participants from the community & younger health care workers	Laboratory study	Community	51 participants; N=24, <80 years; N=27, >80 years; median age 81	Inadequate vaccine-elicited serum antibody neutralization activity at least 3 weeks after the first dose of vaccine measured as a dilution of serum required to inhibit infection by 50% in an in vitro neutralization assay	B.1.1.7	UK	Age was statistically correlated with serum neutralization. There was a significantly higher risk of a suboptimal neutralizing antibody response following first dose vaccination with BNT162b2 in those above the age of 80, cautioning against extending the dosing interval in this high risk population.

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
Jangra, 2021	Not Reported	MedRxiv	To investigate the impact of the E484K mutation in the neutralizing activity of SARS-CoV-2 specific antisera	laboratory study	N/A	A total of 34 sera were selected from study participants based on their SARS-CoV-2 S enzyme linked immunosorbent assay antibody titer (negative [N=4] versus weak [N=8], moderate [N=11] or strong positive [N=11]). Sera from five individuals who received two doses of the Pfizer SARS-CoV-2 vaccine was included.	Serum neutralization efficiency	Non-specific, similar to B.1.351 and P.1	United States	These data indicate that the E484K mutation present in circulating SARS-CoV-2 strains that belong to the B.1.351 and P.1 lineages reduces the neutralizing activity of human polyclonal sera induced in convalescent (infected with previous strains) and vaccinated individuals. It is important to aim for the highest titers possible induced by vaccination, as this should enhance the chances for protection even in the case of antigenic drift of circulating SARS-CoV-2 strains
Borges, 2021	Week 49 2020 to week 3 2021	Eurosurveillance	To investigate the proportion of SGTF cases to gain insight on B.1.1.7 frequency and geographical	Modeling study	Community	Of the 36,651 positive results, 3,367 (9.2%) corresponded to SGTF tests (i.e., proxy for B.1.1.7); Equivalent to	Proportion of COVID-19 cases likely classified as B.1.1.7, based on SGTF, from RT-PCR tests with TaqPath COVID-19 assay; and impact on number of cases due to	B.1.1.7	Portugal	Physical distancing measures implemented in weeks 2 and 3 strongly decelerated the growth rate with the proportion of SGTF and SGTL remaining below 50% until week 7 2021. This reinforces the need to implement robust public health measures adapted to

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			spread in Portugal			9.5% of COVID-19 positive tests in the same time frame	lockdown measures in week 2/3			this new variant to mitigate the impact of COVID-19 in terms of hospitalizations and deaths.
Domenico, 2021	Jan 2021 start date used for projected modelling	medRxiv	To assess the impact of implemented measures on two COVID strains (B.1.1.7 & wild type) through modeling	Modelling study	Community	N/A	Estimated # cases of historical strain and VOC based on various social distancing measures using data from a large-scale genome sequencing initiative conducted in France	B.1.1.7	France	Social distancing and nightly curfews would bring down the R of historical strain, however VOC would continue to increase. It is important to continue strong social distancing measures while increasing vaccination to reduce hospitalization.
Giordano, 2021	model estimated using data collected within a 110-day window ending on Feb 7th, 2021	Research Square	Model impact of mass vaccination campaigns, different transmission rates due to new variants and different enforced countermeasures and assess associated healthcare costs	Modeling study	N/A	NR	fraction of successfully immunised people within one year.	B.1.1.7, B.1.135	Italy	Non-pharm interventions (Physical distancing, testing and contact tracing) are critical throughout a mass vaccination campaign to keep the reproduction numbers low until a sufficient population immunity is achieved.
Munitz, 2021	Dec 6th, 2020-Feb 10th, 2021	medRxiv	To explore the transmission dynamics of B.1.1.7 &	Modeling study	Community & nursing homes	primary data of >300,000 RT-PCR samples	SGTF data from RT PCR tests, effective reproduction number	B.1.1.7	Israel	Our data confirmed that pro-active surveillance programs of populations at risk such as those found in nursing homes were

