Molecular Approaches for Clinical and Public Health Applications to Detect Influenza and SARS-CoV-2 Viruses

Clinician Outreach and Communication Activity (COCA) Call

Thursday, December 9, 2021

Free Continuing Education

- Free continuing education is offered for this webinar.
- Instructions on how to earn continuing education will be provided at the end of the call.

Continuing Education Disclaimer

- In compliance with continuing education requirements, CDC, our planners, our presenters, and their spouses/partners wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

- Planners have reviewed content to ensure there is no bias.

- The presentation will not include any discussion of the unlabeled use of a product or a product under investigational use.

- CDC did not accept commercial support for this continuing education activity.

Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Explain the meaning and potential use cases of Ct values for SARS-CoV-2 testing.
2. Discuss the value of SARS-CoV-2 sequencing in public health compared to clinical practice.
3. Describe clinical test ordering and utilization for seasonal influenza in the context of SARS-CoV-2 co-circulation.

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

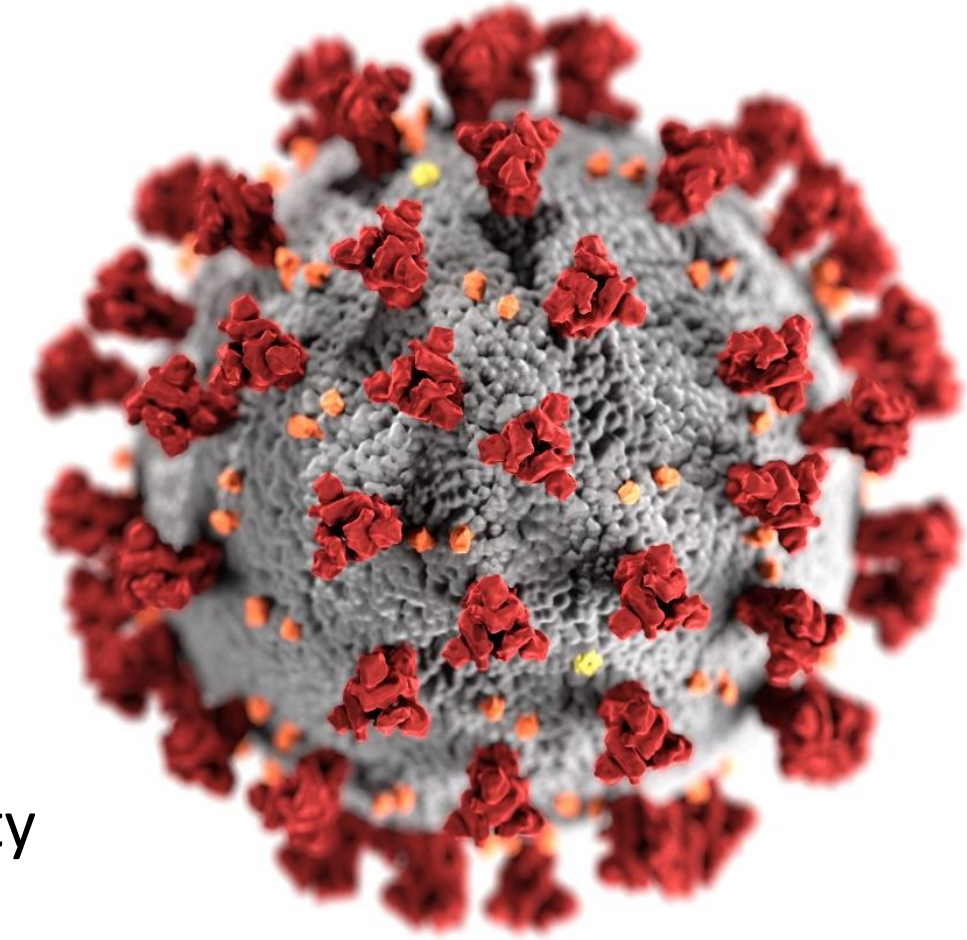
Today's Presenters

- **Manish Patel, MD, MSc**
  Team Lead, Influenza Prevention and Control Team
  Influenza Division
  Centers for Disease Control and Prevention

- **John Barnes, PhD**
  Team Lead, Strain Surveillance and Emerging Variants
  COVID-19 Response
  Centers for Disease Control and Prevention

- **Alison Laufer Halpin, PhD**
  CDR, U.S. Public Health Service
  Task Force Lead, Laboratory and Testing Task Force
  COVID-19 Response
  Centers for Disease Control and Prevention

2021-2022 Influenza Season Testing Issues



Manish Patel, MD

December 9, 2021

Clinician Outreach and Communication Activity (COCA) Call

cdc.gov/coronavirus

Objectives: 2021-2022 Influenza Season Testing Issues

- **Provide high level overview of CDC guidance** on testing for influenza in clinical settings during the 2021-2022 winter season
  - Focus on influenza and SARS-CoV-2 testing, if the two co-circulate
- **Provide recommendations by patient setting**
  - Outpatient clinics and emergency departments
  - Hospitals
  - Nursing homes
- **Not covered today**
  - Available diagnostic tests or validity of tests
  - SARS-CoV-2-related testing issues, except as it relates to possible co-circulation with influenza

Influenza Activity in the United States During 2021-2022

- **Unpredictable**, might vary by extent of COVID-19 control measures
  - Influenza activity can vary geographically and over time

