

LABORATORY TRENDS



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A Report from the BCCDC Public Health Laboratory



Inside this Issue

COVID-19 SPECIAL

This issue summarizes how the BCCDC Public Health Laboratory addressed the COVID-19 pandemic, showcasing the efforts of dedicated staff for over 2 years.

SARS-COV-2 testing preparedness

Early on in the coronavirus disease 2019 (COVID-19) pandemic the Molecular Microbiology & Genomics Program at BCCDC Public Health Laboratory (PHL) was able to support the provincial response by rapidly developing and validating an assay to detect Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Led by Dr. Agatha Jassem, program head and Frankie Tsang, team lead for the Virology Laboratory, this assay was then adopted at the BCCDC PHL and further shared with validation materials with other regional laboratories. Since then, multiple new assays have been developed, refined^{1,2} and validated³ to support detection efforts and to

detect new variants of the virus. In February 2021, a quantitative polymerase chain reaction (PCR) assay detecting the N501Y spike gene mutation was deployed for surveillance purposes to provide rapid variant of concern (VOC) detection. Soon after, a dual assay detecting both N501Y and E484K mutations was made available as a presumptive indicator of B.1.1.7 (Alpha), B.1.351 (Beta) and P.1 (Gamma) VOCs. Nearly 50,000 samples were assessed for these mutations before whole genome sequencing was used routinely to determine the presence of VOCs. In November 2021, BCCDC PHL implemented a nucleic acid test that simultaneously detects SARS-CoV-2/influenza A/influenza B/RSV. This pentaplex assay not only streamlines testing by the Virology Laboratory but further provides enhanced respiratory surveillance for samples submitted to BCCDC PHL.



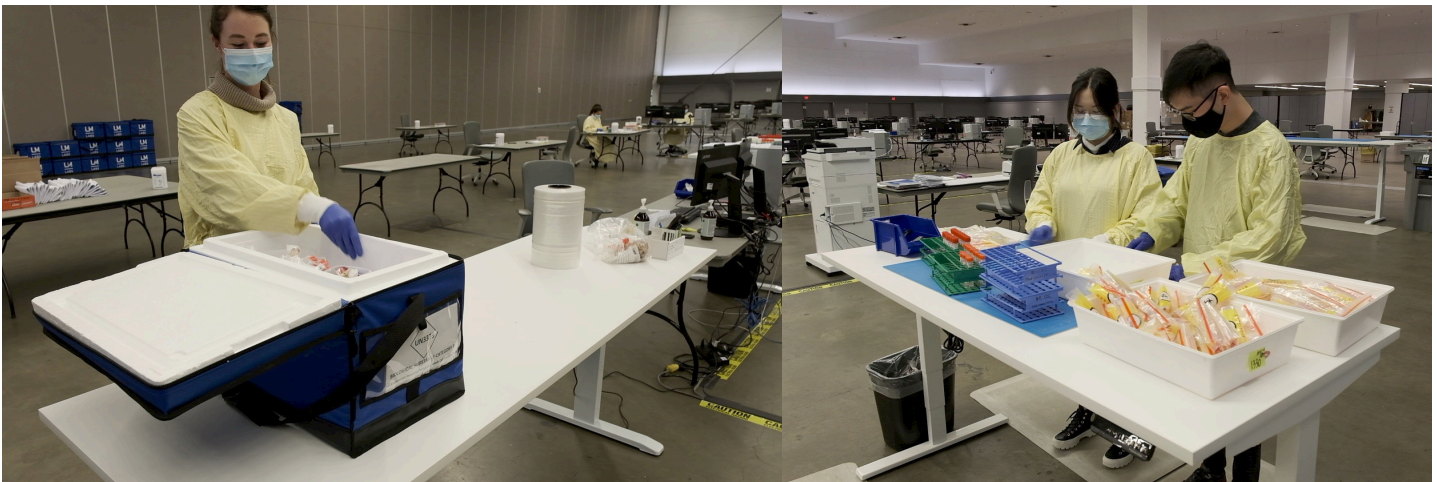
Left to Right: Drs. Agatha Jassem and Catherine Hogan
Photo credit: M. Donoghue.



