COVID-19 FOCUS REPORT

COVID-19 Variants: Update #1

Prepared by BlueDot, March 16, 2021

In this report, we provide an update on the global spread of three current Variants of Concern (VoCs) and highlight several variants that have emerged (referred to as Variants Under Investigation). In addition, we summarize the scientific research available thus far on the clinical impact of the VoCs. Finally, as Denmark is a country with high genomic surveillance capacity and relatively high-quality genomic data, we provide an outlook on its COVID-19 situation based on the domestic spread of the VoCs, epidemiological indicators, implemented control measures, vaccination efforts, and related public sentiment in the country.

Executive Summary

- In this report, we focus on three variants of concern:
    - **B.1.1.7** (initially detected in the U.K.),
    - **B.1.351** (initially detected in South Africa), and
    - **P.1** (initially detected in Brazil).
- We also highlight five newly identified variants carrying mutations that may have a clinical implication. These include:
    - **A.23.1** initially detected in Uganda,
    - **B1.525** initially detected in Nigeria,
    - **B.1526** initially detected in New York, USA,
    - **B1.427/B1.429** initially detected in California, USA, and
    - **B.1.1.7 variant that has gained the E484K mutation** in Oregon, USA and the United Kingdom (independently emerged in these two locations).
- The detection and reporting of genomic surveillance data are biased by a number of factors, including individual country-level access to healthcare, COVID-19 testing rates, and genomic testing capacity. As a result, the known VoCs are likely a sample of variants that may have developed improved fitness through evolutionary change. As of March 15, 2021, 101 countries have detected the B1.1.7 variant, 55 countries have detected the B.1351 variant, and 26 countries have detected the P.1 variant. **Figures 1- 3** are maps highlighting countries whose transmission type of each VoC is monitored; these include all 26 countries that have detected P.1, and a subset of countries that have detected the B.1.1.7 (88/101 countries) and B.1.351 (48/55 countries for B.1351).

- Based on most recent data available on transmission type, Belgium is the only country that has reported local transmission of all three VoCs (B.1.1.7, B.1.351, and P.1). Thirteen countries have reported local transmission of both the B.1.1.7 and B.1.351 variants. Brazil and Sweden are the two countries that have reported local transmission of both the B.1.1.7 and P.1 variants. A map and table of each country's local transmission status of VoC(s) can be found in **Figure 4** and **Table A1**, respectively.
- Scientific evidence around the clinical impact of the VoCs is continually emerging. At this time, there is evidence from multiple, independent analyses to suggest that B.1.1.7 is more transmissible and causes increased severity of disease. Early evidence suggests that B.1351 is likely better at evading vaccine-acquired and natural immunity.
- For Denmark, we synthesized data on the proportion of sequenced cases that are VoCs alongside multiple epidemiological indicators, vaccine-related indicators, travel and local control measures currently implemented, and survey results around vaccine sentiment to speculate on the country's COVID-19 outlook. We conclude that although Denmark's overall COVID-19 outbreak was recently stable with early signs of an increase (7-day rolling average number of new cases per day = 714 as of March 10, 2021), local transmission of the B.1.1.7 variant and the rapid increase of proportion of sequenced cases identified as this variant are causes for concern. In the most recent week, over 80% of sequenced cases of SARS-CoV-2 were identified as B.1.1.7. This high proportion indicates that the existing public health measures to control COVID-19 in Denmark may need to be maintained or very gradually relaxed as vaccination coverage improves in the weeks ahead if a resurgence is to be avoided.

What does this mean?

- The global spread of the three current Variants of Concern has increased in geographic scope and extent of transmission (i.e., more local transmission instead of travel-related only) since our February 3, 2021 Focus Report on Variants of Concern. As exemplified by the spread of these three VoCs, the emergence of new variants can have global impact and risk.
- Several new variants have been identified though they remain "under investigation" and have not been elevated to the status of VoC at this time.
- Countries must continue to implement public health measures appropriate to their domestic epidemiological situation and risk while increasing their vaccination efforts (if supplies are available and there is access). These continued efforts towards minimizing viral transmission will not only prevent the spread of existing variants but also mitigate the emergence of new variants. Countries that are earlier in the domestic spread of the VoC should heed the epidemiological situation and experiences of countries further along their outbreak of VoC (e.g., B.1.1.7 in European countries, B.1.351 in South Africa, and P.1 in Brazil).

Key Questions

Question 1:
What are the Variants of Concern thus far? What are some Variants Under Investigation thus far?

Question 2:
Where have the Variants of Concern been reported globally?

Question 3:
What does the scientific evidence say about the clinical impact of the B.1.1.7, B.1.351, and P.1 variants?

Question 4:
What is the COVID-19 outlook for Denmark (a country with high genomic sequencing capacity) given its current spread of the variants?

Results

Question 1: What are the Variants of Concern thus far? What are some Variants Under Investigation thus far?

Table 1 highlights several SARS-CoV-2 variants that are raising concerns among the scientific community at the time of this report. These do not reflect all SARS-CoV-2 variants that are circulating globally.

- We refer to **Variants of Concern** (VoCs) as variants with mutations in the genomic sequence that may have clinical implications, with scientific evidence (available at the time of this report) to support this. The quality of evidence varies and further research is underway, which BlueDot continues to monitor.
- We refer to **Variants Under Investigation** (VUIs, previously referred to as **Potential Variants of Concern** in the first Focus Report on Variants) as emerging variants with mutations in the genomic sequence that may have clinical implications, though supportive data is not currently available.

The three existing Variants of Concern and Variants Under Investigation represent only a few of the thousands of SARS-CoV-2 variants that have emerged since the pandemic began. As variants are differentiated by the subset of mutations they carry, a telling characteristic of these variants are the one or multiple common mutations shared by a few VoCs and VUIs. It is important to remember that mutations in the SARS-CoV-2 virus may: 1) have a neutral, 2) advantageous, or 3) deleterious effect on the virus' ability to reproduce, spread, or evade immune responses. From a public health standpoint, it is useful to follow newly emerging mutations and the fitness of new variants containing those mutations, particularly variants with mutations that may be advantageous to the virus. In **Table 2**, we highlight some of the most common mutations that confer or may confer (i.e., insufficient evidence to prove) an advantage. Several of these mutations have been identified in the VoCs recognized to date and noted in VUIs being identified. However, it is important to note that the potential clinical implications have been based on experimental laboratory studies of the individual mutations. To truly understand the clinical impact of a given variant, all mutations in a variant need to be studied together to assess how their interactions affect the variant's function and potential clinical implications.