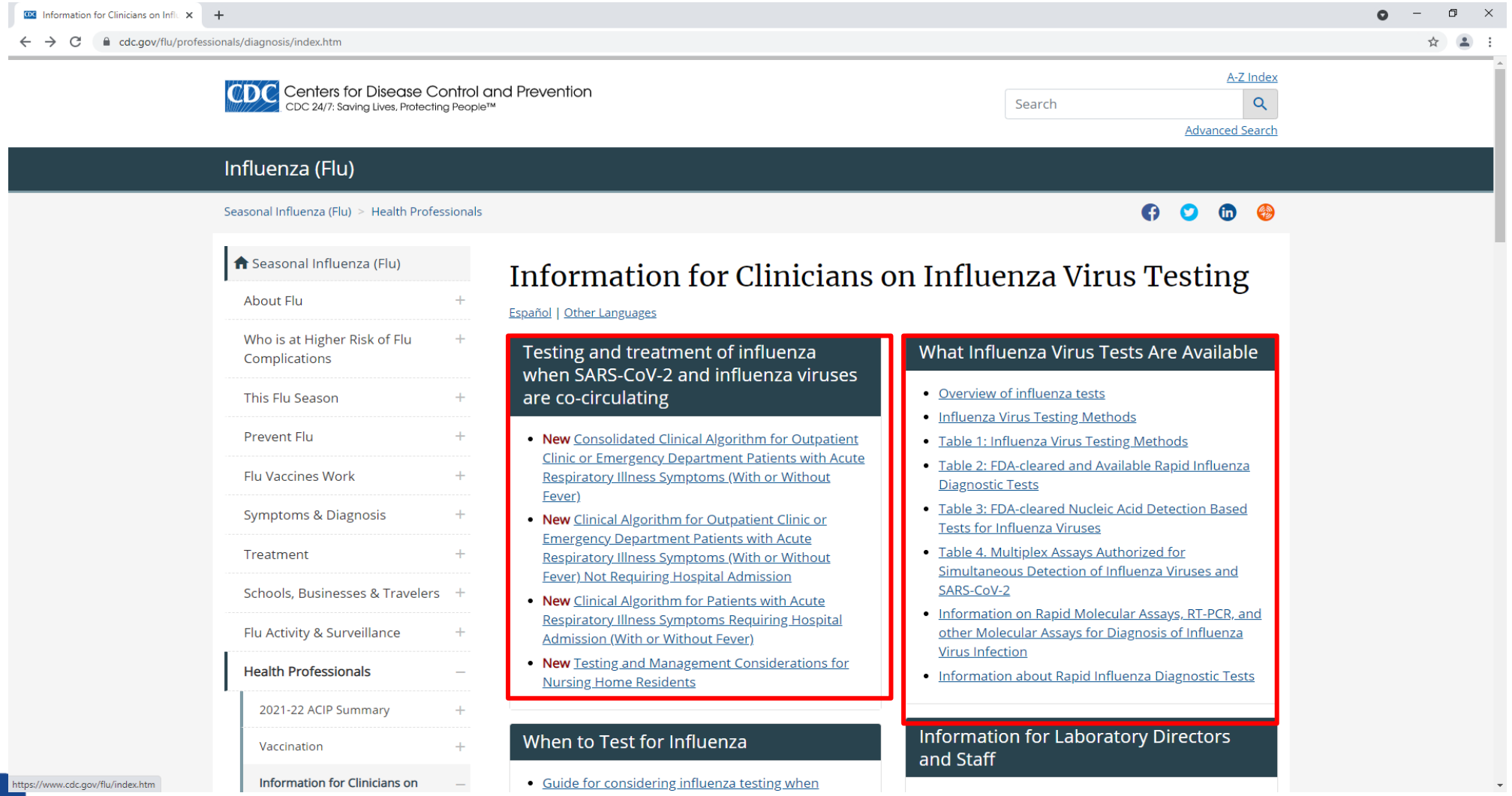
- **Monitoring of viral co-circulation is essential**
  - Public health surveillance (local, state, national)
    - SARS-CoV-2
    - Influenza A and B viruses
  - Local clinical laboratories, hospital testing results

- **Prepare for viral co-circulation**
  - Prevention and control strategies are needed for both SARS-CoV-2 and influenza viruses

Co-circulation of Influenza Viruses and SARS-CoV-2

- **Co-infection might occur** with influenza viruses and SARS-CoV-2
  - Documented in case reports, case series
  - Frequency, severity, and risk factors are unknown
- **Overlapping signs, symptoms**, some differences with either infection
  - Incubation period is shorter with influenza (1-3 days) than COVID-19 (2-14 days)
  - Viral shedding, period of viral RNA detection is generally shorter for influenza
  - Ageusia/dysgeusia, anosmia are more common with COVID-19 than influenza
  - Timing of onset of complications/severe disease is earlier with influenza
- **Implications**
  - Testing is needed to distinguish influenza from COVID-19
    - Consider influenza virus infection, SARS-CoV-2 infection, co-infection

Information for Clinicians on Influenza Virus Testing

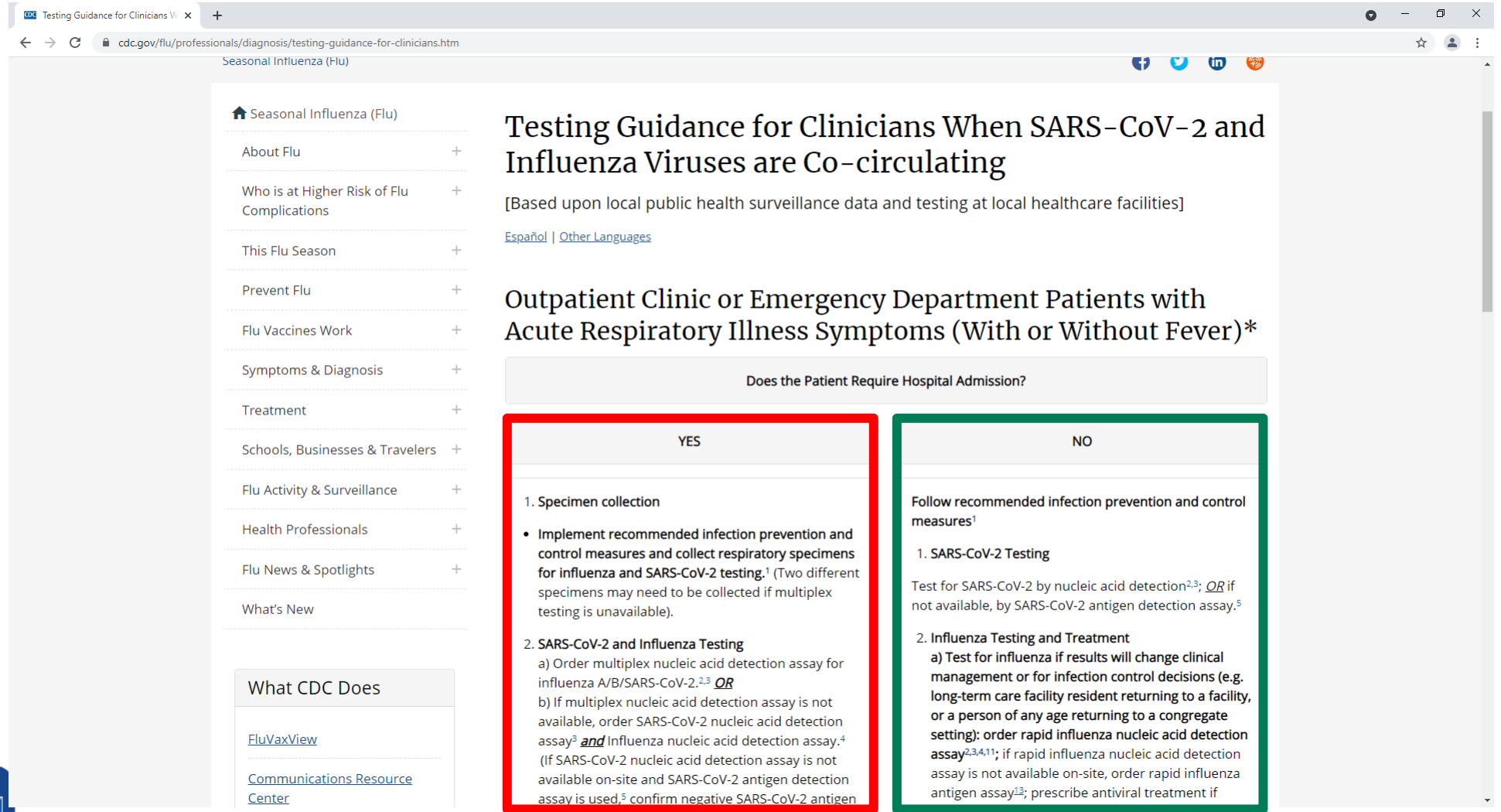


https://www.cdc.gov/flu/professionals/diagnosis/index.htm

Influenza Testing Strategies During Co-circulation of Influenza Viruses and SARS-CoV-2