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			estimate the success of screening, surveillance & vaccination on mitigating risk in the general public & elderly				(Rt) and cycle threshold values (ct)			capable of early detection, which likely enabled containment of further viral spread within this housing community. This is observed by the significant difference in Ct threshold levels, which were higher in nursing homes in comparison with the general population. Thus, proactive protection programs such as routine surveillance and monitoring of populations at risk combined with prioritized vaccination, is achievable and will result in a reduction of severe illness and subsequent death.
Scherbina, 2021	Not Reported	SSRN	Whether the United States would benefit from a COVID lockdown similar to the lockdowns imposed in a number of European countries using the most recent data.	Modeling study	Community	N/A	Future monetary cost of the pandemic based on: 1) loss of productivity due to missed work of the symptomatically ill, 2) the cost of medical interventions that could have been used elsewhere, 3) the value of lives of the projected fatalities. Measured based on value of statistical life (VSL) and discounted QALY	B.1.1.7	United States	In a hypothetical scenario in which the more contagious U.K. variant of the virus becomes predominant in the U.S. one month from now, a lockdown would be substantially more valuable than for the currently prevailing variant; its optimal duration will lengthen, and the associated net savings will nearly triple. Even with vaccinations, a lockdown will generate significant net benefits and that it should optimally last four weeks under the baseline assumptions.

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
Smith, 2021	Oct 19th-Dec 7th, 2020	medRxiv	To assess the impact of environment on VOC transmission	Modelling study	Community	N/A	Transmission intensity estimates (R)	B.1.1.7	UK	Like other SARS-CoV-2 strains, B.1.1.7 spread with greater transmission in colder and more densely populated parts of England. However, there is evidence of B.1.1.7 having a transmission advantage at warmer temperatures compared to other strains. This implies that spring and summer conditions are unlikely to slow B.1.1.7's invasion in Europe and across the Northern hemisphere - an important consideration for public health interventions.
Vazquez, 2021	Not reported	medRxiv	To estimate the rate of transmission per proximity contact, a generative model to simulate infectious disease outbreaks within workplaces, estimates of the rate of super-spreading events per	Modeling study	Modeling of workplace transmission	605 Individuals in a workplace	Using Bluetooth button devices, they tracked when the distance between two coworkers was less than 1.5m for 15 seconds. This data was used to model the spread of virus. They estimated disease transmission rates and examined super-spreading events (where # of secondary cases equals or exceeds 10). A procedure was developed to simulate	B.1.1.7	Germany	Workplace proximity contact data can be used to develop a tailored model to simulate the spread of B 1.1.7 and the impact of containment strategies

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			imported case and an evaluation of mask use as an example of non-pharmaceutical interventions within the workplace.				the disease transmission given the proximity contact data, the disease infectious period and the probability of disease transmission after repeated contacts			
Zimerman, 2021	Jun 1st, 2020, and Jan 10th, 2021	Cureus	To assess if social isolation into small family or groups is associated with the emergence of new severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) variants, particularly the P.1 lineage and E484K mutants, in Brazil and in the state of Amazonas	Modelling study	Community	A total of 773 samples were obtained throughout the period encompassed by the present analysis in Brazil	For the evaluation of the prevailing SARS-CoV-2 genomes present in Brazil and in the state of Amazonas, all human related sequences available on the GISAID collected between June 1, 2020, and January 31, 2021. Social isolation was measured by the daily values of the Social Isolation Index (SII), which shows the percentage of individuals who stayed within a distance of 450 meters from their homes on a given day. Daily SII was collected from the In Loco© website between	P.1	Brazil	In the present study, SII was found to be positively associated with a substantial rise in the prevalence of these new variants. However, this correlation could only be observed when SII was above 40% (from November 2020 to January 2021), suggesting that the SARS-CoV-2 ability to mutate was dependent on high levels of SII in the state of Amazonas, Brazil. Findings reinforce the hypothesis that forced prolonged cohabiting may boost viral ability to generate mutation.

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
							February 1, 2020, and January 24, 2021, for Brazil and the state of Amazonas. Number of daily COVID-19 deaths was noted between March 12, 2020, and January 24, 2021, through the official database of the Brazilian Ministry of Health.			
Pageaud, 2021	N/A	medRxiv	To analyze the expected dynamics of COVDI-19 epidemic after applying protective measures and considering the increasing proportion of more infectious variants and several vaccination strategies	Modeling study	Community	N/A	Cumulative # of individuals removed, cumulative # of deaths in hospital, daily prevalence in ICU beds and its saturation indicator. Saturation of ICU beds was calculated as the cumulative # of new cases requiring ICU when all beds were already occupied.	B.1.1.7, B.1.351, P.1	France	This race against the COVID-19 historical strain and its variant strains is an issue of vaccination strategy. It is mandatory to vaccinate most of the population within a year, and preferably within 6 months. Should a 6-month vaccination campaign not be feasible, then reinforced NPI should be considered.
Phiantham and Ito, 2021	Sep 1st, 2020-Feb 19th, 2021	medRxiv	To propose a method to estimate the selective	Modelling study	Community	71,692 of B.1.1.7 strains vs. 65,850 non-B.1.1.7 strains	The serial interval is the time from illness onset in a primary case	B.1.1.7	UK	The result indicated that the control measures against B.1.1.7 strain needs to be strengthened by 33.7% from that against previously

