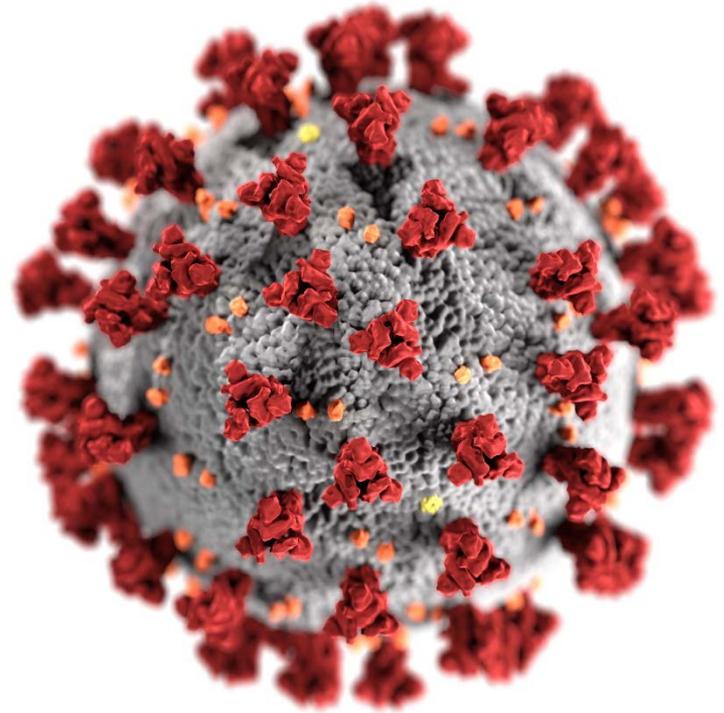# Confirming SARS-CoV-2 reinfection with whole genome sequencing

COVID-19 Genomic Epidemiology Toolkit:
Module 2.5

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Orange County Public Health Laboratory

Toolkit map

Part 1: Introduction

Part 2: Case Studies

Part 3: Implementation

COVID-19 reinfection cases

- Reinfection cases have been reported, but they are rare:
  - Risk was estimated at 0.02%, and the reinfection incidence rate was 0.36 per 10,000 person-weeks (Abu-Raddad *et al.* 2020)

- CDC protocol for investigating suspected SARS-CoV-2 reinfection:
  - Persons with or without COVID-19-like symptoms ≥90 days after initial infection/illness
  - Persons with COVID-19-like symptoms 45-89 days after initial infection/illness
  - Sequencing of paired respiratory specimens (one from each infection episode) is recommended for confirmation

Abu-Raddad et al. (2020) Assessment of the risk of SARS-CoV-2 reinfection in an intense re-exposure setting, PMID: 33315061
CDC Common Investigation Protocol: www.cdc.gov/coronavirus/2019-ncov/php/reinfection.html

Reinfection case overview

32-year-old-person experiencing homelessness

- June 2020 - Shelter A
  - Tested in response to on-site staff with positive test
  - Symptoms: fever, sore throat, cough, headache
  - Recovered, no hospitalization required

- October 2020 - Shelter B
  - Tested in response to resident with positive test
  - Symptoms: general cold symptoms, reported feeling very ill
  - Recovered, no hospitalization required