- **Options for testing of respiratory specimens** in patients with acute respiratory illness
  - **Outpatient clinic and emergency department patients**
    - Test for SARS-CoV-2 and use judgment to clinically diagnose influenza and prescribe antiviral treatment of influenza if needed, OR
    - Test for both SARS-CoV-2 and influenza viruses
  - **Hospitalized patients**
    - Test for SARS-CoV-2 and for influenza viruses
  - **Nursing home residents**
    - Test for SARS-CoV-2 and for influenza viruses
- **Do not order viral culture** for initial or primary diagnosis of influenza
- **Do not order serology** for influenza
  - Results from a single serum specimen cannot be reliably interpreted, and collection of paired acute and convalescent sera 2-3 weeks apart are needed

Outpatient Clinic or Emergency Department Patients



https://www.cdc.gov/flu/professionals/diagnosis/testing-guidance-for-clinicians.htm

Outpatient Clinic or Emergency Department Patients

Testing Guidance for Clinicians When SARS-CoV-2 and Influenza Viruses are Co-circulating
[Based upon local public health surveillance data and testing at local healthcare facilities]
Outpatient Clinic or Emergency Department Patients with Acute Respiratory Illness Symptoms (With or Without Fever)*

Does the Patient Require Hospital Admission?

YES

1. Specimen collection

***Implement recommended infection prevention and control measures and collect respiratory specimens for influenza and SARS-CoV-2 testing.[1]** (Two different specimens may need to be collected if multiplex testing is unavailable).

2. SARS-CoV-2 and Influenza Testing

a) Order multiplex nucleic acid detection assay for influenza A/B/SARS-CoV-2.[2,3] ***OR***

b) If multiplex nucleic acid detection assay is not available, order SARS-CoV-2 nucleic acid detection assay[3] ***and*** Influenza nucleic acid detection assay.[4]
(If SARS-CoV-2 nucleic acid detection assay is not available on-site and SARS-CoV-2 antigen detection assay is used,[5] confirm negative SARS-CoV-2 antigen detection results by SARS-CoV-2 nucleic acid detection assay at an outside laboratory). (Note: Rapid influenza antigen detection assays are not recommended for hospitalized patients due to low sensitivities.)

(Note: Because SARS-CoV-2 and influenza virus co-infection can occur, a positive influenza test result without SARS-CoV-2 testing does not exclude COVID-19, and a positive SARS-CoV-2 test result without influenza testing does not exclude influenza.)

3. Treatment

*If bacterial pneumonia or sepsis is suspected, consider testing recommendations and empiric antibiotic treatment per American Thoracic Society-Infectious Diseases Society of America Adult Community-acquired Pneumonia Guidelines[6], and **administer supportive care and treatment for suspected or confirmed COVID-19 patients per NIH COVID-19 Treatment Guidelines.[7]** (Note: community-acquired bacterial co-infections can occur but appear to be uncommon with COVID-19,[8,9,10] and may be more common with influenza.[11])

*Start empiric oseltamivir treatment for suspected influenza as soon as possible regardless of illness duration, without waiting for influenza testing results, per Infectious Diseases Society of America Influenza Guidelines[11,12], and administer supportive care.

NO

Follow recommended infection prevention and control measures[1]

1. SARS-CoV-2 Testing

Test for SARS-CoV-2 by nucleic acid detection[2,3]; ***OR*** if not available, by SARS-CoV-2 antigen detection assay.[5]

2. Influenza Testing and Treatment

a) Test for influenza if results will change clinical management or for infection control decisions (e.g. long-term care facility resident returning to a facility, or a person of any age returning to a congregate setting): order rapid influenza nucleic acid detection assay[2,3,4,11]; if rapid influenza nucleic acid detection assay is not available on-site, order rapid influenza antigen assay[13]; prescribe antiviral treatment if positive.[11,12] ***OR***

b) Prescribe empiric antiviral treatment as soon as possible without influenza testing based on a clinical diagnosis of influenza for patients of any age with progressive disease of any duration, and for children and adults at high risk for influenza complications.[11,12,14]

*For adult patients with suspected community-acquired pneumonia who do not require admission, see American Thoracic Society-Infectious Diseases Society of America Adult Community-acquired Pneumonia Guidelines[6]

*For otherwise healthy non-high-risk persons with influenza-like illness (fever and either cough or sore throat) with illness ≤2 days, empiric antiviral treatment can be prescribed based upon clinical judgement.[11,12]

*For otherwise healthy non-high-risk persons without influenza-like illness or with illness duration >2 days, antiviral treatment of influenza is unlikely to provide significant clinical benefit.[11]

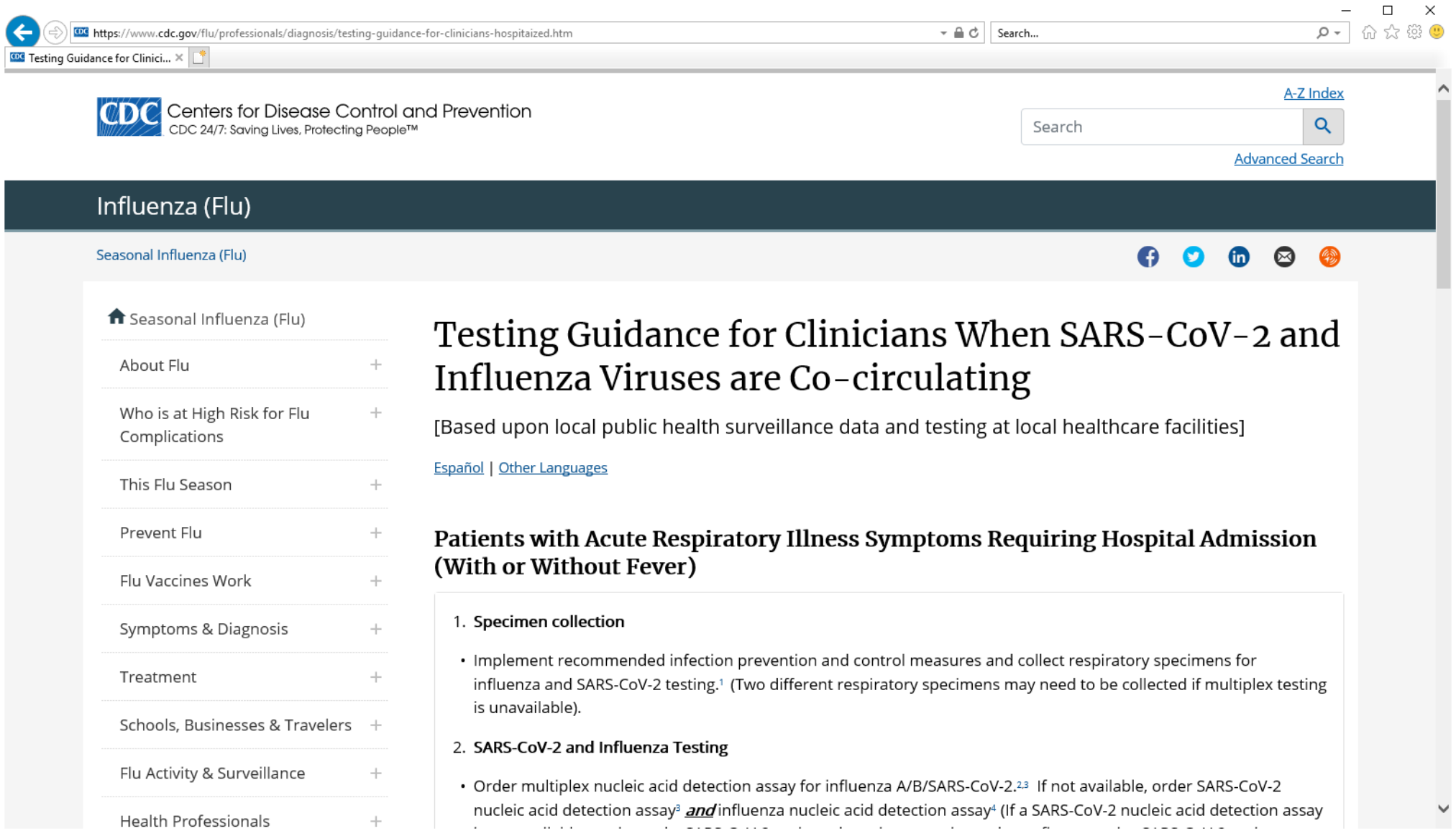
3. Follow isolation and quarantine recommendations for SARS-CoV-2[15]