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			advantage of a mutant strain over previously circulating strains using the time course of B.1.1.7 strain frequencies and the distribution of serial intervals.				to illness onset in a secondary case			circulating strains. To get the same control effect as before, contact rates between individuals needed to be restricted to 0.748 of the contact rates that had been achieved by the control measures taken for previously circulating strains.
CDC, 2021	No primary data collection	CDC	To communicate areas of importance and challenges in genomic epidemiology to CDC officials	Government recommendations	Community	N/A	N/A	B.1.1.7, B.1.351, P.1	US	N/A
Public Health Ontario, 2021	N/A	Public Health Ontario	To communicate PHO's current actions in mitigating VOC in the province	N/A	Community	N/A	N/A	B.1.1.7, B.1.351, P.1	Canada (Ontario)	N/A
Public Health Ontario, 2021	Feb 2nd-3rd, 2021	Public Health Ontario	To review and synthesize policies comparing the use of medical vs. non-medical	Environmental scan	Community	N/A	N/A	B.1.1.7, B.1.351, P.1	International	N/A

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			masks or respirators							
U.S Food & Drug Administration, 2021	N/A	US FDA	To recommend & address possible false negative results for clinical laboratory staff and health care providers who use molecular tests for the detection of SARS-CoV-2	Letter to healthcare providers	Healthcare settings & community	N/A	N/A	B.1.1.7, B.1.351, P.1	US	N/A

Table 2: *Summary of Health Systems Sources*

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
Challen, 2021	Oct 1st, 2021-Feb 12th, 2021	BMJ	To establish whether there is any change in mortality from infection with B.1.1.7 compared with circulating SARS-CoV-2 variants	Matched cohort study	Community - genomic surveillance data and death records	54,906 matched cohort pairs (on age, sex and ethnicity) of participants who tested positive for SARS-CoV-2	Death within 28 days of the first positive SARS-CoV-2 test result	B.1.1.7	UK	Probability that the risk of mortality is increased by infection with B.1.1.7 is high; infection with B.1.1.7 has the potential to cause substantial additional mortality compared with previously circulating variants.
Graham, 2021	Sep 8th-Dec 31st, 2020	medRxiv	To examine the association between the regional proportion of B.1.1.7 and reported symptoms, disease course, rates of reinfection, and transmissibility.	Cross-sectional study	Community	36,920 COVID-19 positive users of the COVID symptom app. Surveillance data from the (COG-UK) and a SGTF correlate in community testing data.	Regional proportion of B.1.1.7 and symptoms, disease course, rates of reinfection and transmissibility. Disease burden was also examined by assessing self-reported hospital visits and long reported symptom duration	B.1.1.7	UK	No evidence of changes in reported symptoms, disease severity and disease duration associated with B.1.1.7.
Grint, 2021	Nov 16th, 2020-Jan 11th, 2021	medRxiv	To estimate the risk of death following SARS-CoV-2 infection in England, comparing	Cross-sectional observational cohort study, chart review	Community - health admin database	SGTF status was known for 184,786 people (n=91,775 non-VOC and n=93,011 VOC)	All-cause mortality based on relative hazard of death ratio and absolute risk of death by 28 days, comparing VOC to non-VOC	B.1.1.7	England	B.1.1.7 was associated higher mortality than the wild type, which increases with age and comorbidities, and males have a higher risk than females.