Phylogenetic tree of case specimens
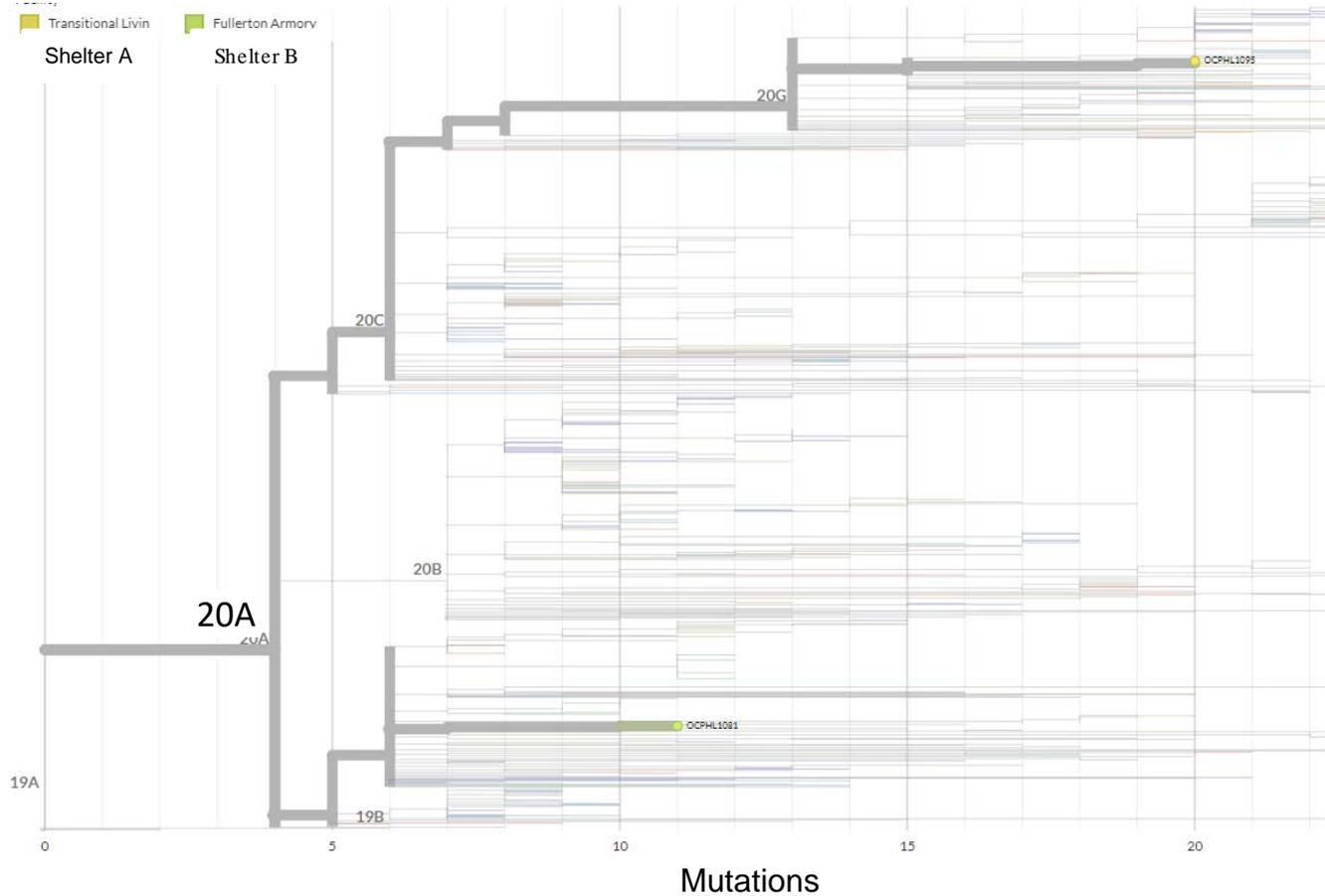
October 2020
Specimen

Specimens taken
138 days apart

June 2020
Specimen

Genotypic characterization of sequences

	June 2020	October 2020
Nextclade Designation	20A	20G
Pangolin Lineage	B.1 (Version 2021-04-14)	B.1.2 (Version 2021-04-14)
GISAID ID	EPI_ISL_672360	EPI_ISL_672367
Amino Acid Substitutions	**Spike: D614G**, T1231A N: S194L NS3: A110S **NSP12: P323L** NSP13: G203C, P82T	**Spike: D614G**, K1191N M: D209Y N: P67S, P199L NS3: G172V, Q57H NS7a: A8T NS8: S24L NSP2: T85I NSP3: E1801K, M102I NSP5: L89F **NSP12: P323L** NSP14: N129D NSP16: R216C

Confirming reinfection findings

- The patient was part of separate, larger outbreaks

- Outbreak in Shelter A, June 2020
  - Exposure dates May 22 – July 7, 2020
  - Included 19 residents and 7 staff
  - WGS performed on 4 specimens

