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Commentary

Public health actions to control new SARS-CoV-2 variants

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Recent reports suggest that some SARS-CoV-2 genetic variants, such as B.1.1.7, might be more transmissible and are quickly spreading around the world. As the emergence of more transmissible variants could exacerbate the pandemic, we provide public health guidance for increased surveillance and measures to reduce community transmission.

Introduction

In December of 2019, a previously unknown respiratory illness was discovered in China. As the culprit, a novel coronavirus named SARS-CoV-2 that causes the disease COVID-19, was being identified, the virus had already started to spread around the world. Now, more than a year later, there have been close to 100 million reported COVID-19 cases. Shortcomings in public health authorities' understanding of the virus and their ability to respond contributed to the severity of the pandemic. With the discovery of new SARS-CoV-2 genetic variants that could increase transmissibility (Lauring and Hodcroft, 2021), the concern is that their spread will be faster than vaccine production and distribution, allowing variants to intensify ongoing COVID-19 outbreaks. Thus, many public health authorities are again in need of guidance to protect their communities. Here, we address these needs by first summarizing what is known about the emergence of variants of concern and the evidence for increased transmissibility. By using the B.1.1.7 variant as an example, we provide recommendations for robust public health responses to new SARS-CoV-2 variants, even as the data to fully understand their potential impacts are still being collected.

Emergence of novel SARS-CoV-2 genetic variants

SARS-CoV-2 is prone to making errors in its genetic code during replication, accumulating 1–2 nucleotide changes (mutations) every month (nextstrain.org/ncov/global?l = clock). Although most mutations are not worrisome, over the course of the pandemic, some have arisen that can be of public health concern. Dedicated sequencing and open data sharing are allowing us to track the emergence and spread of SARS-CoV-2 genetic variants in near real time (e.g., nextstrain.org). Tracking these variants becomes critically important when they can be associated with changes in epidemic dynamics (Lauring and Hodcroft, 2021).

The first SARS-CoV-2 mutation of concern located at amino acid position 614 of the spike protein (changing an aspartic acid to a glycine, aka "D614G") was identified early in the pandemic. The SARS-CoV-2 spike protein is an important structural region of the virus for entry into cells and recognition by antibodies and has hence received a lot of attention. Viruses with the D614G mutation quickly became the globally dominant form by June 2020, and many subsequent studies indicated that it is more infectious (Korber et al., 2020). The rapid rise of D614G during the early COVID-19 pandemic, before many viral genomic surveillance systems were in place, meant that most of what we know about the mutation came after it was already globally established.

In late 2020, genomic surveillance in South Africa revealed a new SARS-CoV-2 variant (designated B.1.351 or 501Y.V2) associated with a concerning rise in local COVID-19 cases (Tegally et al., 2020). One of the mutations in this variant, N501Y, is located in the important receptor-binding domain (RBD) of spike protein and is predicted to increase binding to human cells and reduce viral neutralization by the monoclonal antibody LY-CoV016 (Greaney et al., 2021; Starr et al., 2020). The concern is that if the mutation is the cause of this rapid rise in cases, it could be more transmissible and rapidly spread, similar to D614G during the early pandemic. Following South African scientists alerting others to the N501Y mutation, it was soon found to have arisen independently in a SARS-CoV-2 variant expanding quickly in the southeast of England, in the UK, designated B.1.1.7 (also 501Y.V1).