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			VOC to non-VOC							
Frampton, 2021	Nov 9th Dec 20th, 2020	Lancet	To describe emergence of B.1.1.7 in two North Central London hospitals including comparing virological characteristics and clinical outcomes.	Cohort study	Hospital	Of 496 patients with samples positive for SARS-CoV-2 on PCR and who met inclusion criteria, 341 had samples that could be sequenced. 58% had B.1.1.7	Severe disease (defined as point 6 or higher on the WHO ordinal scale within 14 days of symptoms or positive test) and death within 28 days of a positive test,	B.1.1.7	UK	While length of stay, risk of hospitalization within 14 days of a test, and time to hospital admission from symptom onset were similar, B.1.1.7 patients were younger, had fewer comorbidities and more likely to be from an ethnic minority compared to non-B.1.1.7 patients. There was no increased risk of mortality or severe disease with B.1.1.7 compared to non-B.1.1.7.
Courjon, 2021	Dec 2020-Feb 2021	Research Square	To analyze modification in clinical profile and outcome traits.	Cohort study	Hospital	ED (n=1247) & Infectious disease ward or ICU (n=232)	Timeline of UK-variant spreading; Profile of COVID-19 patients admitted in ED; Assessment comparison of hospitalized patients in Infectious Diseases and ICU departments	B.1.1.7	France	There was no significant difference on time from first symptoms to ED admission, severity, need for immediate ICU management, ICU admission, or severity score on admission between B.1.1.7 and non-B.1.1.7.
Bager, 2021	Jan 1st-Feb 9th, 2021	Lancet – preprint	To link SARS-CoV-2 genomic data with Danish health registers and estimate the risk of hospitalisation	Observational cohort study	Community & hospital (linked national surveillance data to	A total of 35,887 test-positive individuals were identified, 11.6% with B.1.1.7.	Hospital admission within 14 days after a positive SARS-cov-2 PCR test or 48hr before a positive test	B.1.1.7	Denmark	Infection with B.1.1.7 was associated with a 64% increased risk of hospitalization compared with individuals infected with wild type SARS-CoV-2.

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			among cases with B.1.1.7 compared with cases detected with other SARS-cov-2 lineages		hospital admission data)					
Patone, 2021	Nov 1st, 2020-Jan 27th, 2021	medRxiv	To estimate the risk of critical care admission, mortality in critically ill patients, and overall mortality associated with B.1.1.7 compared with the original variant. We also compare clinical outcomes between these variants' groups.	Retrospective cohort design, using mathematical modeling in analysis	Community & Hospital - critical care	The 'primary care cohort' was patients in primary care with a positive community COVID-19 test reported between 1 November 2020 and 26 January 2021. The first cohort included 198,420 patients. Of these, 80,494 had VOC B.1.1.7	The outcomes of interest for the primary care cohort were receipt of critical care and 28-day mortality. The outcomes of interest for the critical care cohort were duration of organ support (respiratory, cardiovascular, renal, neurological and liver) in critical care, duration of critical care and mortality at the end of critical care.	B.1.1.7	England	There was an increased risk of COVID-19 28-day mortality and admission for critical care associated with B.1.1.7 in the primary care cohort. In the critical care cohort, after adjusting for confounders, critical care mortality did not differ significantly between B.1.1.7 and non-VOC B.1.1.7 groups.
Snell, 2021	Mar 13th, 2020 and Feb 17th, 2021	medRxiv	To compare admission characteristics of hospitalised cases during the two dominant	Retrospective cohort study	Hospital	2341 total; n=838 in wave 1 and 1503 in wave two	Comparison of the demographic, physiological and laboratory parameters of hospitalised SARS-CoV-2 positive cases during Wave 1/non-	B.1.1.7	UK	While there was double the admissions in Wave 2 (B.1.1.7), patients with B.1.1.7 were similar in age and ethnicity compared to non-B.1.1.7. Significant differences were B.1.1.7 patients were less likely to be frail but more likely to

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			waves of infection for local healthcare planning				B.1.1.7 and Wave2/primarily B.1.1.7 extracted from hospital electronic health record.			be obese hypoxic on admission, the main indicator of severe disease, than non-B.1.1.7 patients.
Haas, 2021	Jan 24th-Mar 6th, 2021	Lancet – preprint	To provide nationwide estimates of the effectiveness of two doses of Pfizer against SARS-CoV-2 outcomes, including deaths, and document the first evidence of nationwide public-health impact following the widespread introduction of the vaccine at the population level	Observational study	Community	There were 202 684 SARS-CoV-2 infections in Israel, of which 93.9% was B.1.1.7. There were 6,040 hospitalizations, 3,470 severe and critical hospitalizations, and 754 deaths among persons aged >15 years.	Range of SARS-CoV-2 outcomes, including all SARS-CoV-2 infections (symptomatic and asymptomatic), hospitalizations (severe and critical) and deaths	B.1.1.7	Israel	Two doses of Pfizer >7 days after admission were highly effective in preventing initial COVID-19 infection, hospitalizations, severe and critical hospitalizations, and deaths at a time when B.1.1.7 was the dominant strain.
Jabłońska, 2021	Mid-June and mid-August 2020 to	medRxiv	To detect potential association between COVID-19	Cohort study, involving multiple	Community	A dataset of 3971 SARS-CoV-2 virus strains identified	COVID-19 deaths during the second wave of COVID-19 pandemic	B.1.1.7 and 11 other variants	38 European countries	Findings suggest that the development and spread of (B.1.1.7) had a significant impact on the mortality during the second

