Klachkova, Anastasiya (CSC/SCC)

From: Dunn Kathleen (NHQ-AC)
Sent: March 5, 2021 11:40 AM
To: Heurter Dan (ONT); Potvin Megan (NHQ-AC); Kom Emily (NHQ-AC); Varsaneux Olivia (NHQ-AC)
Cc: Ma Kristina (NHQ-AC); VanDalen Madison (NHQ-AC); Clement Chris (NHQ-AC)
Subject: RE: a couple of VoC resources
Attachments: UK Variant What we know so far.pdf

Here is info on the UK variant (Dec 2020), which is the more commonly circulated VoC at this time.

Previous attachment was specific to P1 (Brazil)

From: Dunn Kathleen (NHQ-AC)
Sent: March 5, 2021 9:57 AM
To: Heurter Dan (ONT) <Dan.Heurter@csc-scc.gc.ca>; Potvin Megan (NHQ-AC) <Megan.Potvin@CSC-SCC.GC.CA>; Kom Emily (NHQ-AC) <Emily.Kom@CSC-SCC.GC.CA>; Varsaneux Olivia (NHQ-AC) <Olivia.Varsaneux@CSC-SCC.GC.CA>
Cc: Ma Kristina (NHQ-AC) <Kristina.Ma@CSC-SCC.GC.CA>; VanDalen Madison (NHQ-AC) <Madison.VanDalen@CSC-SCC.GC.CA>; Clement Chris (NHQ-AC) <Chris.Clement@CSC-SCC.GC.CA>
Subject: a couple of VoC resources

Good morning Epi Investigation Team,

Sharing a couple of documents that may be of interest (mentioned on the call this morning)
The UK doc attached is from Barb – it is a nice summary of PHMs and mechanisms of transmission

Public Health Ontario has also released a number of new products.
From an IPC perspective, this is an important statement in the guidance.
"Commonly overlooked areas associated with substantial transmission risk include break rooms and other spaces where staff congregate to eat and drink."

The other place to consider is physical layout, any workflow or movement (people, equipment / things), ventilation, and overall compliance with measures
Appendix A of the interim IPC guidance summarizes key recommendations that may helpful; key measures are also clues to where breaches / risk of exposure & transmission may occur

- Screening, diagnosis & testing
- Transfer & Placement
- PPE (Note that ON has no changes to recommended PPE practices for VoC)
- Duration of precautions
- Environmental cleaning
- Outbreak management

The PHO doc also highlights a few more unanswered questions

key questions that must be answered to understand the potential impact of any new VOC:
• For each VOC, is the VOC associated with increased transmissibility?
• Do current diagnostic tests have sensitivity for detection of each of the VOC equivalent?

• Does infection with each of the VOC result in increased disease severity and higher case fatality as compared to infection?
• Does natural or vaccine-induced immunity to NVSC2 protect against infection and severe disease due to each VOC?

Link to docs:
https://www.publichealthontario.ca/en/diseases-and-conditions/infectious-diseases/respiratory-diseases/novel-coronavirus?_cldee=aXBhY290dGF3YXJlZ2lvbkBnbWFpbC5jb20%3d&recipientid=contact-ec2ca7d82b92e6119af70050569e0009-709061c2220940bf910534dd70b3464a&esid=61efedda-6078-eb11-976d-0050569e118f