https://www.cdc.gov/flu/professionals/diagnosis/testing-guidance-for-clinicians.htm

Influenza Testing in Outpatient Clinic or Emergency Department Patients

- **Testing of respiratory specimens for influenza** in patients with acute respiratory illness
  - If results will change clinical management
    - For example, patients at increased risk for complications who might benefit from antiviral treatment
    - For example, patients not at increased risk where testing might reduce unnecessary antibiotics, further diagnostic testing, time in the facility, or influence antiviral treatment
  - For infection control (e.g., long-term care facility resident)
- **What influenza tests are recommended?**
  - Rapid influenza molecular (nucleic acid detection) assays are recommended
  - Rapid antigen assay okay if molecular assays are not available
- **Assays**
  - By single-plex assays (collect two different specimens if multiplex not available on site)
  - By multiplex assay

Hospitalized Patients

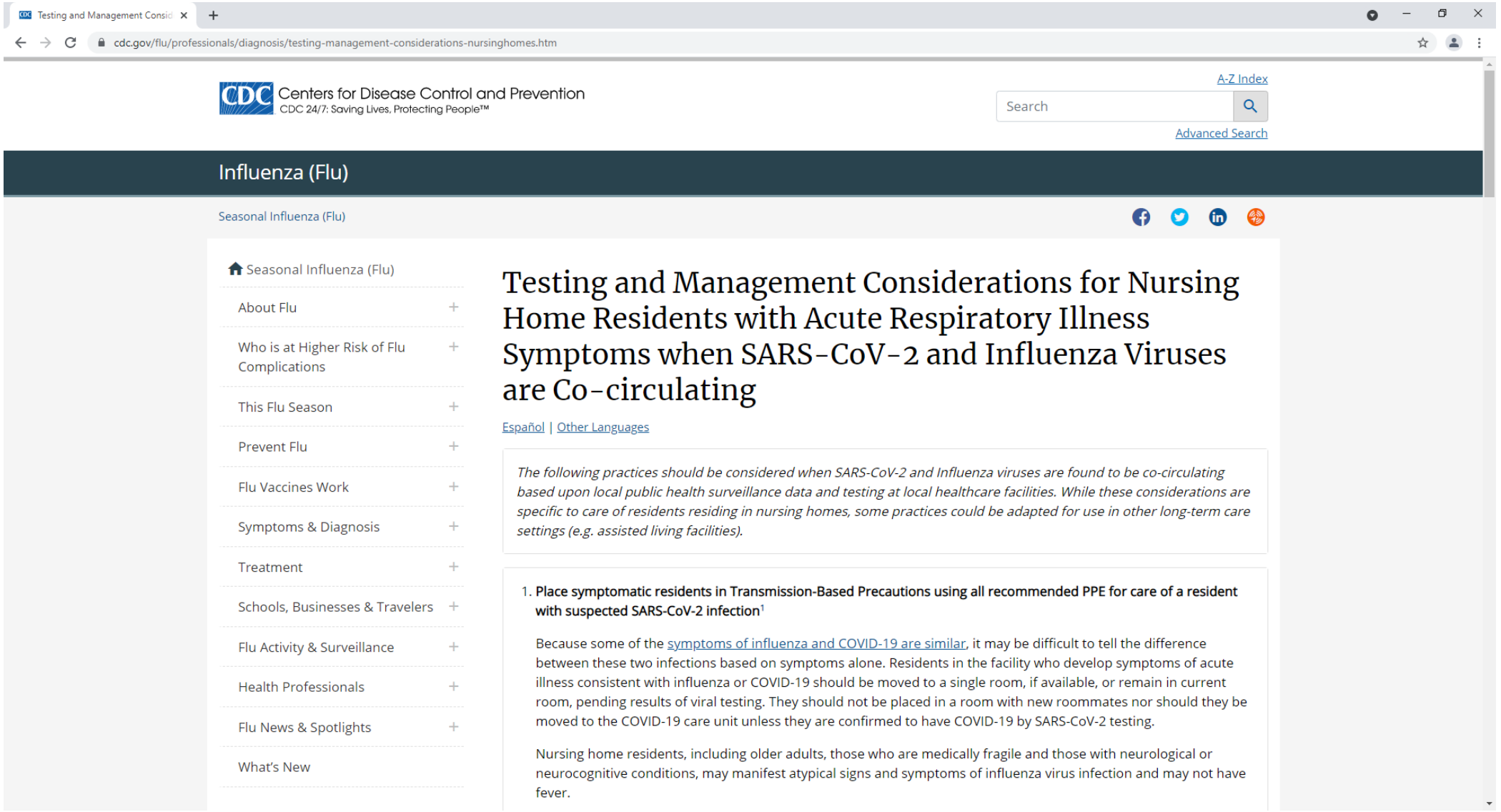


https://www.cdc.gov/flu/professionals/diagnosis/testing-guidance-for-clinicians-hospitaized.htm

Influenza Testing in Hospitalized Patients

- **Testing of respiratory specimens** in patients with acute respiratory illness
  - Testing for both influenza and SARS-CoV-2 is recommended
  - Order multiplex nucleic acid detection assay for influenza and SARS-CoV-2
  - Single-plex is okay if multiplex not available (might need two respiratory specimens)
- **What influenza tests are recommended?**
  - Rapid influenza molecular (nucleic acid detection) assays are recommended
- **What influenza tests are not recommended?**
  - Rapid influenza antigen assay are not recommended due to lower sensitivities
- **Special considerations for immunocompromised patients**
  - Multiplex RT-PCR assays targeting a panel of respiratory pathogens, including influenza viruses are recommended

Influenza Testing Considerations for Nursing Home Residents



https://www.cdc.gov/flu/professionals/diagnosis/testing-management-considerations-nursinghomes.htm