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
	Feb 25th, 2021		mortality and proportion of B.1.1.7 through the second wave of the pandemic in Europe with the use of multivariate regression models.	cross-sections		between December 2019 and March 2021				wave of COVID-19 pandemic in Europe.
Dabrera, 2021	Oct 2020-January 2021	SSRN	To assess whether infection with B.1.1.7 was associated with more severe clinical outcomes compared to wild-type infection	Matched cohort study	Community	63,609 genomically sequenced COVID-19 cases	Risk in hospitalisation and risk of mortality within 28 days of test	B.1.1.7	UK	There was a 34% increased risk in hospitalization associated with B.1.1.7 compared to wild-type cases, however, no significant difference in the risk of mortality was found after adjusting for confounders.
De Oliveira et al., 2021	Sep 1st, 2020 and Mar 17th, 2021	medRxiv	To assess recent trends in mortality data among different age-grouped populations in Brazil.	Cross-sectional	Community	553,518 individuals infected with SARS- CoV-2 in Parana between September 2020 and March 2021	Case fatality rates (CFRs)	P.1	Brazil	There was an 80-215% increased risk of mortality for adults in different age categories between 20-59 years between February 2020 and January 2021, when P.1 was prominent.

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
De Andrade et al., 2021	Feb 16th 2020 - Feb 20, 2021	medRxiv	To compare, during the first year of the pandemic the age profile of patients hospitalized by COVID-19, as well as hospital mortality and use of ICUs, by age group, in large geographic regions of Brazil.	Cross-sectional	Hospital	720,36 completed records of patients hospitalized by Covid-19	Hospital mortality and use of ICUs	P.1	Brazil	Each geographical region of Brazil varied in terms of their mortality over the three periods, with the North region being the hardest hit, experiencing a collapse in the provision of healthcare in the first wave and last periods (associated with P.1) with high mortality in all age groups.
Davies, 2021	Sep 1st, 2020-Feb 14th, 2021	medRxiv	Describe association between SGTF and hazard of death/disease severity	Modeling study	Community	2,245,263 individuals with a positive community test, 51.1% of which had a conclusive SGTF reading and, of these, 58.8% had SGTF (suggesting B.1.1.7).	COVID-19 death occurring within 28 days of an individual's first positive COVID test	B.1.1.7	UK	The hazard of death in the 28 days following a positive test is 55% (39– 72%) higher for B.1.1.7 than for non-B.1.17 cases. Correcting for misclassification of SGTF and missingness in SGTF status, this increases to 61% (42–82%). B.1.1.7 is not only more transmissible than pre-existing SARS-CoV-2 variants but may also cause more mortality.
Domenico, 2021	Jan 7-8 2021	medRxiv	To assess the impact of implemented	Modelling study	Community	N/A	Estimated # cases of historical strain and VOC based on various	B.1.1.7	France	Social distancing implemented in January 2021 would bring down the R of historical strain, however VOC

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			measures on two COVID strains (i.e., B.1.1.7 and wild type) through modeling				social distancing measures using data from a large-scale genome sequencing initiative conducted in France			would continue to increase. School holidays also slowed down dynamics. Accelerating vaccinations will help but won't be sufficient to stop the spread of the VOC, even with optimistic vaccination rates
Mitze and Rode, 2021	December 15, 2020 to February 4, 2021.	MedRxiv	To provide estimates of the epidemiological trends associated with the reporting of B.1.1.7 and non-B.1.1.7 for two key indicators: i) the 7-day incidence rate, and ii) the hospitalization rate.	Modelling study	Community, hospital	Data on daily SARS-CoV-2 infection data for each of the health regions from the COVID-19 dashboard of the Robert Koch Institute. The number of hospitalized patients in intensive care was taken from the INFAS corona database.	Comparing the development in epidemiological outcome variables of two groups (non-B.1.1.7 and B.1.1.7). Outcomes of interest were i) the 7-day incidence rate (SARS-CoV-2 infections per 100,000 population over the last seven days) and ii) the hospitalization rate (hospitalized patients in intensive care per 100,000 population).	Pooled information on VOC	Germany	There was a significant increase in the hospitalization rate in regions in the top 10% percentile of reported VOC cases with an estimated increase of 1.29 [CI: 0.5, 2.1] additional COVID-19 patients in intensive care per 100,000 population.
Pham, 2021	Feb-Aug 2020	medRxiv	To explore the effectiveness of different infection prevention strategies for HCWs in	Modeling study	Hospital	N/A	We computed the effective reproduction number for patients and HCWs to evaluate an intervention's effectiveness. Also measured HCW	B.1.1.7	Netherlands	In response to the emergence of more transmissible SARS-CoV-2 variants, universal PPE use in all hospital wards is the most effective in preventing nosocomial transmission and is the most effective intervention to reduce the