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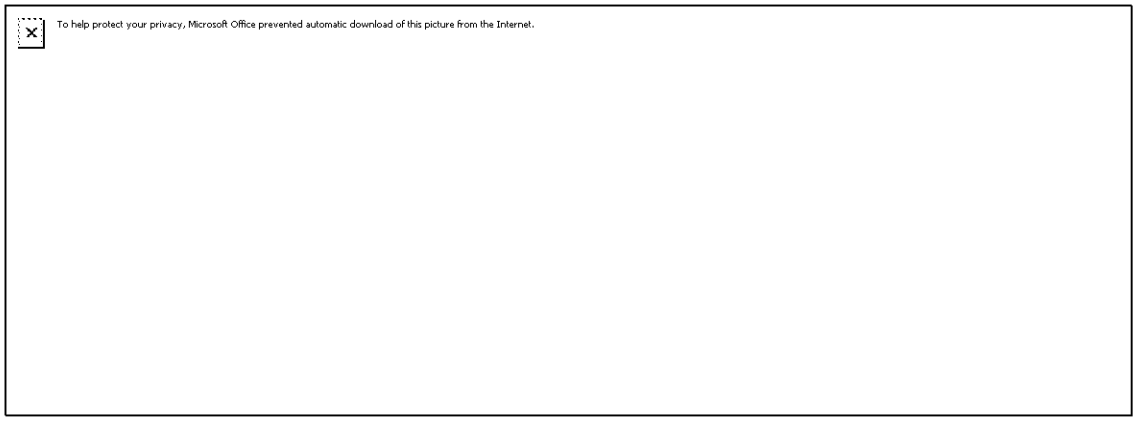
COVID-19 Variants of Concern (VOCs)



Public Health Ontario (PHO) is working with the Ministry of Health, the provincial testing network for COVID-19 and other lab, research and health care partners to test for and monitor COVID-19 variants of concern (VOCs) in Ontario.

About VOCs

- COVID-19 B.1.351 (501Y.V2) Variant of Concern
- COVID-19 P.1 Variant of Concern

Data and Surveillance

- VOC screening volumes and percent positivity at the provincial-level are now available in our COVID-19 Daily Epidemiological Summary
- Enhanced Epidemiological Summary: COVID-19 Variants of Concern in Ontario: December 1, 2020 to February 15, 2021: This new report provides a descriptive summary of COVID-19 VOC cases circulating in Ontario including laboratory data, case data and case characteristics. This report will be updated monthly.
- SARS-CoV-2 Variants of Concern: Results of Point Prevalence Study: This report provides results of a single day point prevalence study of SARS-CoV-2 VOCs, specifically SARS-CoV-2-positive samples from January 20, 2021 in Ontario that were submitted to PHO.

Public Health Measures and Re-opening

- Evidence on Public Health Measures Required for Rapid Control of Variants of Concern
- Using COVID-19 Data to Inform Reopening Decision-making in the Context of Variants of Concern
- Lockdown Duration and Re-opening including Considerations for COVID-19 Variants of Concern

Infection Prevention and Control

- Interim Guidance for Infection Prevention and Control of SARS-CoV-2 Variants of Concern for Health Care Settings

We are continuously producing resources as we learn more about VOCs. Please keep checking our Variants of Concern web page for our most up-to-date resources.

Public Health Ontario | Santé publique Ontario

SYNTHESIS

12/29/2020

COVID-19 UK Variant VOC-202012/01 – What We Know So Far

Introduction

PHO is actively monitoring, reviewing and assessing relevant information related to Coronavirus Disease 2019 (COVID-19). "What We Know So Far" documents are intended to provide a rapid review of the evidence related to a specific aspect or emerging issue related to COVID-19.

The development of these documents includes a systematic search of the published literature as well as scientific grey literature (e.g., ProMED, CIDRAP, Johns Hopkins Situation Reports) and media reports, where appropriate. Relevant results are reviewed and data extracted for synthesis. All "What We Know So Far" documents are reviewed by PHO subject-matter experts before posting.

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in these documents is only current as of the date of posting.