Dr. Paul Levett with staff from the Virology Laboratory
Photo credit: M. Donoghue.

SARS-COV-2 testing preparedness

Capacity building also necessitated having an infrastructure capable of handling large volumes with rapid intake into laboratory information systems. This included, along with staff from health authorities across the Lower Mainland, reimagining accessioning and hiring enough auxiliary staff for a centralized location that was large enough to handle the surge of samples from across BC and Yukon. The Provincial Laboratory Medicine Services (PLMS) COVID-19 Processing (Central Accessioning) site located at the Vancouver Convention Centre was established to address this need. It was supported by a small team of various staff from across PHSA, Vancouver Coastal Health, Fraser Health and Providence Health Care sites, including BCCDC PHL's technical coordinator Andrew Balbirnie. It operated as a hub intaking SARS-CoV-2 and other respiratory samples. The site operated from October 2020 to March 2022 to support testing performed at Vancouver General Hospital, St Paul's Hospital, BC Children's Hospital and BC Women's Hospital + Health Centre Hospital and the BCCDC PHL. This centralized pre-analytical approach was complemented on the diagnostic side with the hiring of many additional technologists, laboratory assistants and clerks at BCCDC PHL, while directly linking the laboratory information systems in the province. With extended hours and technological improvements, at the height of the Dec 2021 Omicron variant wave, the site peaked intake of approximately 7000 samples a day and enabled BCCDC PHL itself to test more than 3,000 samples per day at its peak. This site also included intake of SARS-CoV-2 positive specimens to support Canada's leading SARS-CoV-2 variant screening and whole genome sequencing effort.



Accessioning staff handling respiratory samples at the Vancouver Convention Centre.

Alternative sample and test types for SARS-COV-2 testing

Saline gargle

The threat of nasopharyngeal swab shortages loomed globally in 2020. Coupled with a need to source a self collection alternative for individuals in remote locations it became clear that another sampling method was needed for COVID-19 testing. Working with the BC Children’s Hospital laboratory, the BCCDC PHL was able to validate the [use of saline gargles](#) as a less invasive, alternative sample type for testing. Saline gargle was initially deployed in the province as a nasopharyngeal swab substitute for school-aged children but soon after it was made available for the adult population as well. Since September 2020, this new sample collection method has been so successful it is now a routine offering at collection centres across the province, used in other provinces and was even [outside the country](#).



Rapid testing program

The BCCDC PHL is also at the forefront of assessing multiple SARS-CoV-2 rapid antigen and nucleic acid tests as alternate testing solutions. The five different rapid antigen test kits provided by the federal government each required evaluation through an analytical validation in the laboratory and a clinical validation at diverse sites before their deployment. This is done to ensure that the performance matches the manufacturer’s claims and isn’t affected by the different circulating variants.

Distribution of these kits involved the joint efforts of other Provincial Health Services Authority departments, such as Provincial Laboratory Medicine Services, BCCDC Knowledge Translation, BCCDC Chee Mamuk, PHSA Printing Services and PHSA Supply Chain which has now received and distributed over 24 million tests. These kits became essential in rural, remote, and indigenous communities, for various industries and for home use over the winter holiday season during the onset of the Omicron wave when testing sites were overwhelmed. A resource for rapid testing is available on the [BCCDC website](#) with the instructional video closing in on 50,000 views now. These kits are now a mainstay for COVID-19 diagnosis in the province.