Influenza Testing in Nursing Home Residents

- **Special considerations**
  - Promptly notify health department per guidelines (e.g., SARS-CoV-2 or influenza virus infection in a resident or healthcare personnel)
- **Testing recommendations are the same as hospitalized patients**
  - **Testing of respiratory specimens** in patients with acute respiratory illness
    - Testing for both influenza and SARS-CoV-2 is recommended
    - Order multiplex nucleic acid detection assay for influenza and SARS-CoV-2
    - Single-plex is okay if multiplex not available (might need two respiratory specimens)
  - **What influenza tests are recommended?**
    - Rapid influenza molecular (nucleic acid detection) assays are recommended
  - **What influenza tests are not recommended?**
    - Rapid influenza antigen assay are not recommended due to lower sensitivities

Summary

- **Hospitalized and nursing home patients**
  - Test for influenza and SARS-CoV-2 in all with acute respiratory symptoms
- **Non-hospitalized outpatients and emergency department patients**
  - Test for influenza when results will change clinical management (e.g., influenza antiviral treatment) or for infection control decisions (e.g., long-term care facility resident)
- **Influenza assays**
  - Rapid influenza nucleic acid detection assays are preferred
- **Guidelines might evolve**
  - To date, co-circulation of SARS-CoV-2 and influenza has been uncommon and so recommendations could evolve as data accumulate on co-circulation or co-infection

Self-knowledge Check

What influenza assays are **not recommended** for diagnosis of influenza infection in **hospitalized patients** with acute respiratory illness?

A. Viral culture
B. Antigen assay
C. Serology
D. A and B only
E. All of the above

Self-knowledge Check

The correct answer is: E - All of the above

- Viral culture is not practical or sensitive for detecting influenza viruses (A)
- Antigen assays have low sensitivity compared with RT-PCR (B)
- Serology assays require acute and convalescent sera which is not practical for diagnosing acute infection (C)

References (Influenza Testing During 2021-2022 Season)

- Cuadrado-Payán E, Montagud-Marrahi E, Torres-Elorza M, Bodro M, Blasco M, Poch E, Soriano A, Piñeiro GJ. SARS-CoV-2 and influenza virus co-infection. Lancet. 2020 May 16;395(10236):e84. doi: 10.1016/S0140-6736(20)31052-7.
- Azekawa S, Namkoong H, Mitamura K, Kawaoka Y, Saito F. Co-infection with SARS-CoV-2 and influenza A virus. IDCases. 2020 Apr 21;20:e00775. doi: 10.1016/j.idcr.2020.e00775.
- Simin Ma, Xiaoquan Lai, Zhe Chen, Shenghao Tu, Kai Qin. Clinical characteristics of critically ill patients co-infected with SARS-CoV-2 and the influenza virus in Wuhan, China. Int Jo of Infectious Diseases;96;2020:683-687, https://doi.org/10.1016/j.ijid.2020.05.068.
- Ding Q, Lu P, Fan Y, Xia Y, Liu M. The clinical characteristics of pneumonia patients coinfected with 2019 novel coronavirus and influenza virus in Wuhan, China. J Med Virol. 2020 Sep;92(9):1549-1555. doi: 10.1002/jmv.25781.
- Wu X, Cai Y, Huang X, Yu X, Zhao L, Wang F, Li Q, Gu S, Xu T, Li Y, Lu B, Zhan Q. Co-infection with SARS-CoV-2 and Influenza A Virus in Patient with Pneumonia, China. Emerg Infect Dis. 2020 Jun;26(6):1324-1326. doi: 10.3201/eid2606.200299.
- Beltrán-Corbellini Á, Chico-García JL, Martínez-Poles J, et al. Acute-onset smell and taste disorders in the context of COVID-19: a pilot multicentre polymerase chain reaction based case-control study. Eur J Neurol 2020; 27: 1738-1741.
- Uyeki, TM et al. “Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza.” Clinical infectious diseases;68,6 (2019): 895-902. doi:10.1093/cid/ciy874
- Centers for Disease Control and Prevention. Information for Clinicians on Influenza Virus Testing. Accessed September 28, 2021. https://www.cdc.gov/flu/professionals/diagnosis/index.htm?web=1&wdLOR=c326CD6B1-3783-4BA2-8CC0-C46134DA0632
- Centers for Disease Control and Prevention. People at High Risk for Flu Complications. Accessed September 28, 2021. https://www.cdc.gov/flu/highrisk/index.htm

Thank you

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

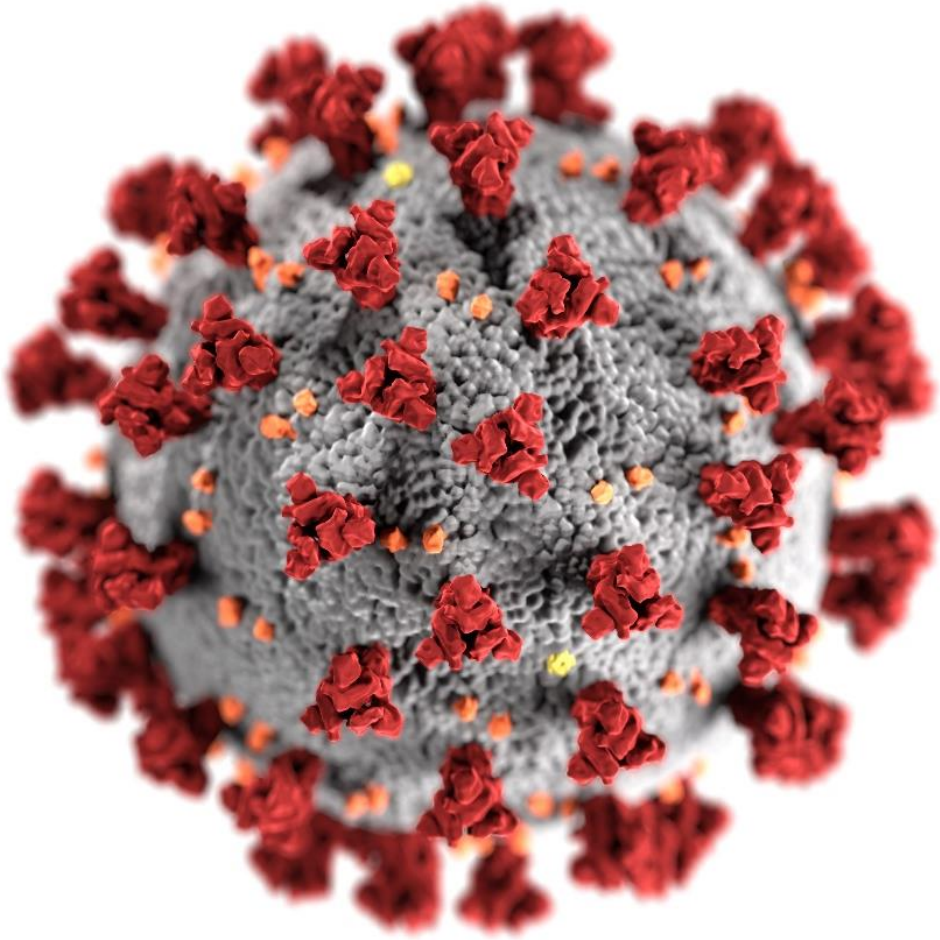
For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Cycle Threshold (Ct) Values and Correlations to Viral Titer and Infectiousness- Real or Red Herring?