Author, date	Date of data collection	Source	Objective	Study design	Setting	Sample size	Outcome measures	Variant	Country	Main finding
			hospitals in the absence of vaccination using an agent-based model of nosocomial SARS-CoV-2 transmission.				absenteeism and numbers of nosocomial infections			reproduction number and absenteeism. Regular screening and contact tracing of HCWs are also effective interventions, but critically depend on the sensitivity of the diagnostic test used.

Table 3: *Summary of Guidance Documents*

Author, Date	Source	Objective	Setting	Variant	Country	Audience
ECDC & WHO, 2021	ECDC & WHO	To present the available methods (screening and sequencing) for identification of circulating SARS-CoV-2 VOC	N/A	B.1.1.7, B.1.351, P.1	Europe	Laboratories, microbiology experts and relevant stakeholders making decisions on establishing or scaling up capability and capacity to detect and identify circulating VOC, and making decisions on which technologies to use and for which objective
Health Canada, 2021	Health Canada	To communicate guidance on testing protocols in primary and secondary schools, including communities with high levels of VOC	Primary and secondary schools	B.1.1.7, B.1.351	Canada	Health/government workers responsible for planning testing in schools

Author, Date	Source	Objective	Setting	Variant	Country	Audience
Ontario Ministry of Health, 2021	Ontario Ministry of Health	This document details case, contact and outbreak management guidance for ALL confirmed and probable cases of COVID-19, as well as additional guidance for VOC screen positive cases when timely intervention is feasible for the case, contacts, and/or outbreaks	Community	B.1.1.7, B.1.351, P.1	Canada (Ontario)	Public health units (PHUs) in Ontario
Public Health Ontario, 2021	Public Health Ontario (Provincial Infectious Diseases Advisory Committee group)	This document provides interim guidance for how infection prevention and control (IPAC) practices in Ontario health care settings should be modified in light of the emergence of B.1.1.7 in Ontario, and the potential for the emergence of other known or as yet unknown VOC.	Community and health care settings	B.1.1.7, B.1.351, P.1	Canada (Ontario)	Government, public health units and health care providers
Callan, 2021	medRxiv	To report on a taxonomy created to categorize disease dynamics across different countries to show the evolution of COVID-19 relative to disease control measures	Community	B.1.1.7, B.1.351, P.1	International	All
Health Protection Surveillance Centre, 2021	Health Protection Surveillance Centre	To communicate public health updates/guidance for Ireland regarding VOC	Community	B.1.1.7, B.1.351, P.1	Ireland	Decision makers
Public Health England, 2021	Public Health England - Department of Health and Social Care	To communicate guidance about surge testing to the public	Community	B.1.1.7, B.1.351, P.1	UK	UK population
Public Health England, 2021	Public Health England	To communicate public health guidance for people entering the UK and/or suspected to be infected with a VOC	Health system and community	B.1.1.7, B.1.351, P.1	UK	Healthcare staff in primary and secondary care
Public Health Ontario, 2021	Public Health Ontario	This document aims to provide information about the recent changes to the Public Health Ontario's laboratory (PHO) process for detecting SARS-COV-2 VOC.	Community	B.1.1.7, B.1.351, P.1	Canada (Ontario)	Ontario's government, public health organizations and health care providers, and general public