BC Centre for Disease Control
An agency of the Provincial Health Services Authority

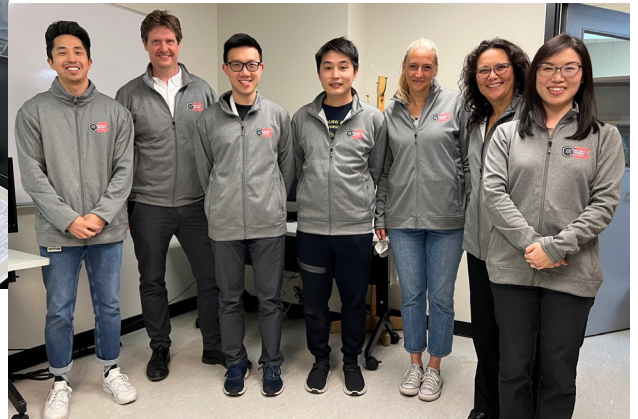


Whole Genome Sequencing

With support from the National Microbiology Laboratory, the COVID-19 pandemic has provided the opportunity to invest in a routine sequencing program at the BCCDC PHL. The SARS-CoV-2 sequencing program is headed by Dr. Natalie Prystajecky and Dr. Linda Hoang, also co-program heads of the Molecular Microbiology & Genomics Program. Staff in the Public Health Advanced Bacteriology & Mycology Laboratory form the core of the program, while the Molecular Microbiology & Genomics Program was and continues to be active in optimizing⁴ genomic methods, particularly in the face of emerging variants. The program is supported by a multitude of personnel such as the Genomics Liaison Technical Officers (GLTOs) Kim Macdonald, Dan Fornika and Kimia Kamelian and genomics specialist Sherrie Wang, who provide expertise in the analysis and management of genomics data. The GLTOs are Public Health Agency of Canada (PHAC) personnel who assist with co-ordination between the BCCDC PHL and PHAC, within the context of the Canadian Public Health Laboratory Network COVID Genomics Program

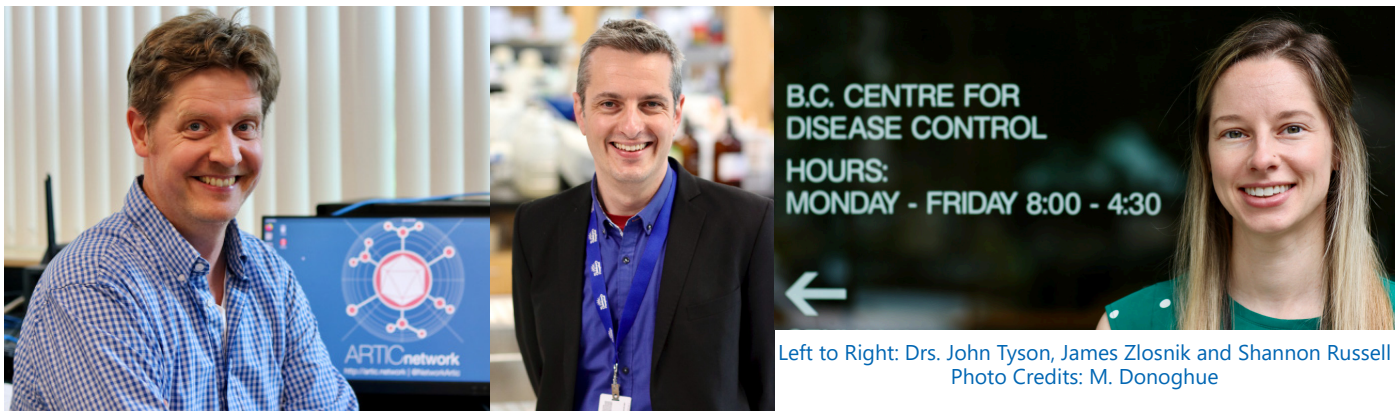


Staff in the Public Health Advanced Bacteriology & Mycology Laboratory.
Photo Credit: C. Howarth



Dr. Linda Hoang (second from right) with senior staff in the Public Health Advanced Bacteriology & Mycology Laboratory.
Photo Credit: M. G. Cheah

(CCGP). GLTOs support a lot of the automation required for these routine processes, developing the genomics analysis pipelines for SARS-CoV-2 and processes for rapid data sharing with both provincial and federal partners. Senior scientists Dr. John Tyson, Dr. Shannon Russell and Dr. James Zlosnik play central roles in monitoring emerging strains and variants and their impacts on sequencing operations and outbreak reporting, as well as ensuring that updates to software tools are integrated in the analysis pipelines.