John R. Barnes, Ph.D.

Team Lead, Genomics and Diagnostics Team

Virology Surveillance and Diagnosis Branch, Influenza Division, National Center for Immunization and Respiratory Diseases



cdc.gov/coronavirus

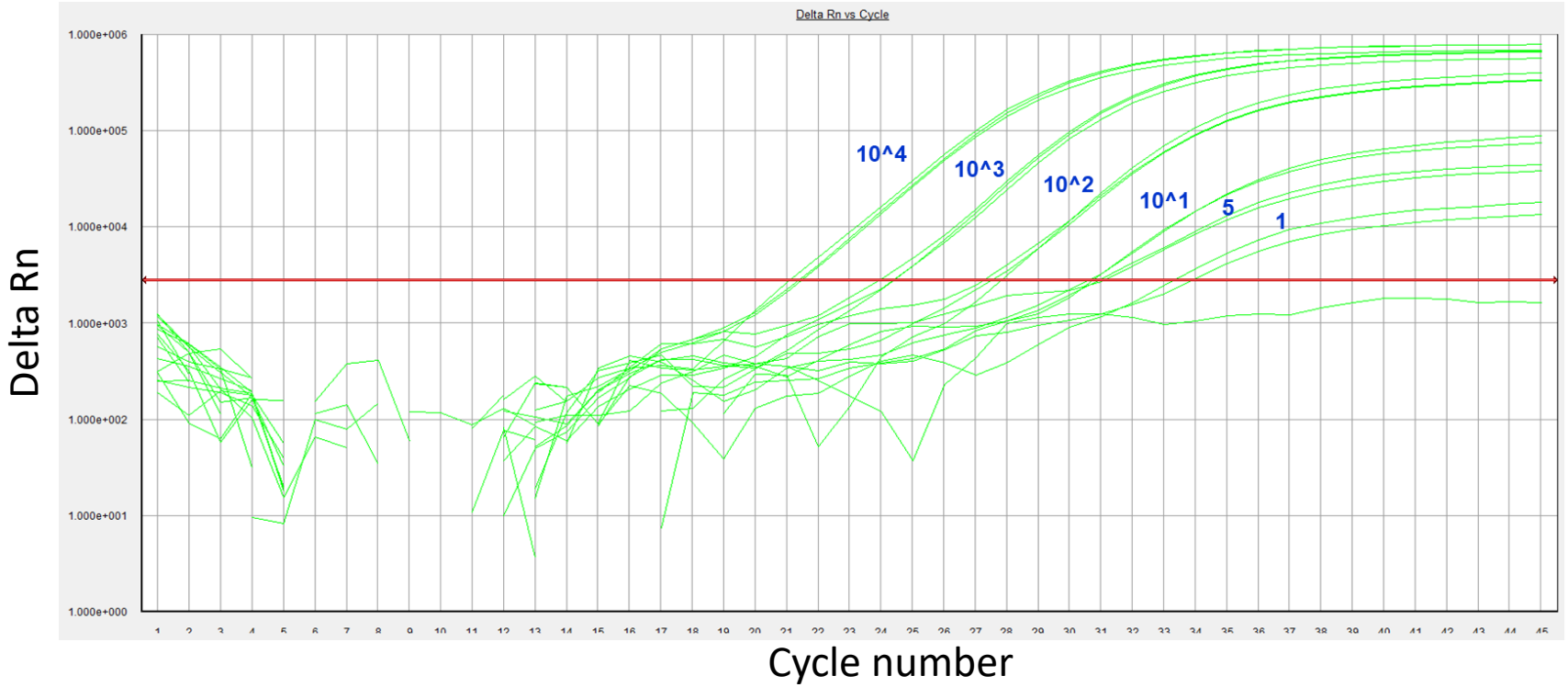
Variability vs. Bias

- Individual (symptoms, inhibitors, time since infection)
- Specimen quality
- Specimen storage and transport
- Specimen extraction
- Reverse transcription efficiency
- Assay platform (hardware, enzymes, primers/probes)
- Assay performance
- Assay interpretation (e.g., threshold setting)
- RT-PCR dynamics (higher Ct = higher variability)

Ct Values can be Related to Genome Copies

- **Control measures**:
  - Same instrument
  - Same run conditions/ assay
  - Same operator
  - Same quality
  - Same material
  - Same analysis
- **Assumptions**:
  - Test maintains a linear relationship in varying concentrations
  - Assay site is intact (no mutation)

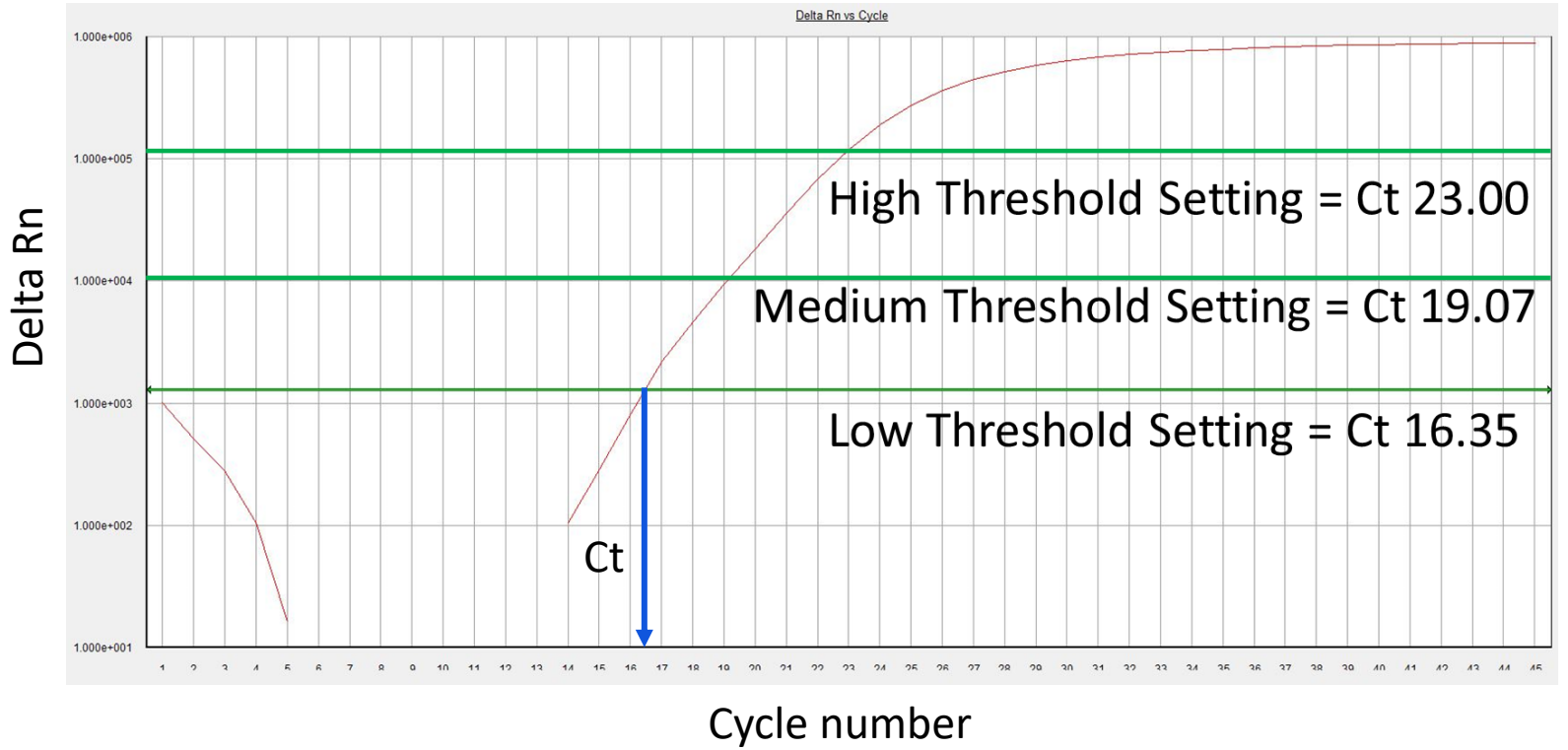
Twist RNA	Total Copies in Reaction	Control #2 (WT)
10^4 copies/ul	50,000	19.27/19.43/19.37
10^3 copies/ul	5000	22.86/22.74/22.64
10^2 copies/ul	500	26.22/26.34/26.21
10 copies/ul	50	30.14/29.83/29.70
5 copies/ul	25	30.46/31.15/31.01
1 copy/ul	5	33.86/33.05/32.85