Key Findings

- A new variant of SARS-CoV-2, called **'VOC-202012/01' or lineage B.1.1.7**, was recently identified in the United Kingdom (UK).
- The variant was detected after the UK observed a rapid increase in COVID-19 notification rates since late September 2020, with an ongoing increase as of December 2020.
- Epidemiological findings and modelling data suggest that this strain may be more transmissible. Contact tracing and genomic sequencing data in the UK suggests that the secondary attack rate may be higher for cases with VOC-202012/01 compared to cases with other variants (15.1% vs 9.8%). Further laboratory-based investigations are underway to determine the impact of this strain on virulence and transmissibility.
- Early analyses suggests that there is **no increased risk for hospitalization, 28-day case fatality, or reinfection with the UK variant**.
- The UK variant contains a high number of genomic mutations; however, laboratory-based assays and Health Canada-approved rapid tests currently available for COVID-19 detection are still likely to detect the UK variant.
- To date, there is **no indication that the vaccines will be less effective** against this variant, although studies are ongoing.

- **As of December 29, 2020, six cases of the UK variant have been identified in Canada** (three in Ontario, one in British Columbia, one in Quebec, one in Alberta).

- Ongoing genomic surveillance efforts in Ontario will be important to identifying this and other new variants of SARS-CoV-2.

Background

A new variant of SARS-CoV-2, the virus that causes COVID-19, was identified in the United Kingdom (UK) in early December 2020, and is now reportedly spreading rapidly across the UK. Initially, a few cases were documented in a small number of other countries including Denmark (n=9), Belgium (n=4), Australia (n=1) and the Netherlands (n=1); however, as of December 29, 2020, cases have been identified in a least 14 different countries, including Canada.[1,2]

- The variant was initially named **'VUI-202012/01'** ("the first Variant Under Investigation in December 2020").[3,4] On December 18, 2020, public health authorities in the UK re-designated this as a Variant of Concern (VOC), and renamed it **'VOC-202012/01'**. The UK variant is also known as **lineage B.1.1.7**.

- The variant was identified as part of a genomics surveillance program in the UK, which was used to investigate increasing incidence of COVID-19 in Kent in early December 2020. Genomic epidemiological analyses identified cases from as early as September 2020.[1]

- The concern about the potential increased transmissibility of this variant has resulted in stricter public health measures in the UK with restriction on movement within and between more and less heavily affected areas.

- As of December 22, 2020, many countries around the world have imposed a travel ban on individuals arriving from the UK. On December 20, 2020, Canada also banned flights originating from the UK until at least January 6, 2021.[5]

- Current studies are underway to determine what impact this new variant may have on human health including, transmissibility, severity, diagnostic testing, and on vaccine effectiveness.

Epidemiology

Epidemiological data are so far limited to reports from the UK.

- Between September 20 (the earliest case identified retrospectively) and December 15, 2020, 1,623 cases of this variant have been identified in England, mostly in Kent and South East England.[4]

- Preliminary modelling results suggest a strong association between the presence of the new variant in the Kent/South East England region and an increasing incidence of COVID-19.[6,7]

- Transmission of the new variant has occurred in other regions of the UK, with 20 cases reported in Wales. In recent weeks, over 10% of UK SARS-CoV-2 sequences belong to the variant, with higher proportions observed in South East England.[1]

- The new variant has mostly been identified in individuals younger than 60 years of age; however, the increase of overall COVID-19 cases in England is also seen in this age group.[1]

- So far, enhanced transmissibility of this lineage has been suggested based on early epidemiological and modelling data and analysis of secondary attack rate originating from the UK; however, the scope is not yet known.[1,6-8]

- The investigations into the properties of the new variant are ongoing, and worse clinical outcomes or particularly affected groups have not been reported to date.

Genomic Features

SARS-CoV-2 mutations occur regularly with estimates suggesting that circulating lineages accumulate genetic changes (mutations) at a rate of about 1-2 mutations per month.[9] Most mutations are silent and do not result in any change to the amino acid sequence that code viral proteins (called **"**synonymous"). Some mutations do change the amino acid sequence and result in changes in viral proteins (called "non-synonymous"). Most lineages of SARS-CoV-2 show only a few mutations. However, the novel UK lineage carries a large number of mutations and therefore, is unusual in comparison to what is seen in the global virus genomic data available.