Left to Right: Drs. John Tyson, James Zlosnik and Shannon Russell
Photo Credits: M. Donoghue

COVID-19 Surveillance

Serological Surveillance

COVID-19 antibodies are also being evaluated to monitor trends in certain populations of the province. A quantitative research platform for serosurveillance^{8,9} and vaccine immunogenicity studies has been validated for both serum and dried blood spot samples^{10,11}. One such study, led by Dr. Inna Sekirov, is the the Antenatal Serostudies Project funded by the COVID-19 Immunity Task Force (Public Health Agency of Canada). The study has enabled the BCCDC PHL High Volume Serology Laboratory to collaborate with Dr. Deborah Money (BC Women’s Hospital & Health Centre) to initiate a COVID-19 serosurveillance program in pregnant women across BC. Since November 2021 a subset of prenatal samples (100-300 per week) in women of childbearing age have been tested for SARS-CoV-2 antibodies. These include anti-nucleocapsid and anti-spike antibodies, elicited by natural SARS-CoV-2 infection and/or vaccination, respectively. Results demonstrate an exponential increase (from <10% to almost 50%) in anti-nucleocapsid antibody by the end of February 2022, persisting at the end of April 2022 (Figure 1). These data coincide with the emergence of the Omicron variant. Quantitative levels of anti-spike antibodies have also significantly risen in 2022 relative to November and December 2021 levels. Samples positive for anti-nucleocapsid antibodies have significantly higher levels of anti-spike antibodies than those negative for anti-nucleocapsid antibodies, demonstrating antibody boosting by natural infections. Continued monitoring is underway as is applying vaccination status to the analysis of these data.



Drs. Paul Levett, Mel Krajden, Agatha Jassem, and Muhammad Morshed (bottom starting left) with staff from the High Volume Serology Laboratory. Photo credit: M. Donoghue.



Dr. Inna Sekirov with samples for serology. Photo credit: M. Donoghue.

All Health Authority Data

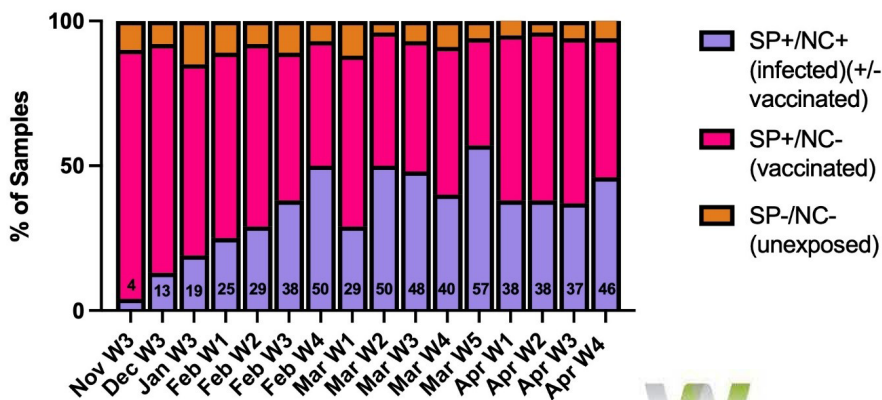


Figure 1. Weekly SARS-CoV-2 serostatus of antenatal samples in British Columbia collected between November 15, 2021 and April 30, 2022. Antenatal samples tested for spike (SP) and nucleocapsid (NC) proteins to determine natural infection and vaccination status. Data represents prenatal samples collected from women residing in Vancouver Coastal, Fraser, Interior, Northern, and Island Health Authorities.