Table 1. A summary of the Variants of Concern and Variants Under Investigation included in this report.

Variant of Concern (VoC)			
Name of Variant	Country of earliest specimen sequenced	Date of earliest specimen sequenced	Clinical significance*
B.1.1.7 (aka. 20B/501Y.V1, VOC 202012/01)	United Kingdom	September 20, 2020	Increased transmissibility of virus Increased severity of COVID-19
B.1.351 (aka. 20C/501Y.V2)	South Africa	October 8, 2020	Increased transmissibility of virus Reduced vaccine efficacy (preliminary) Increased evasion of natural immunity (preliminary)
P.1 (aka. 20J/501Y.V3)	Brazil – Amazonas State (first reported among 4 travellers from this location arriving in Japan)	December 4, 2020 (in Brazil) January 2, 2021 (in Japan, travel-associated)	Potential increased transmissibility of virus Potential reduced vaccine effectiveness
Variants Under Investigation (VUI)			
Name of Variant	Country of earliest specimen sequenced	Date of earliest specimen sequenced	Clinical significance*
B.1.1.207	Nigeria - Osun State	Detected in two samples collected on August 3, 2020 and October 9, 2020	Potential for increased transmissibility as it has the N501Y mutation, but no evidence of increased transmission in Nigeria (as of Dec 2020)
COH.20G/501Y	U.S. (Columbus, Ohio)	Sometime between December 31st, 2020 - January 6th, 2021	Potential for increased transmissibility as it has the N501Y mutation
A.23.1	Uganda – Samaru/Kitgum prison cluster	August 2020	Insufficient evidence – it has been flagged as a VUI as it has the E484K mutation (potentially helps the virus evade antibodies) and the P681R mutation (affects the spike protein and similar to the P681H mutation in the B.1.1.7 variant)
B.1.525 (aka. VUI-202102/03)	Nigeria	December 15, 2020	Insufficient evidence – it has been flagged as a VUI as it has the E484K mutation (potentially helps the virus evade antibodies)
B.1.526	USA - New York State	November 2020, mid-February 2021	Insufficient evidence – it has been flagged as a VUI as it has the E484K mutation (potentially helps the virus evade antibodies) and S477N mutation (potentially increases transmissibility)
B.1427/B1.429 (aka. CAL.20C)	USA – California	July 2020	Insufficient evidence – it has been flagged as a VUI as it has the L452R mutation which affects the viral spike protein which may improve virus binding to human cells. It also has become the new dominant variant in California.

B.1.1.7 with E484K	Independently emerged in: USA – Oregon State (in 1 patient) United Kingdom (a cluster)	March 5, 2021 (in USA) Detected in sequences processed by January 26, 2021 (in England)	It has been flagged as VUI as it also has the E484K mutation (potentially helps the virus evade antibodies).

*Based on current evidence at the time of this report. The term "potential" is used to indicate items that currently have a lack of supportive data at the time of this report but have a hypothesized clinical significance.

Table 2. An overview of several mutations identified in Variants of Concern (VoC) and Variants Under Investigation (VUI) included in this report. **Note:** For most of these mutations, the potential clinical implications have been based on experimental laboratory studies of the individual mutations. To truly understand the clinical impact of a given variant that carries a given mutation, all mutations in a variant need to be studied together to assess how their interactions affect the variant's function and potential clinical impact. Currently, the evidence is still emerging.

Identified Mutations under VOC and VUI		
Name of Lineage(s) that carries this mutation	**Mutation**	**Significance (based on early evidence)**
Variant of Concern: B.1.1.7 B.1.351 P.1	N501Y	Helps the virus bind more tightly to human cells as this mutation changes the shape of the SARS-CoV-2 spike protein[1] - serves as the biological basis to explain why variants with this mutation may have increased transmissibility
Variant of Concern: B.1.351 P.1 **Variant Under Investigation:** B.1.525 B.1.526 B.1.1.7 with E484K	E484K	May help the virus better evade certain antibodies as this mutation changes the shape of the SARS-CoV-2 spike protein which is a target area for some treatments/vaccines[1,2]
Variant of Concern: B.1.351 P.1	K417N (in B.1351 variant), K417T (in P.1 variant)	Insufficient evidence at this time - it is plausible that this mutation helps the virus bind more tightly to human cells as it affects the SARS-CoV-2 spike protein
Variant Under Investigation: CAL.20c	L452R	Insufficient evidence at this time - it is plausible that this mutation helps the virus bind more tightly to human cells as it affects the SARS-CoV-2 spike protein. The L452R mutation has recently been detected in California, especially in the Los Angeles area.

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[1] Yi C, Sun X, Ye J, Ding L, Liu M, Yang Z, Lu X, Zhang Y, Ma L, Gu W, Qu A. Key residues of the receptor binding motif in the spike protein of SARS-CoV-2 that interact with ACE2 and neutralizing antibodies. Cellular & molecular immunology. 2020 Jun;17(6):621-30.

[2] Bamlanivimab does not neutralize two SARS-CoV-2 variants carrying E484K in vitro | medRxiv

Question 2: Where have the Variants of Concern been reported globally?

Global Spread of the B.1.1.7 variant (initially detected in the United Kingdom)

As of March 15, 2021, 101 countries have detected the B.1.1.7 variant based on sequences uploaded to GISAID, an open-data platform.[3] Among the 88 countries whose transmission type of this variant is currently monitored (**Figure 1**),

- Thirty-six countries have only reported cases that are travel-related. These locations must continue to be vigilant in screening, testing, isolating infected travellers and tracing their contacts to mitigate transmission into the community, as well as enhancing genomic surveillance among community cases.
- Forty countries have also reported local transmission. Many of these countries are in Europe where reports suggest that the B.1.1.7 has become or is growing to become the dominant variant in circulation. These countries and others with an effective reproduction number >1 are at high risk of rapidly accelerating number of new COVID-19 cases.
- The type of transmission is unspecified for twelve countries that have reported this variant.