The B.1.1.7 variant is a global concern

Initial observations suggested that the B.1.1.7 SARS-CoV-2 variant rapidly replaced existing variants and became dominant in London and southeast England in less than three months (Figure 1). Subsequent modeling work

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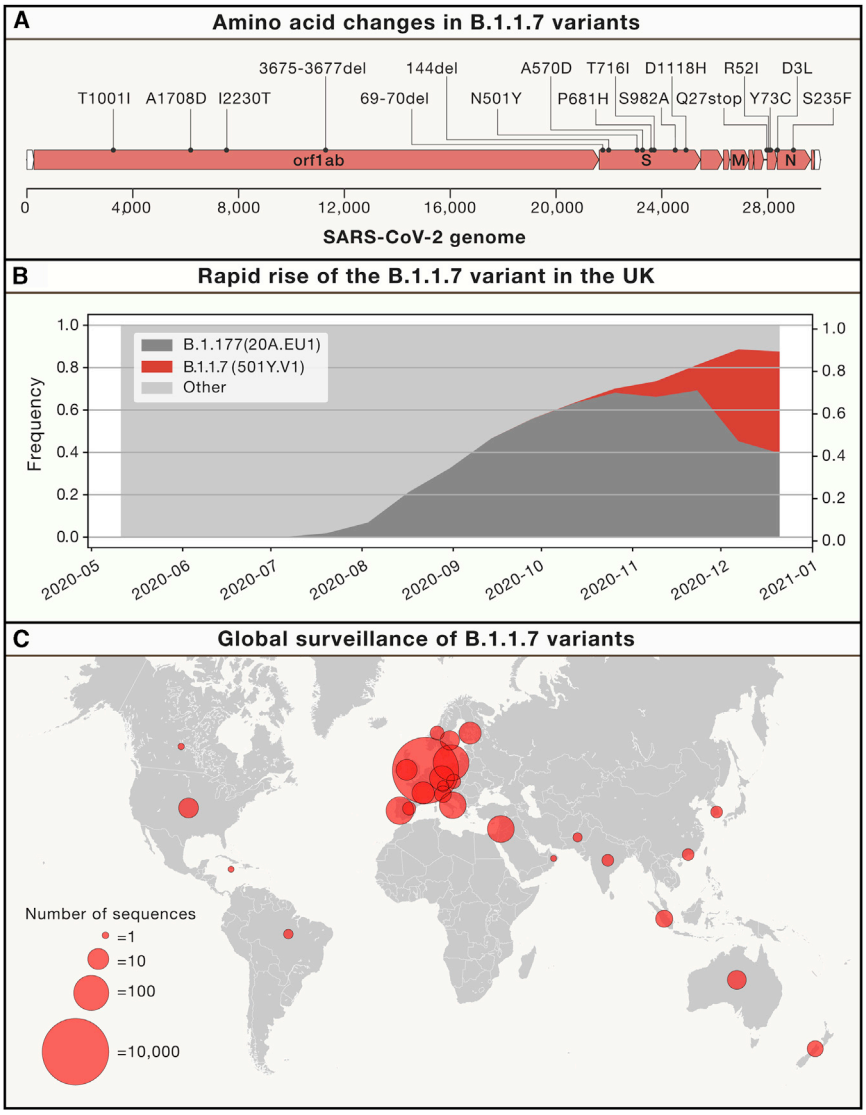

Figure 1. Rising global spread of the SARS-CoV-2 B.1.1.7 variant

(A) Location of the 17 amino acid substitutions that define the B.1.1.7 variant genome. Eight amino acid substitutions are in the important spike gene (S), including N501Y and Δ69/70 HV.

(B) Prior to B.1.1.7, B.1.177 (also called "20A.EU1") was the dominant variant in the UK, although it is not believed to have arisen due to increased transmissibility. Since the earliest sequenced sample of B.1.1.7 (September 20, 2020), it started to displace B.1.177 and other variants in the UK. The rapid rise of B.1.1.7 sequences in the UK alerted officials that this was a variant of concern.

(C) As of January 11, 2021, B.1.1.7 has been detected in 49 countries, of which 30 countries have shared sequences. Germany was the earliest to report local transmission of B.1.1.7 on November 27, 2020 (cov-lineages.org/global_report.html).

has estimated that B.1.1.7 is approximately 50% more transmissible (Davies et al., 2020), which could increase the average number of people that one infected person will pass the virus to (effective reproductive rate) by between 0.4 and 0.7 people (Volz et al., 2021). Public Health England investigated these claims by using contact tracing data and found that the likelihood of infection upon contact (secondary attack rate) is 30%–50% higher with B.1.1.7 than with other variants (PHE, 2020). Although the impact of this variant on disease severity is still uncertain, increased transmissibility of B.1.1.7, or future variants, can still lead to steep rises in hospitalizations and deaths due to a rise in infections.