Change of ~3 Ct = Log change in Nucleic acid concentration

Threshold Settings Impact Ct Value

- Threshold line setting is often left to discretion of the operator
- Exponential phase may cover multiple cycle numbers depending on curve shape
- Differences in threshold setting displayed (High Threshold to Low Threshold) in the figure would lead to two log variance in genome copies estimated



Change of ~3 Ct = Log change in Nucleic acid concentration

Ct Values on Same Amount of Starting Material can Vary Based on Assay Performance

Sample	Synthetic Genome Copies/ Reaction	CDC Flu SC2 Multiplex SC2 Target	Commercial Assay N Gene Target	Commercial Assay RdRp* Gene Target
Twist 10^3 copies/ul	5000	23.19/23.02/23.09	27.63/27.60/27.49	26.35/26.72/26.84
Twist 10^2 copies/ul	500	27.17/27.24/27.62	33.22/33.12/33.46	31.43/32.19/32.53
Twist 10 copies/ul	50	31.69/31.17/30.44	37.76/41.15/37.78	40.98/-/39.07
Twist 5 copies/ul	25	32.11/31.61/31.96	42.51/37.34/38.84	-/-/-
Twist 1 copy/ul	5	33.44/33.74/35.02	-/40.45/42.11	-/-/-
SC2 positive clinical specimen		22.18/21.90	25.93/26.01	26.01/26.09

*RdRp: RNA dependent RNA polymerase

Self-knowledge Check

Which of the following factors can change assay performance and induce variability in Ct values of a molecular test?

A. Specimen site of collection
B. Specimen quality
C. Enzyme used in assay
D. Lab/technician preference for setting threshold line
E. All the above

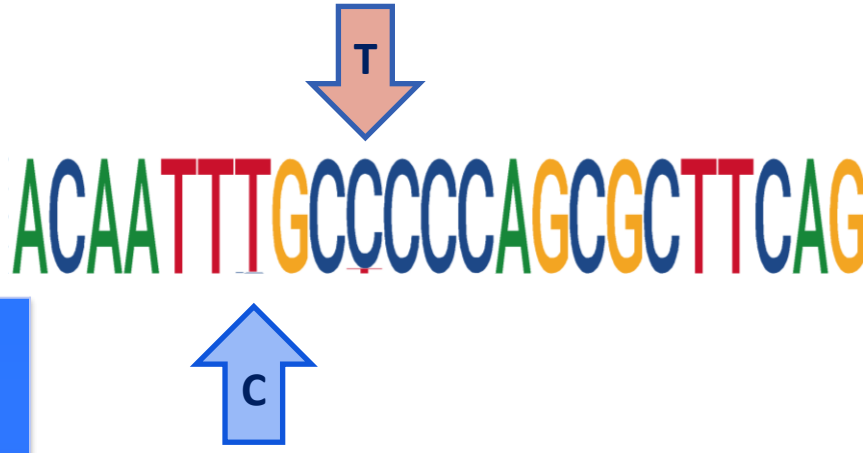
Self-knowledge Check

The correct answer is: E – All of the above

The reason for this is because… All these factors can have a profound effect on the perceived sensitivity of the molecular assay and can serve as sources of variability in Ct values.