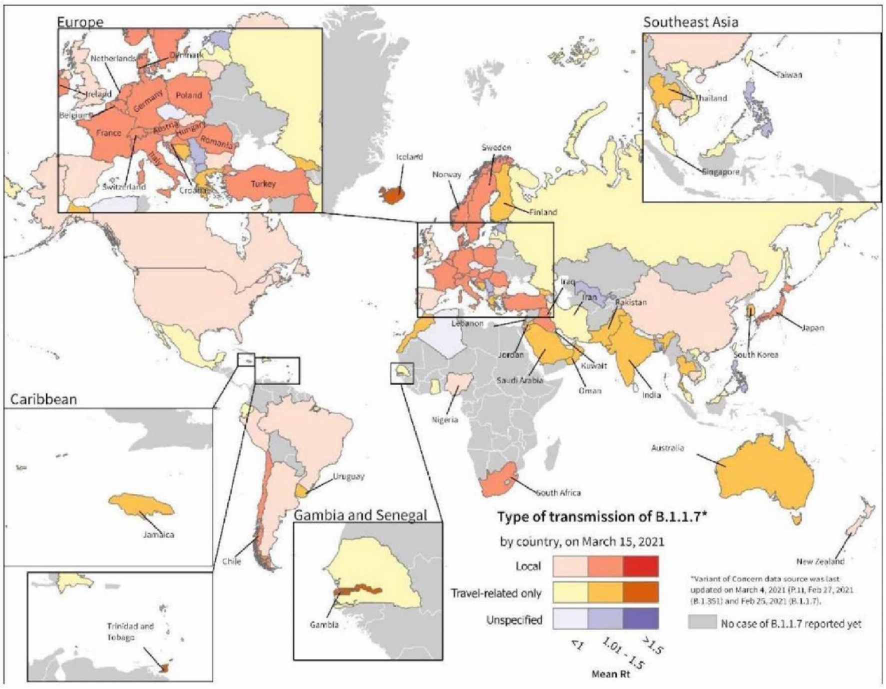

Figure 1. Countries that have reported at least one case of B.1.1.7 (travel-related or locally acquired or unspecified type of transmission) and the estimate of the country's effective reproduction number (R_t) of COVID-19 as of March 15, 2021. Data sources: Transmission type - https://cov-lineages.org/global_report_B.1.1.7.html, Mean R_t - BlueDot COVID-19 Data Suite

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[3] Data from GISAID, presented on https://outbreak.info/situation-reports

Global spread of the B.1.351 variant (initially detected in South Africa)

As of March 15, 2021, 55 countries have detected the B.1.351 variant based on sequences uploaded to GISAID.[4] Among the 48 countries whose transmission type of this variant is monitored (**Figure 2**),

- Twenty-one countries have only reported cases that are travel-related. These locations must continue to be vigilant in screening, testing, isolating infected travellers and tracing their contacts to mitigate transmission into the community.
- Twenty-three countries have also reported local transmission. As preliminary evidence suggests that the B.1.351 VoC may be better at evading antibodies (i.e., potential implication for reduced efficacy of COVID-19 vaccines), these countries should enact control measures and enhance public health messaging to mitigate the risk of viral spread and B.1.351 becoming the predominant variant circulating (already reported in South Africa[5] and Zambia[6]).
- The type of transmission is unspecified for Singapore, Thailand, Viet Nam, and Democratic Republic of Congo.

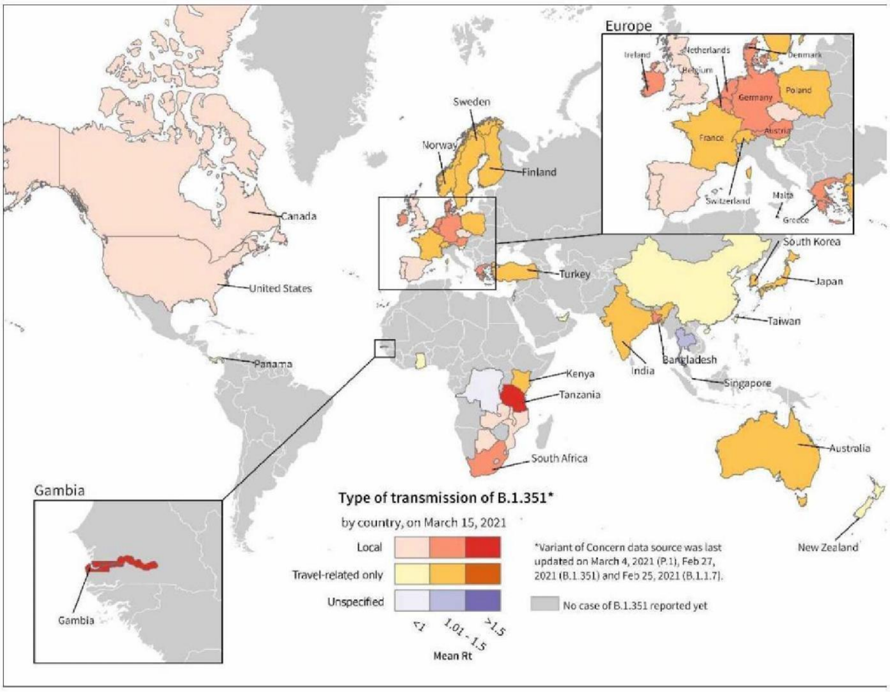

Figure 2. Countries that have reported at least one case of B.1.351 (travel-related or locally-acquired or unknown type of transmission) and the country's effective reproduction number (R_t) of COVID-19 as of March 15, 2021. Data sources: Transmission type – https://cov-lineages.org/global_report_B.1.351.html, Mean R_t - BlueDot COVID-19 Data Suite

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[4] Data from GISAID, presented on https://outbreak.info/situation-reports