The B.1.1.7 variant is characterized by mutations changing 17 amino acids, including eight changes in the spike protein (Figure 1). Besides N501Y, the most notable mutation is a deletion in the spike protein at amino acid positions 69 and 70 (Δ69/70 HV) that increases infectivity and has evolved independently several times during the pandemic (Kemp et al., 2020). It is not yet clear if N501Y, Δ69/70 HV, both, or a larger combination of the 17 mutations that define the B.1.1.7 variant are driving the apparent increased transmissibility. Moreover, studies investigating the impact of the B.1.1.7 mutations on natural and vaccine-mediated immunity are ongoing. Because the immune system creates antibodies to multiple parts of the SARS-CoV-2 spike protein, chances remain high that vaccines will retain efficacy for this variant. However, it is a realistic possibility that over time immune escape variants could emerge, particularly if imperative public health measures to reduce SARS-CoV-2 transmission are not implemented.

As of January 11, 2021, the B.1.1.7 variant has been detected in 49 countries, including many across Europe and also in Asia and the Americas (Figure 1; cov-lineages.org/global_report.html). Increasing detection of linked COVID-19 cases with B.1.1.7 without a direct connection to the UK highlights that the variant is likely spreading locally in many of these locations and that substantial international spread happened weeks or months before it was first recognized. Sequencing efforts to monitor both known variants like B.1.1.7 and novel variants remain inconsistent across the globe, so the known distribution and prevalence of B.1.1.7 is undoubtedly underestimated. Thus, public health authorities currently have a patchy and skewed picture and no clear guidance on which to inform critical decision making to slow variant spread.

Actions to improve variant surveillance

The COVID-19 pandemic has demonstrated how a comprehensive open virus sequencing program is crucial for a robust pandemic response plan. We need up-to-date information on the circulating genetic variants to make timely public health decisions that can

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slow the spread of SARS-CoV-2 variants or make recommendations to update future vaccines. This is fundamentally different than targeted sequencing for outbreak investigations, where the goals are to reveal epidemiological connections (e.g., timing and source of virus, relatedness among cases). For surveillance purposes, a random subset of positive tests should be sequenced to monitor for mutations or variants of concern. Thus, routine genomic surveillance requires strong ties among (1) entities performing diagnostic SARS-CoV-2 testing; (2) labs with the expertise, capacity, and resources to conduct relatively large-scale sequencing; and (3) computational groups who can process and analyze the large genomic datasets. Rarely are all steps conducted in a single laboratory or even at a single institution. In countries where SARS-CoV-2 testing is decentralized, such as the US, building this network often requires partnerships between public institutions, such as state health departments or academic laboratories, hospitals, and private companies. Recommendations for SARS-CoV-2 sequencing can be found in a recent report published by the World Health Organization (WHO) that is available in the web resources.

The prime example of a comprehensive genomic surveillance program is the COVID-19 Genomics UK (COG-UK) Consortium (www.cogconsortium.uk/). COG-UK is a collaboration between government, private, and academic institutions from around the UK, with substantial funding support for large-scale routine SARS-CoV-2 sequencing. Their network of diagnostic labs sends a subset of 5%–10% of the SARS-CoV-2 positive cases for sequencing at regional universities and large sequencing centers. What keeps COG-UK working is structured governance and a series of technical working groups to ensure that samples and data continuously flow. This system, combined with detailed epidemiological investigations, helped detect the B.1.1.7 variant soon after its emergence and provided the world with an early warning.