Author, Date	Source	Objective	Setting	Variant	Country	Audience
Public Health Ontario, 2021	Public Health Ontario	Using available epidemiologic data at Public Health Ontario, this approach considers how these data can be used to guide reopening accounting for what is known (e.g. rates of new cases) and what is unknown (e.g. what is the effect of VOC in Ontario?). The stepwise, data-driven approach could support reopening at low community transmission levels, building on lessons learned in countries that have recently managed exponential VOC growth	Community	B.1.1.7, B.1.351, P.1	Canada (Ontario)	public, policy-makers and researchers
SAGE-EMG/SPIB-B/TWEG, 2020	SAGE Environmental Modelling Group (EMG), the Scientific Pandemic Insights Group on Behaviours (SPI-B) and the Transmission Group (TWEG)	To communicate B.1.1.7 mitigation strategies to Public Health England officials	Community	B.1.1.7, B.1.351, P.1	UK	N/A
Toronto Public Health, 2021	Toronto Public Health	To communicate guidance about strategies to mitigate VOC in the workplace	Workplaces	B.1.1.7, B.1.351, P.1	Canada (Toronto)	People working in Toronto
Alberta Health Services, 2021	Alberta Health Services	To communicate infection control and isolation/quarantine changes resulting from VOC	Community	B.1.1.7, B.1.351, P.1	Canada (Alberta)	Alberta public
CanCOGeN, 2021	CanCOGen	To communicate guidance on genomic surveillance of VOC in Canada	Health system	B.1.1.7, B.1.351	Canada	Laboratories and health/government workers conducting screening/surveillance of VOC
CIDRAP, 2021	University of Minnesota Center for Infectious	To communicate possible strategies for pivoting vaccine rollout in the US	Health system	B.1.1.7, B.1.351, P.1	US	Health/government workers responsible for vaccine rollout

Author, Date	Source	Objective	Setting	Variant	Country	Audience
	Disease Research and Policy (CIDRAP)					
Government of Newfoundland & Labrador, 2021	Government of Newfoundland & Labrador	To communicate infection control measures in settings offering personal services; one piece of guidance is related specifically to VOC	Community - hair salons/barber shops, spa and esthetic services (manicures, pedicures, facials, waxing, make-up, etc.), tattooing and piercing services, tanning salons	B.1.1.7, B.1.351, P.1	Canada (NL)	Workers offering personal services in these settings
Health Canada, 2021	Health Canada	To communicate when updated vaccines should be considered in response to VOC	Health system	B.1.1.7, B.1.351, P.1	Canada	Health/government workers responsible for planning vaccine rollout
Province of Manitoba, 2021	Province of Manitoba	To communicate isolation and testing guidance related to VOC	Community	B.1.1.7, B.1.351, P.1	Canada (Manitoba)	Manitoba public
Saskatchewan Health Authority, 2021	Saskatchewan health authority	To communicate public health recommendations around eye protection for staff, physicians and family members/support persons	Hospital/healthcare settings	B.1.1.7, B.1.351, P.1	Canada (Saskatchewan)	Public and healthcare providers

Author, Date	Source	Objective	Setting	Variant	Country	Audience
Saskatchewan Health Authority, 2021	Saskatchewan health authority	To communicate most recent evidence related to VOC to staff & physicians	Healthcare settings & community	B.1.1.7, B.1.351, P.1	Canada (Saskatchewan)	staff and physicians
Saskatchewan Health Authority, 2021	Saskatchewan health authority	To communicate updates to screening protocols in light of increasing VOC	Healthcare settings & community	B.1.1.7, B.1.351, P.1	Canada (Saskatchewan)	Healthcare professionals, decision-makers, public health

ECDC: European Centre for Disease Control

Appendix 4: *Quality Appraisal*

Table 1. *Quality Appraisal of research articles using the Newcastle-Ottawa scale (NOS) tool*

Author, year	**Pre-print (PP) or Peer Review (PR)**	**Source**	**Average score per category**			**Minus 2* if preprint**	**Total Score (%) out of 9**	**Overall Quality* (low, medium, high)**
			Selection	Comparability	Outcome			
Cohort Study Design								
Bager, 2021	PP	SSRN	3.5	2	2.5	-2	6 (67)	Medium
Buchan, 2021	PP	MedRxiv	3.5	2	2.5	-2	6 (67)	Medium
Challen, 2021	PR	BMJ	4	2	3	N/A	9 (100)	High
Courjon, 2021	PP	Research Square	4	0.5	2.5	-2	5 (56)	Medium
Dabrera, 2021	PP	SSRN	4	2	2	-2	6 (67)	Medium
Frampton, 2021	PR	Lancet	4	2	3	N/A	9 (100)	High
Grint, 2021	PR	Eurosurveillance	4	2	3	N/A	9 (100)	High
Haas, 2021	PP	SSRN	4	2	2	-2	6 (67)	Medium
Jablonska, 2021	PP	MedRxiv	4	1	2	-2	5 (56)	Medium
Lumley, 2021	PP	MedRxiv	3	2	1	-2	4 (44)	Low
Patone, 2021	PP	MedRxiv	4	2	2	-2	6 (67)	Medium
Cross-sectional Study Design								