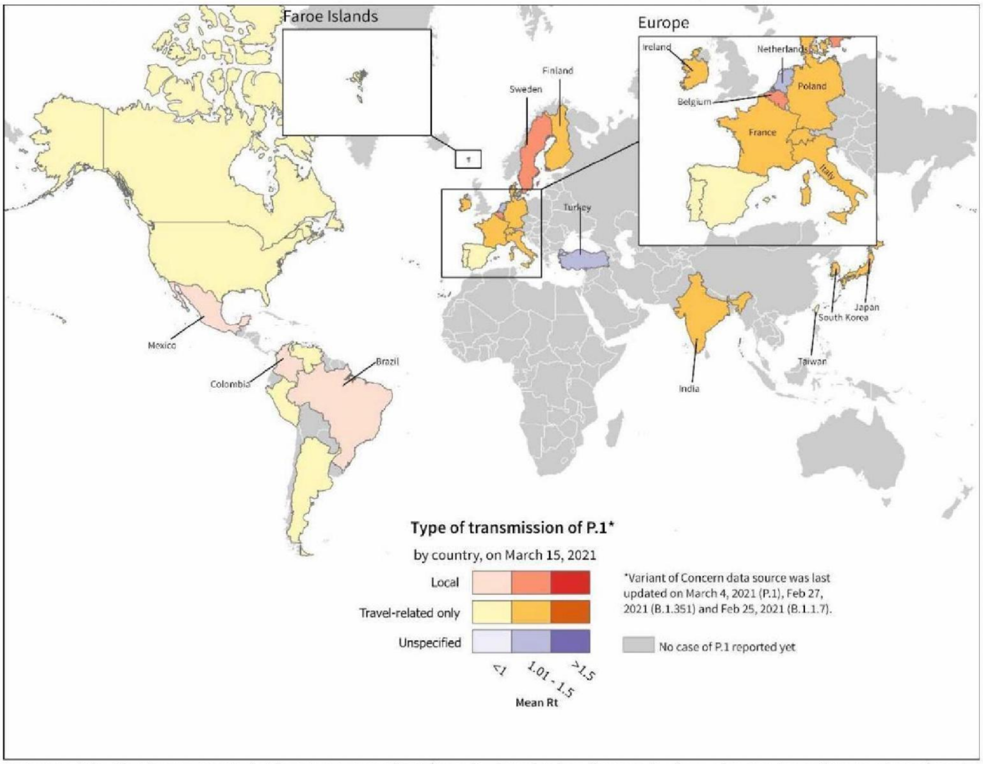
[5] https://www.ecdc.europa.eu/en/current-risk-assessment-novel-coronavirus-situation

[6] https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/scientific-brief-emerging-variants.html

Global spread of the P.1 variant (initially detected in Brazil)

As of March 15, 2021, 26 countries have detected the P.1 variant based on sequences uploaded to GISAID.[7] Among these 26 countries whose transmission type of this variant is currently monitored (**Figure 3**),

- Nineteen countries have only reported cases that are travel-related. These locations must remain vigilant in screening, testing, isolating travellers and tracing their contacts to mitigate transmission into the community.
- Five countries (Belgium, Brazil, Colombia, Mexico, and Sweden) have also reported local transmission. As preliminary evidence suggests that the P.1 may be better able to evade antibodies (i.e., potential implication for reduced efficacy of COVID-19 vaccines), control measures and appropriate public health messaging are needed to prevent further viral spread.
- The type of transmission is unspecified for the Netherlands and Turkey.



*Variant of Concern data source was last updated on March 4, 2021 (P.1), Feb 27, 2021 (B.1.351) and Feb 25, 2021 (B.1.1.7).

Figure 3. Countries that have reported at least one case of P.1 (travel-related or locally-acquired or unknown type of transmission) and the country's effective reproduction number (Rt) of COVID-19 as of March 15, 2021. Data sources: Transmission type - https://cov-lineages.org/global_report_B.1.351.html, Mean R_t - BlueDot COVID-19 Data Suite

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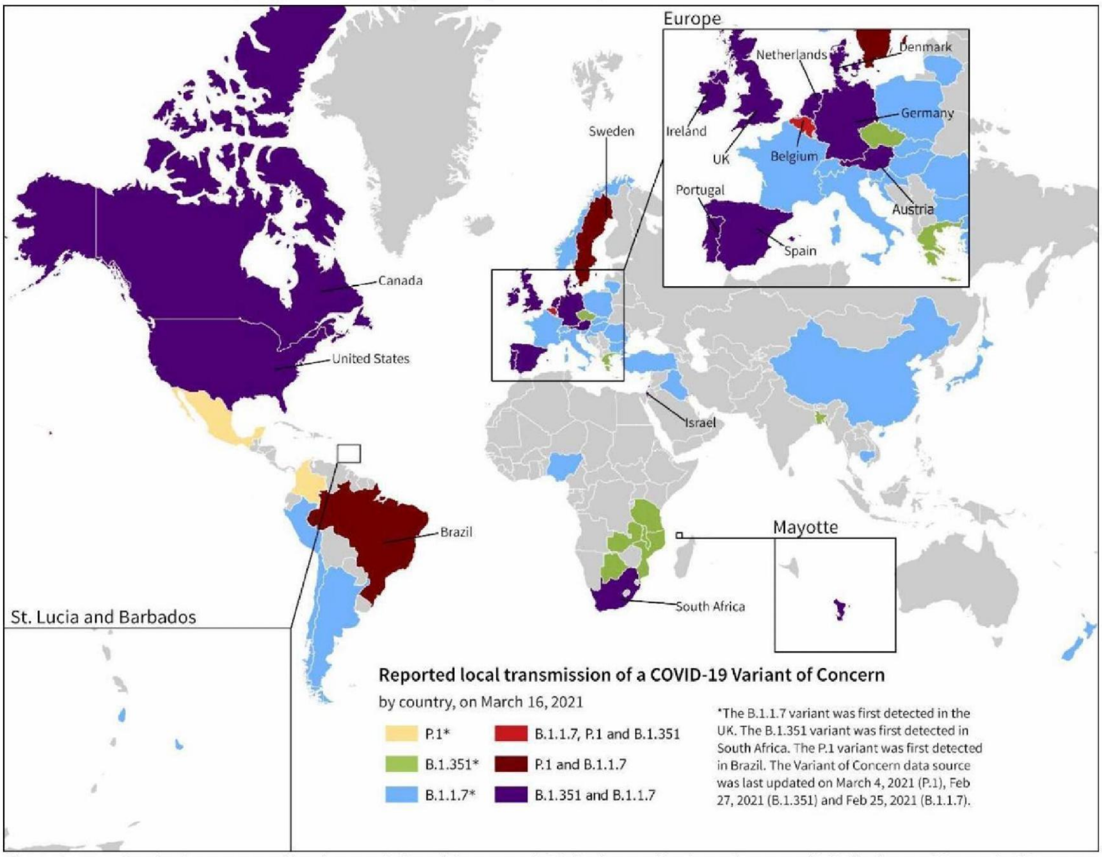
[7] Data from GISAID, presented on https://outbreak.info/situation-reports

Local transmission of the three VoCs, by country

In the prior **Figures 1-3** of this section, we presented all transmission types (i.e., local transmission, travel-related, or unspecified) for the subset of countries whose transmission type if currently monitored for each VoC on https://cov-lineages.org/. Here, **Figure 4** only depicts the countries/territories that have reported local transmission (i.e., cases reported with no travel history or links to travel) of at least one of the VoCs: B.1.1.7, B.1.351, or P.1. The data in this figure, indicating the status of local transmission of each VoC by country/territory, is also presented in **Table A1**.