The problem remains that genomic surveillance is still not available in most countries, leaving us blind to what variants could be circulating in many places. This is often due to a combination of factors, including a lack of infrastructure, technical expertise, political will, and dedicated resources. Many areas without genetic surveillance are those with large previous outbreaks and thus potentially fertile ground for some types of concerning mutations. Given that SARS-CoV-2 variants are a global concern, in addition to high-income countries urgently prioritizing surveillance, the international community should also provide financial and technical support to bolster genomic surveillance in areas that are less resourced. Furthermore, there is insufficient international governance, including no current legal obligations, for rapid sequence data sharing (Rourke et al., 2020). Given that new SARS-CoV-2 variants of concern will likely continue to emerge even after the vaccine rollout, investment in and policies for genomic surveillance should be a priority where feasible.

Standard PCR assays can also help support variant detection when large-scale sequencing is not available. The Applied Biosystems TaqPath COVID-19 assay (ThermoFisher), a PCR test, was discovered to have a distinct signature (“spike gene target failure”) when viruses contain the Δ69/70 HV deletion, like the B.1.1.7 variant. This PCR fault has been useful in the UK to track changes in B.1.1.7 frequency and elsewhere to screen COVID-19 samples for sequencing priority. However, other SARS-CoV-2 variants also have the Δ69/70 HV deletion, so TaqPath PCR alone is not confirmatory for B.1.1.7. By targeting multiple deletions in the B.1.1.7 variant, such as ORF1a Δ3675-3677 SGF (Figure 1A), however, molecular assays can be designed to be more variant-specific. Although not replacements for routine sequencing, easier and cheaper discriminatory PCR tests will likely play an important role in SARS-CoV-2 variant tracking. An example of a PCR assay to detect the variants of concern B.1.1.7, B.1.351, and P1 (also 501Y.V3, detected in Brazil) is available in the web resources.

Local actions to slow variant transmission

There is a growing sense of uncertainty among public health officials and the general public on what actions should be taken to slow the local emergence and spread of the emerging SARS-CoV-2 variants, including B.1.1.7. The primary evidence suggests that B.1.1.7 is equally more transmissible across all age groups (PHE, 2020). There are several hypotheses about the underlying cause of increased transmissibility such as (1) the variant could lead to an infected person producing more virus (increased viral load), (2) it could be more likely to establish infection upon contact (decreased infectious dose), and/or (3) it could prolong the period of infectiousness. Thus, control measures need to be centered around reducing community transmission. Although previously identified mitigation measures will continue to apply to the new variant, some measures might need to be tightened, and gaps in mitigation measures need to be addressed. This is particularly a major challenge in countries where community transmission has not been adequately controlled prior to the variant’s emergence. An example list of public health mitigations is available in the web resources.

With potentially more transmissible SARS-CoV-2 variants circulating globally, public officials should communicate the known health risks and tighten the personal, procedural, engineering, and societal control measures that are known to be effective at decreasing transmission. These include the following: reducing social contacts, effective testing and tracing, robust outbreak identification and control, support to ensure effective isolation and quarantine, and population vaccination. There should also be appropriate messaging to inform the public about specific environments and activities in the community associated with high risk of transmission and the continued use of mitigation measures that will need to be in place even after vaccine rollout. Finally, the messaging should be tailored to the population, ideally by working with community groups and leaders, to ensure that the information is widely disseminated and adequately understood across different backgrounds and ethnic groups.

As COVID-19 cases associated with variants rise in the community, the level of urgency and frequency of the messaging should increase, alongside bolstering local control programs.