- Outbreak in Shelter B, October 2020
  - Exposure dates October 15 – November 2, 2020
  - Included 14 residents and 1 staff
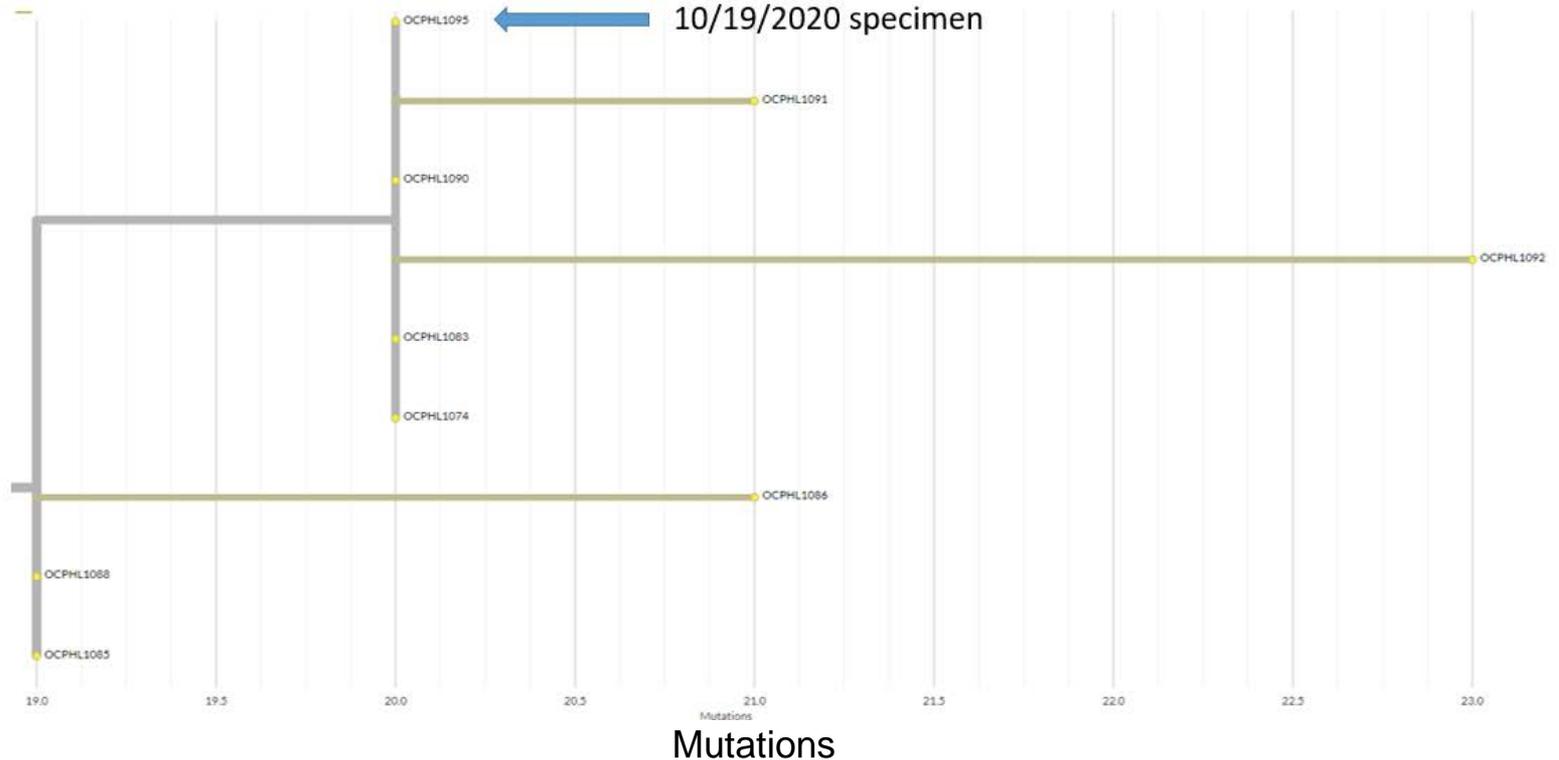 - WGS performed on 9 specimens

Outbreak in Shelter A, June 2020

Specimens (n=4) collected
May 22 – June 3, 2020
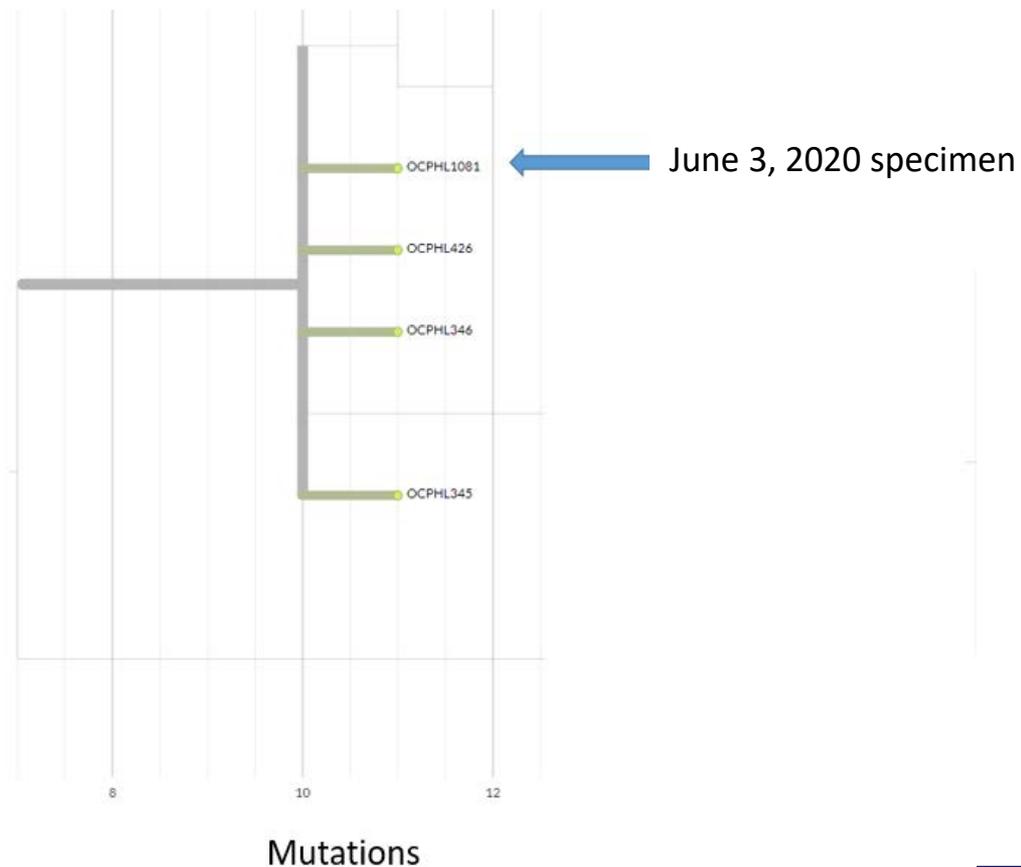
# Outbreak in Shelter B, October 2020