As of March 16, 2021, the 13 countries that have reported local transmission of both the B.1.1.7 and B.1.351 variant are: Austria, Canada, Germany, Denmark, Spain, United Kingdom, Ireland, Israel, Netherlands, Portugal, United States, French overseas territory of Mayotte, and South Africa.

- As of March 16, Brazil and Sweden have reported local transmission of both the B.1.1.7 and P.1 variants.
- As of March 16, Belgium is the only country that has reported local transmission of all three VoCs.



Reported local transmission of a COVID-19 Variant of Concern

by country, on March 16, 2021

*The B.1.1.7 variant was first detected in the UK. The B.1.351 variant was first detected in South Africa. The P.1 variant was first detected in Brazil. The Variant of Concern data source was last updated on March 4, 2021 (P.1), Feb 27, 2021 (B.1.351) and Feb 25, 2021 (B.1.1.7).

Figure 4. Countries that have reported local transmission of the B.1.1.7 (initially detected in the U.K), B.1.351 (initially detected in South Africa, or P.1. variant (initially detected in travellers from Brazil). Data source: https://cov-lineages.org/global_report.html **Note:** Due to limitations in data collection, there may be some countries that have reported local transmission but updates to the data have yet to be made.

Question 3: What does the scientific evidence say about the clinical impact of the B.1.1.7, B.1.351, and P.1 variants?

Key results

What we know so far:

- B.1.1.7 is more transmissible and likely causes increased severity of COVID-19 (i.e., hospitalizations, deaths).
- B.1351 is likely better at evading vaccine-acquired immunity (in other words, reduced vaccine efficacy) and natural immunity (i.e., potential for re-infection).

What we do not know (based on insufficient evidence at this time):

- Whether B.1.351 and P.1 are more transmissible (given biological plausibility) and/or causes increased severity of COVID-19.
- Whether P.1 is better at evading vaccine-acquired immunity (i.e., reduced vaccine efficacy) and/or natural immunity.

Table 3 summarizes the current evidence on the three VoCs are based on risk assessments published by Public Health England (PHE)[8][9], European Centre for Disease Prevention and Control (eCDC)[10], Public Health Ontario (PHO)[11] and our own literature review. It is important to note that the evidence is continuing to emerge. Many of the studies on vaccine efficacy against the VoCs and whether the VoCs can escape natural immunity are based on laboratory studies. At this time, it is difficult to understand how this may translate to the clinical impact of the VoCs in this regard.

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[8] Public Health England - Technical Brief 5

[9] Public Health England - Technical Brief 6

[10] European Centre for Disease Prevention and Control eCDC - February 15th, 2021 Rapid Risk Assessment: SARS-CoV-2 - increased circulation of variants of concern and vaccine rollout in the EU/EEA, 14th update

[11] Public Health Ontario - Rapid Review: COVID-19 B.1.351 (501Y.V2) Variant of Concern

Table 3. A summary of the current evidence on the transmissibility, severity of disease, vaccine efficacy, and escape from natural immunity for each of the three Variants of Concern.

Summary of current evidence				
Variant of Concern	**Transmissibility**	**Severity of disease**	**Vaccine efficacy**	**Escape from Natural Immunity**
B.1.1.7	↑ Evidence from a variety of studies (modelling, laboratory, epidemiological) suggests increased transmissibility.[A]	↑ Multiple updated and new epidemiological analyses suggest increased risk of hospitalization and death.[B]	↔ (preliminary) Early evidence (not yet peer-reviewed) suggests that B.1.1.7 is not strongly associated with escape from vaccine-acquired immunity from Pfizer/BioNTech, Moderna, and AstraZeneca vaccines.[C]	↔ (preliminary) Early evidence (not yet peer-reviewed) suggests that B.1.1.7 is not strongly associated with escape from natural immunity.[D]
B.1.351	? Insufficient evidence currently from laboratory/ epidemiological studies to confirm. However, increased transmissibility is plausible given that this VoC contains N501Y and E484K mutations that have been implicated in increased binding to the angiotensin converting enzyme-2 (ACE-2) receptor. A recent unpublished modelling study estimates that B.1.351 is 50% more transmissible that previously circulating variants.[E]	? Insufficient evidence currently.	↓ (preliminary) Early evidence suggests that AstraZeneca/Oxford University and Johnson & Johnson vaccine may have a reduced efficacy, while reduction of antibodies generated was observed for the Pfzier/BioNTech, Moderna vaccine, and Sinopharm.[F]	↑ (preliminary) Early evidence from an in-vitro study and multiple pre-print studies suggests that the B.1.351 can evade natural immunity, thus has the potential for re-infection.[G]
P.1	? Insufficient evidence currently from laboratory/epidemiological studies to confirm. However, increased transmissibility is plausible given that this VoC contains N501Y and E484K mutations that have been implicated in increased ACE-2 receptor binding. A recent, unpublished modelling study estimates that P.1 is 1.4 - 2.2 times more transmissibility that non-P.1 variants.[H]	? Insufficient evidence currently.	? Insufficient evidence currently. However, one lab study found that serum from individuals fully vaccinated with the Pfizer/BioNTech vaccine was able to comparably neutralize recombinant virus representing P.1 and B.1.1.7 .[I]	? Insufficient evidence currently. However, this VoC contains the E454K mutation, which studies noted may be more resistant to neutralizing antibodies (as seen for the B.1351 VoC that also has this mutation).[J]

A. **Transmissibility of B.1.1.7** - Public Health England - Technical Brief 5, Davies et al. (2021)

B. **Severity of Disease associated with B.1.1.7** - The evidence supporting increased severity of disease has been strengthened by the most recent update from England's NERVTAG Group. In their Feb 12, 2021 update, they concluded that ***"it is likely that infection with VOC [Variant Of Concern] B.1.1.7 is associated with an increased risk of hospitalisation and death compared to infection with non-VOC viruses"*** based on their assessment of multiple, independent analyses of data from England that were updated or added since their first report (summarized in our previous Focus Report on Variants). Furthermore, a pre-print observational cohort study using data from Denmark's national COVID-19 surveillance system also reported that B.1.1.7 was associated with increased risk of hospitalization.