- The UK variant has 14 non-synonymous mutations, 6 synonymous mutations, 3 deletions.[10] This new variant has 29 nucleotide substitutions (changes in the RNA sequence) compared to the first described Wuhan strain. A list of non-synonymous mutations, as well as mutations resulting in shortened protein forms is provided in the Appendix.

- Key mutations in the UK variant occur in the sequence that encodes the 'spike' (or S) protein. The spike protein is the key protein on the viral surface involved with binding to the angiotensin-converting enzyme 2 (ACE2) cell surface receptor and initiating cell entry during infection. It is also a major target of the immune system. Spike mutations may alter virus infectivity, replication and pathogenicity, and can result in an altered host immune response. Three key mutations may change viral properties of SARS-CoV-2:

    - The N501Y mutation, occurs in the receptor binding domain (RBD) of the spike protein and may enhance the binding ability of the spike protein to human and mammalian ACE2 receptors.[11]

    - The deletions at positions 69-70 of the spike protein has been suggested to be involved in potential evasion of the human immune response.[12] It has also been associated with some false negative signals by molecular tests that target the spike gene. These assays often include multiple gene targets so overall detection failure is rare.[13]

    - The P681H mutation in the RBD of the spike protein has potential biological significance as it contributes to a key spike protein (S1/S2) cleavage site that facilitates respiratory cell entry, as well as transmission in animal models.[4,14]

- These mutations are not specific to the UK variant and have occurred spontaneously in other SARS-CoV-2 variants previously. Whether these mutations have significant impacts on transmissibility, infectivity, and clinical severity remains to be fully elucidated.

Potential Source of the UK Variant

Given the rapid emergence of this variant in a localized region of the UK and the high rate of mutations found in VOC-202012/01, it is unlikely that this variant emerged through gradual accumulation of mutations since SARS-CoV-2 usually mutates at a much slower rate per month globally as outlined above. Several hypotheses have been proposed for the potential source:

- Emergence from persistent infection in an immunocompromised host. This may result in accumulation of mutations at a higher rate and promote mutations that evade the immune system (immune escape).[1]
- Adaptation in an animal host and subsequent re-introduction into humans. This was seen with the emergence of the mink strain in Denmark and the Netherlands. There is currently no evidence of an epidemiological link to animals for the UK variant.[1]
- Emergence and circulation in other countries that do not routinely use whole genome sequencing for COVID-19 surveillance. Given the estimated mutation rate for SARS-CoV-2 and the fact that countries that experience high international travel (e.g., the UK) employ genomic surveillance, this explanation is less likely.[1]

Potential Health Impacts

Given the very recent emergence of this new variant and relatively restricted circulation, there is currently limited data on its impact on human health, laboratory testing, and vaccination.

Transmissibility and Disease Severity

- Initial reports of enhanced transmissibility were based on epidemiological data and preliminary modelling analysis, which showed a strong association between the rise in COVID-19 cases and the presence of VOC-202012/01 in the Kent/South East England region of the UK.
- Early modelling studies estimated that transmissibility may be increased by up to 70% with a potential to increase the reproductive number (R_t) by 0.39-0.93.[6,7,15]
- Preliminary findings from a retrospective matched cohort study using the contract tracing system and genomic sequencing in England between October 5 – December 6, 2020, found that the secondary attack rate for index cases who had the UK variant was 15.1% compared to 9.8% for index cases with other COVID-19 variants.[8]
- Clinical information about the UK variant is limited; however, there is currently no indication that infection with VOC-202012/01 is associated with increased disease severity or mortality. Preliminary analysis from a retrospective matched cohort study in the UK comparing VOC-202012/01 cases to non-VOC-202012/01 cases did not find a significant difference between hospitalization and 28-day case fatality.[8]
- It is worth noting that the majority of cases of VOC-202012/01 infection so far have occurred in individuals less than 60 years of age, an age group that is less likely to develop severe disease.[16]
- There is currently no evidence for increased risk of reinfection with the UK variant.[8]