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Moreover, enhanced mitigation measures might be necessary, depending on the level of local community transmission. These include the following: (1) reinforcing the importance of using face coverings in all indoor public spaces, schools, workplaces, and crowded outdoor spaces; (2) considering temporary closure of non-essential indoor spaces where face coverings cannot be worn; (3) considering expanding the distance on the 2 m (6 ft) rule; (4) enhancing indoor ventilation; and (5) addressing socioeconomic inequalities that are the main drivers of background community transmission in many countries. To the last point, governments should implement or bolster sick leave entitlements to avoid undue pressure to work when sick, incentivize sectors to provide safer working environments, financially support temporary business closures where necessary, and provide accommodation for those living in crowded or shared housing. Such measures could help to significantly reduce community transmission. Determining which of these measures should be enacted will be dependent upon the local COVID-19 rates and risk factors.

Congregate living facilities, such as nursing homes, homeless shelters, detention centers, and university dormitories, as well as high-risk occupational settings such as meat-packing plants, warehouses, manufacturing, and distribution could be especially vulnerable to SARS-CoV-2 with enhanced transmissibility. These facilities might need to enforce enhanced mitigation measures earlier than the surrounding communities. This will be especially important with elderly, high-disease-risk, and other vulnerable populations. Although B.1.1.7 and other variants are not known to cause more severe COVID-19 disease, spread of these variants in medically and socioeconomically vulnerable populations could lead to greater hospitalizations and mortality. Thus, it is important that individuals that fit into one of the high-risk categories, and their caregivers, take extra precautions.

Closing schools should be a last resort

There are significant age-related differences in relative susceptibility and infectivity for SARS-CoV-2. According to a review of international data, children less than 10 years of age had significantly lower susceptibility to infection than did adults, and susceptibility increases with age (Goldstein et al., 2020). Although earlier analysis based on data from November in England (when lockdown was in force but schools were open) suggested that the B.1.1.7 variant might have been circulating at higher rates in 10–19 year olds, there are currently four analyses demonstrating B.1.1.7 has similar increases in transmissibility across all age groups (PHE, 2020). Moreover, the contact tracing data from the UK shows that B.1.1.7 still has relatively lower attack rates in children than in adults (PHE, 2020).

Although increased mitigation measures are required to bring down the community transmission when more transmissible variants like B.1.1.7 are circulating, proactively closing schools is not advised as a broad preventative measure. Schools in the UK were closed not based on the increased transmissibility of the variant, but due to high community transmission rates. Therefore, school closures should not be seen as an exit strategy for SARS-CoV-2 variants in the absence of addressing the underlying issues of high community levels of infection. Rather, decisions about school closures should be based on local and school-based data at a given time and only imposed for the duration of the quarantine period.

Prolonged school closures can lead to broad societal damage. Safety of the students, teachers, and staff should be a top priority, and thus authorities should implement mitigation measures (e.g., test and trace, distancing, mask wearing, and ventilation) to reduce the likelihood of within-school transmission and maximize in-person learning days. Remote learning further exacerbates inequities, especially among under-resourced communities, not only in terms of education (e.g., it requires computers, internet, and adult guidance for younger students) but also in reducing access to safe places, social and wellbeing support, and adequate nutrition. Thus, extended periods of remote school could contribute to educational gaps, worsening mental health, and developmental disorders caused by malnutrition, disruption of previously in-place family supports, and domestic violence. Each school district needs to delicately balance and mitigate the risks and not allow public health authorities to close schools down to make up for inadequate community-level control measures for SARS-CoV-2 variants.

Limited effectiveness of travel restrictions

At the beginning of the pandemic, the WHO did not recommend the use of travel bans to control SARS-CoV-2. This was based on considerations under the 2005 International Health Regulations—the international law countries adopted after SARS and more than a century and a half of normative practice that recognized such restrictions are often too delayed and porous to prevent pathogen spread (WHO, 2016). Moreover, travel bans often cause economic harm that could result in countries delaying notification of future health threats, as well as interrupting the flow of essential goods, including medical supplies (Devi, 2020). Over the course of the COVID-19 pandemic, however, some nuance has developed around the utility of travel restrictions in slowing (rather than stopping) spread, giving time for governments to establish a response strategy (Grepin et al., 2020). For example, countries that have managed to approach elimination repeatedly, like New Zealand, Australia, and Taiwan, do not have porous land borders and have been able to use travel restrictions as a way to slow incoming cases to enable quarantine and, if required, contact tracing. Still, the utility of travel restrictions depends on the context because gaps in surveillance could mean variants are already spreading locally. Travel restrictions can also provide a false sense of security, particularly when used by governments to give the appearance of action, and are not effective without the necessary corollary local public health response measures. With the emergence of B.1.1.7 and other variants, countries are still implementing new travel restrictions to exclude or delay virus introductions. The success of these restrictions will depend heavily on the context and local actions.