C. **Vaccine Efficacy against B.1.1.7** - Most emerging studies suggest that there is not significant difference in efficacy of the Pfizer/BioNTech, Moderna, AstraZeneca/Oxford University vaccines against the B.1.1.7 variant compared to existing predominant variants (summarized in our previous Focus Report on Vaccines).
D. **Immune escape of B1.1.7** – eCDC Rapid Risk Assessment, Public Health England – Technical Briefing 6
E. **Transmissibility of B.1.351** - Unpublished modelling study by Pearson et al. (2021) currently under review
F. **Vaccine efficacy against B.1351** - Summarized in our previous Focus Report on Vaccines
G. **Escape from natural immunity by B.1351** - Recently published in-vitro study by Wibmer et al. (2021), pre-print studies highlighted by eCDC, PHO, and PHE. As aptly summarized by PHE, *"Multiple studies with pseudovirus and live virus neutralization assays indicate a significant loss of antibody binding and neutralization to B.1.351..."*
H. **Transmissibility of P.1** - Unpublished modelling study by Faria et al. (2021)
I. **Vaccine efficacy against P.1** - Liu et al. (2021)
J. **Escape from natural immunity by P.1** - Preprint by Greaney et al. (2020)

Question 4: What is the COVID-19 outlook in Denmark (a country with high genomic sequencing capacity) given its current spread of the variants?

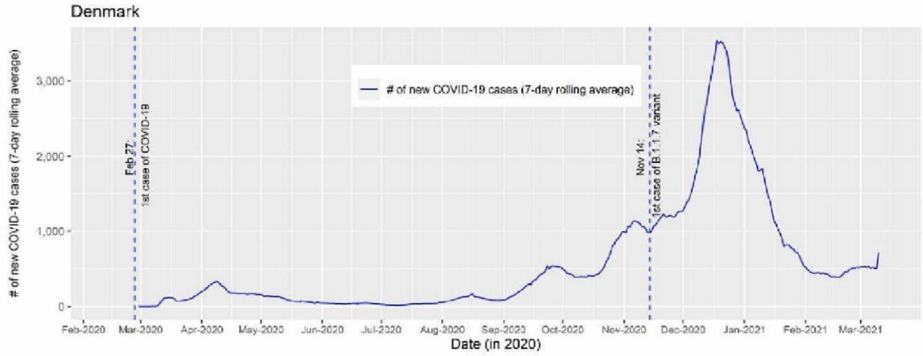
Key results

Speculation of Future Risk: Although Denmark's COVID-19 outbreak was stable throughout February 2021 (with early signs of an increase), the local transmission of the B.1.1.7 variant and the rapid increase in the proportion of sequenced cases identified as this variant are causes for concern. Currently, local transmission of B.1.351 remains at a low level while local transmission of P.1 has not been reported. Thus, public health control measures must be maintained to prevent the further spread of SARS-CoV-2 in light of the low percentage of population having been vaccinated and evidence suggesting that the B.1.1.7 variant is associated with increased transmissibility.

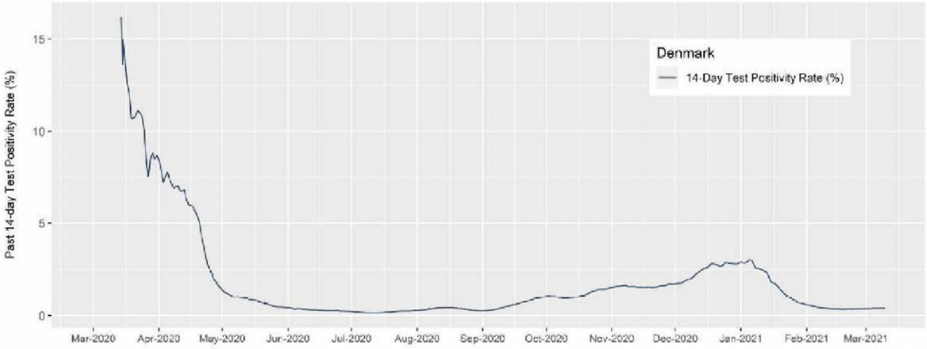
Promisingly, quantitative indicators suggest that there is currently good SARS-CoV-2 testing capacity, an increasing trend in daily vaccinations administered, and the majority of the population is willing to receive a vaccine. Furthermore, scientific evidence suggests that the vaccine brands currently administered do not have appreciable decreased efficacy against B.1.1.7.

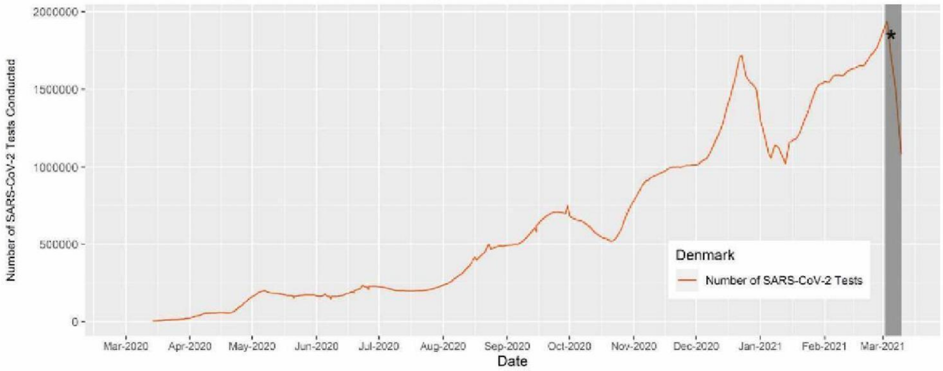
Change in size of COVID-19 Outbreak

- 7-day rolling average in daily new cases has fallen since its peak in late Dec 2020. It remained stable through February 2021, but recently showed early signs of an increase (714 new cases per day, as of March 10 2021).



- 7-day average in test positivity is currently **stable and relatively low** (i.e., <5%), amidst a generally increasing trend in number of tests conducted. Thus, these indicators suggest that Denmark is testing to a sufficient level to capture the extent of outbreak and control spread.





*The grey bar indicates that the most recent data may not be fully completed due to reporting delays.

Distribution of the Variants of Concern [12,13,14]

- As of March 9, 2021, local transmission of the B.1.1.7 variant has been reported in Denmark. Proportion of specimens identified as B.1.1.7 has been **increasing week-over-week** since it was first detected in the country. As of the week of February 28 - March 6, 2021 (i.e., Week 09), the proportion of SARS-CoV-2 cases with sequenced genomes that were identified B.1.1.7 was 84.8%.