COVID-19 IMMUNITY TASK FORCE



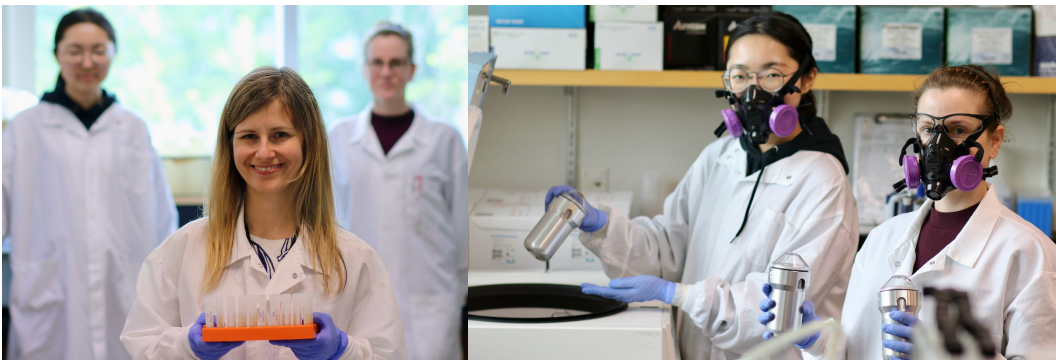
WOMEN'S HEALTH RESEARCH INSTITUTE AT BC WOMEN'S



COVID-19 Surveillance

Wastewater surveillance

Building on an established relationship with Metro Vancouver for the surveillance of viral and enteric illness in wastewater, the BCCDC PHL Environmental Microbiology Laboratory was able to apply similar methods to detect SARS-CoV-2 in sewage effluent as another pandemic response tool. Wastewater surveillance data can be useful for monitoring the spread of COVID-19 at a community level and may be an early warning of increasing or decreasing transmission. This was shown to be the case for the initial emergence of VOCs in our population¹². Dr. Natalie Prystajecy (principal investigator) and Dr. Melissa Grier (lead researcher) have been testing untreated wastewater for the presence of SARS-CoV-2 weekly for over a year and a half now, providing valuable information on the presence of COVID-19 in the [five Metro Vancouver communities sampled](#). This program has become increasingly important with the de-escalation of conventional testing that has been occurring. A broader surveillance program expanded to other health authority sites is in the works.



First photo pictured from left to right: Ziwen-Jo Ran, Dr. Natalie Prystajecy, and Dr. Melissa Grier
Photo credit: M. Donoghue.

Data integration efforts and surveillance outputs

The COVID-19 pandemic has precipitated the need for routine data sharing across all levels: internal to the laboratory, within BC, nationally and internationally. At the onset of the pandemic, it was clear that a coordinated, centralized repository of SARS-CoV-2 testing records would be essential to understanding the impact of this virus in the province. [PLOVER](#), which had been housing provincial respiratory data was commissioned with this undertaking, automatically integrating testing data from all public laboratories and Lifelabs, rapid (Point of Care) tests from PHSA and several large employers, and border testing results outside of BC ([Figure 2](#)). PLOVER was a primary source of test results and patient details for contact tracing and other public health needs across BC, with over 600 total users (120 active at any time). PLOVER has evolved for new needs without significant changes by leveraging an open-source enterprise framework for rapid development. Created and managed by senior clinical scientist Dr. Chris Fjell, PLOVER now has a small team of software developers, Jaideep Singh and Kyle Clarkson, who ensure the maintenance of the system, while continually making improvements and providing new functionality for managing laboratory investigations of other pathogens.