Following the UK government's first report on the potential increased transmission exhibited by B.1.1.7 on December 20, 2020, several countries implemented travel restrictions or required negative COVID-19 tests for travelers from the UK (Kwai et al., 2020). Although the existing disruptions to global travel might have slowed the spread of the variant, it is now clear that the new restrictions did not halt its spread. B.1.1.7 has now been detected around the world, including in countries that implemented additional travel restrictions or test requirements (e.g., France, Japan, and the United States). Many of these infections with B.1.1.7 have been detected in individuals without recent travel history, suggesting that local transmission could have been occurring well before the travel restrictions were in place. Moreover, because genomic surveillance is not widespread, the variant has likely already spread to many other countries that have not yet reported cases. In areas with insufficient local mitigation measures, the variant will likely quickly dominate circulation. This underlines the imperative of all governments to implement already necessary local mitigation measures to reduce community transmission, but now at an urgency that cannot wait or rely solely on travel restrictions to prevent introduction or greater spread of B.1.1.7.

Unlike early in the pandemic, global travel is already significantly disrupted, and the norms against travel bans have significantly shifted, making it easier for governments to implement new restrictions. This could have long-term public health implications. In light of the travel restrictions seen for the B.1.1.7 and B.1.351 variants, there is a real risk that when future variants (or novel diseases) emerge, countries will delay notifying or sharing sequences with the international community, particularly if there is uncertainty about whether a variant is more transmissible, more virulent, or could impact vaccine efficacy. This disincentive is amplified by the unequal impacts of travel bans, inequitable vaccine access, and economic inequalities between countries. Any potential delays in notification and sharing could have significant public health ramifications, particularly if variants that impact vaccine efficacy emerge.

Conclusions

As the COVID-19 pandemic progresses, new SARS-CoV-2 variants of concern will continue to emerge. The concern over these variants is not only that they could exacerbate already crippling outbreaks but also that they could reduce the efficacy of some vaccines or cause increased rates of reinfections, prolonging the pandemic. As the B.1.1.7 variant has demonstrated, these are global issues. Thus, there is urgent need for multilateral cooperation and agreement between countries on building local sequencing capacities and the rapid global sharing of sequence data, along with, but decoupled from, guidance on the swift actions to control local transmission as well as the appropriateness and limits of travel restrictions. Although much of this article uses the B.1.1.7 variant as an example, similar principles can be applied to other SARS-CoV-2 variants of concern, including B.1.351 discovered in South Africa and P.1 discovered in Brazil. With vaccination started, the end is in sight, but that can quickly vanish with poor public health actions in the months to come.

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DECLARATIONS OF INTEREST

The authors declare no competing interests.

WEB RESOURCES

Genomic sequencing of SARS-CoV-2, https://apps.who.int/iris/bitstream/handle/10665/338480/9789240018440-eng.pdf?sequence=1&isAllowed=y

Mitigations to Reduce Transmission of the new variant SARS-CoV-2 virus, https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/948607/s0995-mitigations-to-reduce-transmission-of-the-new-variant.pdf

Multiplexed RT-qPCR to screen for SARS-COV-2 B.1.1.7, B.1.351, and P.1 variants of concern V.2, https://www.protocols.io/view/multiplexed-rt-qpcr-to-screen-for-sars-cov-2-b-1-1-brrhm536

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