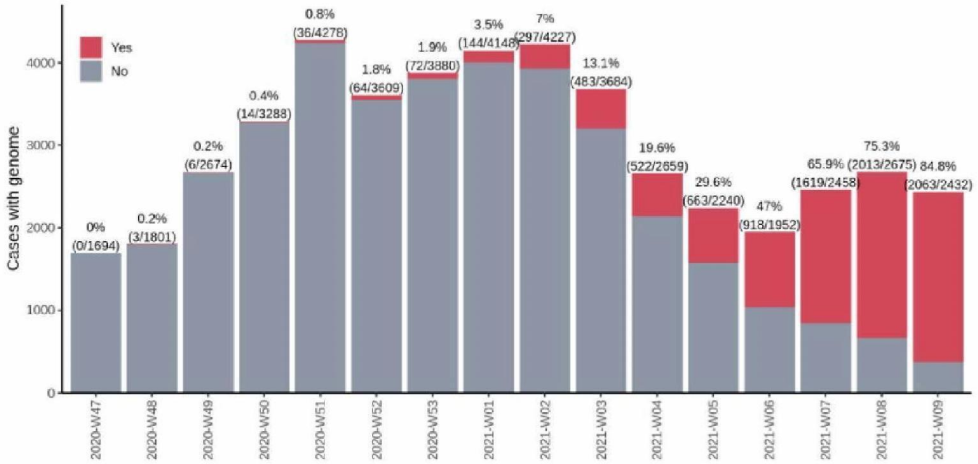


Figure created by the Danish COVID-19 Genome Consortium[7] using data from Statens Serum Institute

- As of March 9, 2021, local transmission of the **B.1.351** has been reported in Denmark since February 17, 2021. The proportion of specimens identified as B.1.351 **remains very low**. As of the week of February 26 - March 6 2021, 0.5% of positive SARS-CoV-2 cases with sequenced genomes have been identified as the B.1351. This weekly proportion has not exceeded 0.5% since the first case of B.1351 was detected.

- P.1 was first detected in Denmark on March 3, 2021. As of March 7, 2021, two cases of P.1 have been detected. At this time, insufficient time has elapsed to explore the temporal trend.

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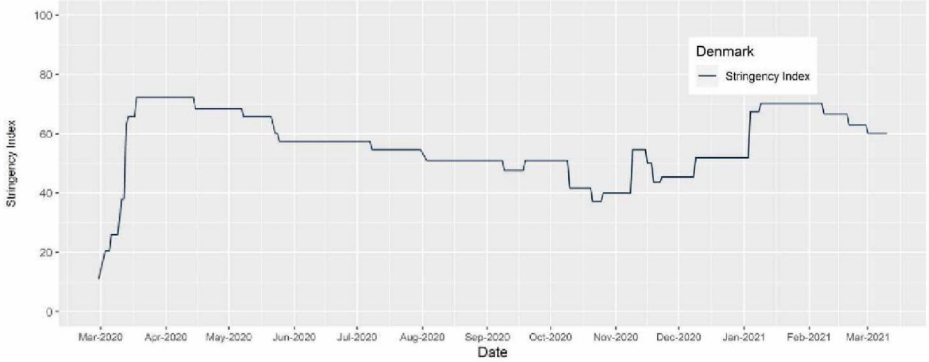
[12] https://cov-lineages.org/global_report_B.1.1.7.html
[13] https://www.covid19genomics.dk/statistics
[14] https://files.ssi.dk/covid19/virusvarianter/status/status-virusvarianter-17022021-2a9s

Change in COVID-19 Control Policies

Policies gradually relaxed throughout February and remain **relatively stringent**. In light of the rising prevalence and dominance of the B.1.1.7 VoC, Denmark is maintaining the current local control measures and travel/border restrictions until at least April 5, 2021.



Local Control Measures[15]:

Since January 6, health authorities tightened restrictions as a measure to curb the spread. As of March 11 2021,

- Public gatherings were limited to five people, a decrease from the previously allowed 10 people.
- Funerals may not exceed 50 attendees.
- Protective face masks are mandatory in all indoor public spaces, public transportation and domestic social-distancing mandates remain in force.
- Bars, clubs, cafes, restaurants, libraries, museums, theatres and concert venues, as well as gyms and fitness centers are closed. However, outdoor cultural institutions (e.g., gardens, zoos) are open to visitors who can provide proof of a negative COVID-19 test taken within the last 72 hours.
- Alcohol sales must cease at 10 p.m. daily.
- Individuals are encouraged to work from home where possible. Industry-specific operating requirements are also still in place for certain sectors.
- There are no restrictions on travel within the country.
- There is region-specific re-opening of schools.

Travel/Border Restrictions[16]:

As of March 11, 2021,

- Non-resident international travellers must have a justifiable purpose, such as work, study, or family reasons to enter Denmark. All non-resident international travellers arriving by air must present a negative COVID-19 test result upon arrival. The test must have been taken no more than 24 hours before boarding their flights; children under 12 are exempt from this requirement.
- Danish nationals and residents are not required to present a negative COVID-19 test result upon arrival. However, all passengers must present proof of a negative COVID-19 test result taken no more than 24 hours earlier before they are permitted to board flights to Denmark.
- Passengers who have previously been infected with COVID-19, and therefore may not achieve a negative result in a COVID-19 test, must present proof of a positive COVID-19 test result that is more than 14 days old.
- Exceptions are made for flights from Greenland and the Faroe Islands.
- Authorities continue to recommend against all travel abroad.

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[15] https://en.coronasmitte.dk/rules-and-regulations/national-measures

[16] https://en.coronasmitte.dk/rules-and-regulations/entry-into-denmark/regarding-persons-travelling-to-denmark-by-air

Vaccination Rate

Vaccine manufacturers: Moderna, Oxford/AstraZeneca*, Pfizer/BioNTech

*As of March 11 2021, the Danish Health Authority has stopped the administration of the AstraZeneca/Oxford vaccine for 14 days as a precautionary measure due to an unconfirmed link between the vaccine and development of severe blood clots.[17] Investigations by drug regulatory authorities are currently underway.