COVID-19 Surveillance

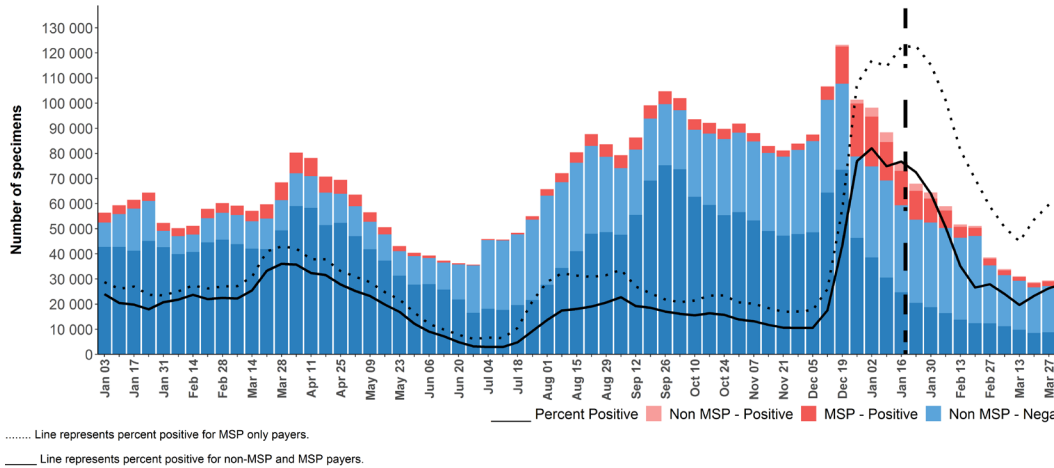
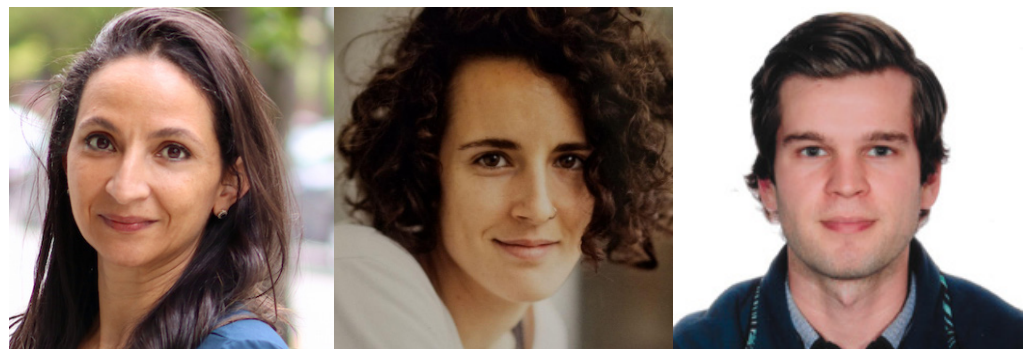


Figure 2. BC SARS-CoV-2 testing, January 2021-May 2022.

Surveillance teams are also critical in being able to provide the up-to-date situational data needed to not only drive laboratory, but public health response as well. Dr. Hind Sbihi, senior scientist with BCCDC Data and Analytics Services, leads a team consisting of Yayuk Joffres, Braeden Klaver and Geetika Gill. Their efforts combine and automate provincial laboratory NAT testing (Figure 2) and BCCDC PHL sequencing results together with available clinical and administrative data, including information on hospitalization, travel, vaccination and outbreak associations. This integrated data populates public and regional dashboards and has been the backbone of informing vaccine efficacy work^{13,14,15,16,17,18}. This team also contributes to and produces a myriad of COVID-19 reports for BC. Combining genomic VOC data with epidemiological, clinical and immunization data we have been able to analyze breakthrough infections and reinfection events during the multiple waves of this pandemic. The ability to monitor SARS-CoV-2 variant introductions and evolution has been key for outbreak response during cluster investigations in the province, while mutational profiling has been used to monitor evolution of the virus in immunocompromised patients¹⁹ and the population as a whole. Because of his continual observation, Dr. John Tyson was even able to resolve that different primers would need to be manufactured by Integrated DNA Technologies to accommodate the variant changes.



Left to Right: Dr. Hind Sbihi, Yayuk Joffres and Braeden Klaver
 Left photo credit: M. Donoghue.

COVID-19 Surveillance

Data sharing on the national level is via the [Canadian COVID-19 Genomics Network](#) (CanCOGeN) while international efforts to track variants and their mutations are shared through the [Global Initiative on Sharing All Influenza Data](#) (GISAID) database. Data sharing promotes threat response and capacity-building through collaboration and has been an integral component in observing the emergence and transmission of variants globally. In BC, five VOCs have been detected: Alpha, Beta, Gamma, Delta and Omicron (Figure 2). These variants and the sublineages (Figure 3) that arise are actively monitored as they are indicators of higher transmissibility, immune escape, severity, or a combination of the three.