Laboratory Testing

- Current diagnostic molecular assays used in Ontario will still be able to identify SARS-CoV-2 if the UK variant is present, although they cannot distinguish it from other SARS-CoV-2 lineages.
- PCR targets directed at the S gene may not detect the virus due to the mutations in this gene. Such assays in use in Ontario also include other gene targets, so they will still detect the UK variant.
- Gene sequencing or whole genome sequencing is required to identify the actual variant viruses.
- The rapid antigen tests currently licensed by Health Canada and in use in Ontario detect the SARS-CoV-2 nucleocapsid (N) protein; therefore, they are likely to be unaffected. Preliminary laboratory analysis indicates that that rapid antigen tests that target the N protein are able to detect the UK variant.[17]
- A number of serological assays that are used to detect COVID-19 antibodies use the S protein or a part of it as a target. Data are not yet available to determine whether antibodies against the UK variant may be missed by these antibody assays.
- Health Canada is currently working with other regulators and manufacturers of COVID-19 test devices to determine what, if any, impact this variant will have on the effectiveness of tests (December 21, 2020 email communication from Michelle Lefebvre, Health Canada to Public Health Ontario; unreferenced).

Vaccine Effectiveness

- How the various mutations in the UK variant impact the ability of the human immune system to recognize and develop antibodies to the virus (i.e. antigenicity) is currently being explored.
- COVID-19 vaccines that are currently available in Canada are based on the spike protein. There is not yet any information to determine whether vaccine-induced antibodies have a reduced ability to neutralize the UK variant.
- Ongoing vaccine effectiveness data coupled with genome sequencing will be important for assessing vaccine failure and breakthrough infections by the UK variant.

Provincial and National Response in Canada

As of December 29, 2020, six cases of VOC-202012/01 have been identified in Canada.

- Three cases have been identified in Ontario, one in British Columbia, one in Quebec, and one in Alberta. All cases report recent travel to the UK or recent contact with travellers from the UK.[18-21]
- So far, the UK variant has not been identified in cases prior to December 2020 in Ontario or Canada.

- Rapid screening of 4,446 epidemiologically representative SARS-CoV-2 genome sequences (~14% of all positives tested at PHO) generated by the PHO's genomic surveillance program did not identify this variant up to November 28, 2020.
- The variant has not been identified among additional genome sequences (N=2,200) originating from partner sequencing programs in Ontario.
- The variant has so far not been identified in genome sequences generated by the National Microbiology Laboratory (NML), or among genomic surveillance programs in Quebec, Alberta and British Columbia. These data represent ~5% of all sequences in Canada.

- To further assess potential introductions of the UK lineage and other variants, including a recently described South African variant, into Canada, the provincial and national response will prioritize screening of positive specimens recovered from returned travelers for SARS-CoV-2 variants of concern, retrospective to December 1, 2020, and on an ongoing basis.

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Appendix

Table 1. Genomic mutations leading to amino acid changes (non-synonymous) found in the UK variant, VOC-202012/01 (Lineage B.1.1.7)

Gene	Nucleotide substitution or deletion	Amino acid substitution or deletion
ORF1ab	C3267T	T1001I
	C5388A	A1708D
	T6954C	I2230T
	11288-11296 deletion	SGF 3675-3677 deletion
Spike	21765-21770 deletion	HV 69-70 deletion
	21991-21993 deletion	Y144 deletion
	A23063T	N501Y
	C23271A	A570D
	C23604A	P681H
	C23709T	T716I
	T24506G	S982A
	G24914C	D1118H
Orf8	C27972T	Q27stop
	G28048T	R52I
	A28111G	Y73C
N	28280 GAT->CTA	D3L
	C28977T	S235F

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). COVID-19 UK variant VOC-202012/01– what we know so far. Toronto, ON: Queen's Printer for Ontario; 2020.

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