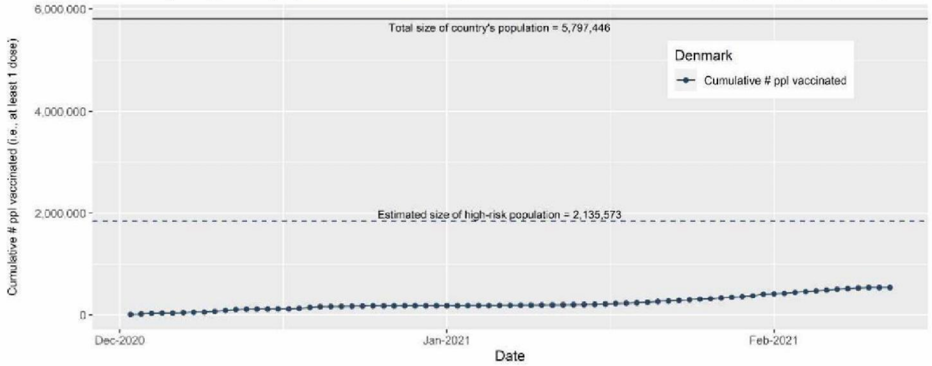
Timeline to Vaccination: Denmark's vaccination timeline will **be affected by whether the AstraZeneca/Oxford vaccine may be administered**, pending investigations by the drug regulatory authorities. If the AstraZeneca/Oxford vaccine is deemed unsafe and removed, the country's population ≥16 years old is expected to be eligible to receive a vaccine by the second week of July 2021.[11] If the AstraZeneca/Oxford vaccine is deemed safe, this timeline will be earlier.

% of country's population vaccinated, as of March 11, 2021: **9.48%**

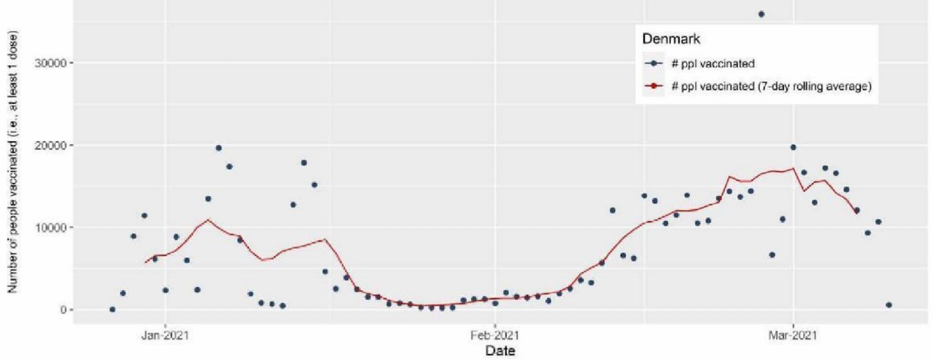
Population Eligible to receive vaccination, as of March 11, 2021: Key workers, elderly, clinically vulnerable

- As the eligible population in Denmark's vaccination campaign has consisted of at least two of the three groups listed above, we assume that all vaccinations have been among Denmark's high-risk population.

Estimated % country's high-risk population vaccinated, as of March 11, 2021 = **27.1%** (549,062/2,135,573[18])



- The **7-day rolling average number of daily people vaccinated** is increasing. As of March 7 2021, the 7-day rolling average number of daily individuals who receive a vaccination is 11,587 (i.e., 0.2% of country's population).



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[17] https://www.ssi.dk/aktuelt/nyheder/2021/vaccinationer-med-astrazeneca-saettes-paa-pause-indtil-videre

[18] Size of high-risk population (i.e., ≥1 health condition that increases risk of severe disease or ≥65 yrs) based on estimated calculated by Clark et al. (2020).

Vaccine Hesitancy/General Risk Perception

An ongoing study is being conducted by Imperial College London and YouGov to understand population behaviour related to COVID-19.[19] This study surveys a nationally-representative sample of respondents in Denmark:

- As of the survey on February 24, 2021 – **82%** of respondents answered "**Yes**" to the question "*If a COVID-19 vaccine is available to you will you get it?*".
    - This is an increase compared to the 79% of respondents who answered similarly on the January 7, 2021 survey administered shortly after Denmark began administering vaccines.

- As of the survey on February 24, 2021, **65%** of respondents answered, "**Strongly Agree**" to a 5-point Likert scale question of "*To what extent do you agree or disagree that… if a COVID-19 vaccine were made available to me this week, I would definitely get it.*"
    - This was an increase from 59% of respondents who answered similarly on the January 7, 2021 survey disseminated shortly after Denmark began administering vaccines.

What does this mean? Assuming that these study results can be generalized to Denmark's population, the majority of Denmark's population (~80% or higher) has consistently been willing to receive a COVID-19 vaccine. Furthermore, the extent to which the population is immediately willing to receive a vaccine has increased since Denmark began administering vaccines. This suggests the country will be able to reach a high level of vaccine coverage of their population to control COVID-19 as supply improves.

Appendix

Table A1. Reported local transmission of at least one variant of concern, as of March 16, 2021, by country/territory. Countries/territories that have not reported local transmission of at least one variant of concern are not included. *Note:* We manually revised the data for Denmark to indicate that local transmission of the B.1.351 VoC was reported as of February 17, 2021 but not indicated by the data source.

Country/Territory	Local transmission of B.1.1.7 reported	Local transmission of B.1351 reported	Local transmission of P.1 reported
Argentina	Yes		
Austria	Yes	Yes	
Barbados	Yes		
Bangladesh		Yes	
Belgium	Yes	Yes	Yes
Bulgaria	Yes		
Brazil	Yes		Yes
Botswana		Yes	
Canada	Yes	Yes	
Switzerland	Yes		
Chile	Yes		
China	Yes		

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[19] Imperial College London and YouGov

Colombia			Yes
Czech Republic		Yes	
Germany	Yes	Yes	
Denmark	Yes*	Yes	
Spain	Yes	Yes	
France	Yes		
United Kingdom	Yes	Yes	
Gambia		Yes	
Greece		Yes	
Croatia	Yes		
Hungary	Yes		
Ireland	Yes	Yes	
Israel	Yes	Yes	
Iraq	Yes		
Italy	Yes		
Japan	Yes		
Cambodia	Yes		
St Lucia	Yes		
Lithuania	Yes		
Malawi		Yes	
Mexico			Yes
Mozambique		Yes	
Nigeria	Yes		
Netherlands	Yes	Yes	
Norway	Yes		
New Zealand	Yes		
Peru	Yes		
Poland	Yes		
Portugal	Yes	Yes	
Romania	Yes		
Sweden	Yes		Yes
Slovenia	Yes		
Slovakia	Yes		
Turkey	Yes		
Tanzania		Yes	
United States	Yes	Yes	
Mayotte	Yes	Yes	
South Africa	Yes	Yes	
Zambia		Yes	