Summary

- Reinfections seem to be rare, but previous SARS-CoV-2 infection may not confer immunity against a different variant

- WGS of paired specimens can confirm reinfection of SARS-CoV-2:
  - Case study specimens from June 2020 and October 2020 exhibited
    1. Distinct clade and lineage assignments
    2. Specific mutation patterns
  - Alternative: similar sequences would suggest persistent infection

- Additional epi data can inform the genomic epidemiologic investigation:
  - Both positive tests reported during outbreaks more than 3 months apart at separate facilities

Learn more

- Other introduction modules
    - Community Transmission – Module 2.3
    - Superspreading Event– Module 2.4

- COVID-19 Genomic Epidemiology Toolkit
    - Find further reading
    - Complete a feedback survey
    - Subscribe to receive updates on new modules as they are released
    go.usa.gov/xAbMw
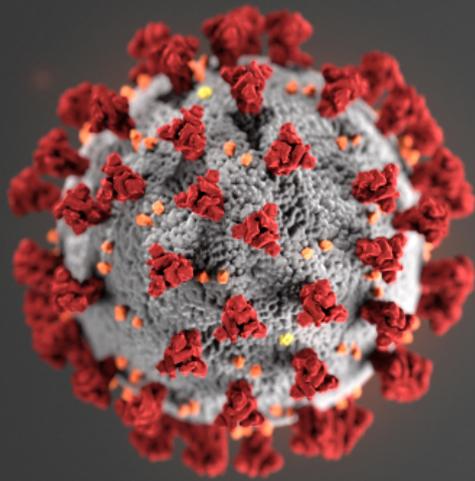
For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348   www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

FOR WEBSITE

- **Further Reading:**
  - Assessment of the risk of SARS-CoV-2 reinfection in an intense re-exposure setting. Abu-Raddad *et al.* 2020 Clinical Infectious Diseases. https://pubmed.ncbi.nlm.nih.gov/33315061/
  - Symptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reinfection by a phylogenetically distinct strain. Elslande *et al.* 2020 Clinical Infectious Diseases. https://pubmed.ncbi.nlm.nih.gov/32887979/
  - COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. To *et al.* 2020 Clinical Infectious Diseases. https://pubmed.ncbi.nlm.nih.gov/32840608/
  - Evidence of severe acute respiratory syndrome coronavirus 2 reinfection after recovery from mild coronavirus disease 2019. Lee *et al.* 2020 Clinical Infectious Diseases. https://pubmed.ncbi.nlm.nih.gov/33219681/
  - Genomic evidence for reinfection with SARS-CoV-2: a case study. Tillett *et al.* 2021 The Lancet Infectious Diseases. https://pubmed.ncbi.nlm.nih.gov/33058797/
  - Case Study: Prolonged infectious SARS-CoV-2 shedding from an asymptomatic immunocompromised individual with cancer. Avanzato *et al.* 2020 Cell. https://pubmed.ncbi.nlm.nih.gov/33248470/

- **Resources:**
  - CDC Common Investigation Protocol for Investigating Suspected SARS-CoV-2 Reinfection: www.cdc.gov/coronavirus/2019-ncov/php/reinfection.html