Author, year	**Pre-print (PP) or Peer Review (PR)**	**Source**	**Average score per category**			**Minus 2* if preprint**	**Total Score (%) out of 9**	**Overall Quality* (low, medium, high)**
			Selection	Comparability	Outcome			
Bachtiger, 2021	PP	MedRxiv	2	1	0	-2	1 (10)	Low
DeAndrade, 2021	PP	MedRxiv	2.5	1	2.5	-2	4 (40)	Low
DeOliveira, 2021	PP	MedRxiv	2	0	2	-2	2 (20)	Low
Graham, 2021	PR	Lancet	3	2	3	N/A	8 (80)	High
Snell, 2021	PP	MedRxiv	3	1	3	-2	5 (50)	Medium

*High quality: 80-100%; Medium quality: 50-80%; Low quality: <50%

Table 2. *Quality Appraisal of guideline documents using the AGREE II tool*

Author/Organization, Year	**Domain Scores (%)**						**Domain 7: Overall Quality (%)***	**Overall Quality (low, medium, high)****
	1	2	3	4	5	6		
Alberta Health Services, 2021	30.5	13.9	0.0	72.2	16.7	0.0	25.0	Low
Callan, 2021	13.9	13.9	11.5	47.2	33.3	25.0	50.0	Medium
CanCOGeN, 2021	18.8	25.0	5.2	38.9	18.8	62.5	25.0	Low
CIDRAP, 2021	44.4	41.7	13.5	33.3	20.8	8.3	41.7	Low
ECDC & WHO, 2021	86.1	80.5	35.4	52.8	41.7	12.5	66.7	High
Government of Newfoundland and Labrador, 2021	44.4	25.0	0.0	63.9	20.8	0.0	16.7	Low
Health Canada, 2021	36.1	27.8	8.3	33.3	29.2	16.7	16.7	Low
Health Canada, 2021	44.4	63.9	22.9	69.4	47.9	16.7	66.7	High
Health Protection Surveillance Centre, 2021	44.4	25.0	12.5	44.4	37.5	41.7	58.3	Medium
Ontario Ministry of Health, 2021	58.3	47.2	22.9	80.6	35.4	16.7	75.0	High
Province of Manitoba, 2021	44.4	25.0	2.0	38.9	14.6	0.0	25.0	Low
Public Health England, 2021	47.2	22.2	3.1	75.0	20.8	16.7	58.3	Medium
Public Health England, 2021	86.1	50.0	3.1	63.9	27.1	8.3	50.0	Medium
Public Health Ontario, 2021	72.2	69.4	24.0	77.8	35.4	8.3	83.3	High
Public Health Ontario, 2021	69.4	47.2	8.3	55.6	25.0	16.7	41.7	Medium
Public Health Ontario, 2021	69.4	44.4	18.7	52.8	37.5	16.7	41.7	Medium
SAGE-EMG/SPIB-B/TWEG, 2020	27.8	27.8	22.9	55.6	29.2	12.5	58.3	Medium

Author/Organization, Year	**Domain Scores (%)**						**Domain 7: Overall Quality (%)***	**Overall Quality (low, medium, high)****
	1	2	3	4	5	6		
Saskatchewan Health Authority, 2021	8.3	8.3	3.1	50.0	10.4	0.0	25.0	Low
Saskatchewan Health Authority, 2021	44.4	22.2	4.2	47.2	6.2	8.3	16.7	Low
Saskatchewan Health Authority, 2021	25.0	19.4	2.1	44.4	4.2	4.2	16.7	Low
Toronto Public Health, 2021	41.7	30.6	3.1	75.0	41.7	8.3	58.3	Medium

*Subjective overall score calculated as an average between two appraiser scores

**Low: Low overall score & appraisers do not recommend use; Medium: middle overall score and/or appraisers have mixed views on whether guideline is recommended; High: middle to high score & appraisers both recommend guideline