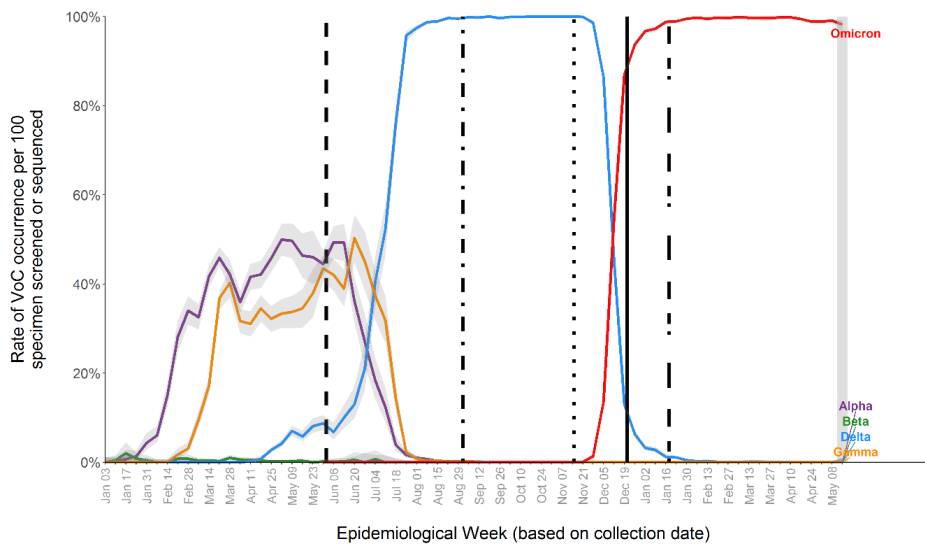


Figure 3. Estimated sample prevalence* of VOCs by lineage Jan 2021-May 14, 2022.

*Sample prevalence is calculated as the rate of occurrence of a given VOC lineage per 100 positive lab samples. It was estimated from the proportion of presumptive VOC from screening and the proportion of confirmed VOC via sequencing (excluding outbreaks and targeted surveillance) until May 30th, 2021 when BC transitioned to WGS on all positive cases. From week 13 (March 28, 2021), VOC screening results with both E484K and N501Y mutations are assumed to be Gamma, given a very low prevalence of Beta in BC. As of week 22 (May 30, 2021), prevalence of VOC is estimated from sequencing results only. Grey shaded box can reflect partial data due to a lag in receipt of positive samples from front line laboratories and turn around time of 7 to 11 days from sample collection to WGS analysis; estimates are expected to change as more specimens are received and sequenced. Dotted line indicates the time of transition to WGS of all positive samples on November 15, 2021 (epi week 46). Solid line indicates the time of transition to WGS of a subset of representative positive samples in addition to priority cases (including outbreaks, long-term care, vaccine escape, travel-related, hospitalization) on December 21st, 2021 (epi week 51). Dashed-dotted line indicates transition to the most recent change in testing guidelines and exclusion of RAT. Trends from Jan 18th onwards represent those in targeted populations (health care workers, clinically extremely vulnerable, etc).

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The Public Health Laboratory at the BC Centre for Disease Control (BCCDC) provides consultative, interpretative testing and analyses for clinical and environmental infectious diseases in partnership with other microbiology laboratories and public health workers across the province and nationally. The BCCDC PHL is the provincial communicable disease detection, fingerprinting and molecular epidemiology centre providing advanced and specialized services along with international defined laboratory core functions. The Provincial Toxicology Centre conducts toxicology testing and analysis for clinical patients, including therapeutic drug monitoring, drug screening tests and forensic toxicology analyses for the BC Coroners Service.

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