Viral Mutations within Primer or Probe Region can Impact Ct Value

CDC N2 probe

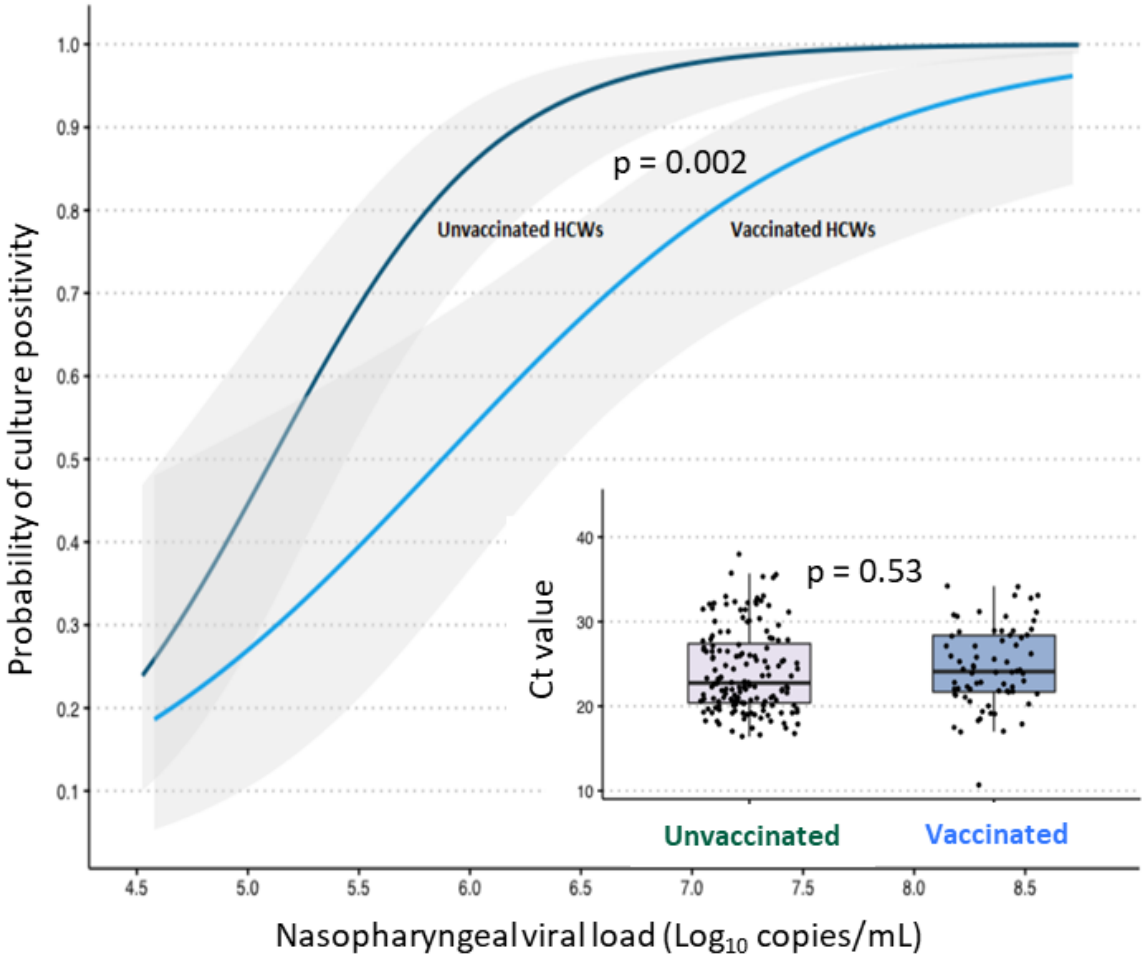


Sample	Number of Viral Mutations in Assay Target 2 Region	N1 Ct Value (no mutation)	N2 Ct Value
1	1	27.3	28.21
2	1	20.17	19.27
3	1	22.7	22.3
4	2	21.55	24.23
5	2	27.69	31.27
6	2	21.09	23.89

N1 and N2 give similar Ct values, even in the presence of one mutation (red arrow)

As mutations in N2 region increase from 1 to 2 mutations, Ct value between N1 and N2 starts to differ (red arrow and blue arrow)

Infections in Unvaccinated and Vaccinated Dutch Healthcare Workers



Data from the Dutch Healthcare Workers

- Unvaccinated: January to April 2020 → D614G
- Vaccinated: January to April 2021 → B.1.617.2

For the same Ct values, specimens from vaccinated persons with Delta variant **yielded less replication-competent virus**

- Suggests that despite more infectious variant, full vaccination improves neutralization of virus during infections in previously vaccinated persons
- In fully vaccinated persons, breakthrough infections may be less infectious

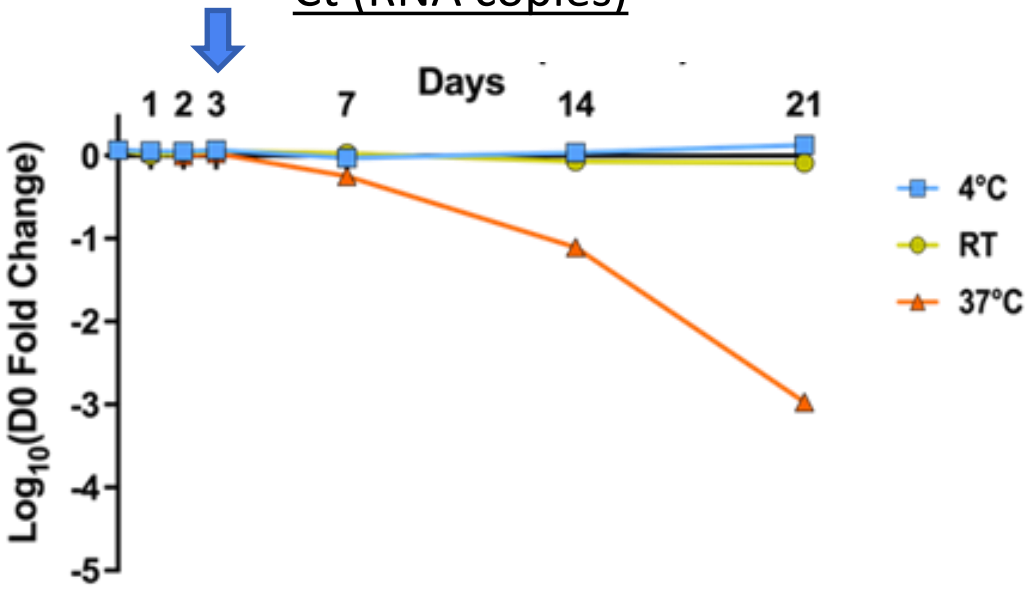
Shamier et al. 2021, medRxiv: Virological characteristics of SARS-CoV-2 vaccine breakthrough infections in health care workers (medrxiv.org).

Ct Does Not Always Correlate with SARS-CoV-2 Infectivity

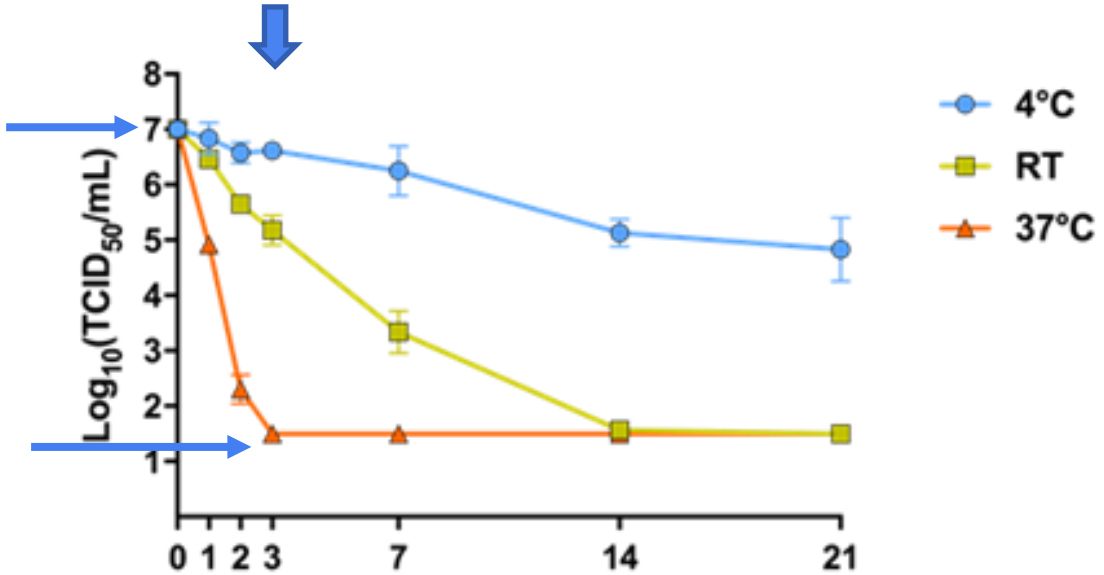
Comparing RNA copies determined by Ct with standard curve and infectivity under various conditions (e.g., D3 & D7)

- Day 3
  - Day 3 **Ct values equal** at all temperatures, yet there are **100,000 less infectious virus particles** at 37°C
  - Day 7 Ct very similar at 4 C and 37 C, but again **100,000 fewer infectious virus particles** at 37°C

Ct (RNA copies)



Infectious Virus Titer



Similar phenomenon also identified by Eyre *et al. The impact of SARS-CoV-2 vaccination on Alpha and Delta transmission. medRxiv* https://doi.org/10.1101/2021.09.28.21264260.

"Hence, observed viral loads [determined by Ct] may not be representative of viral loads at transmission"

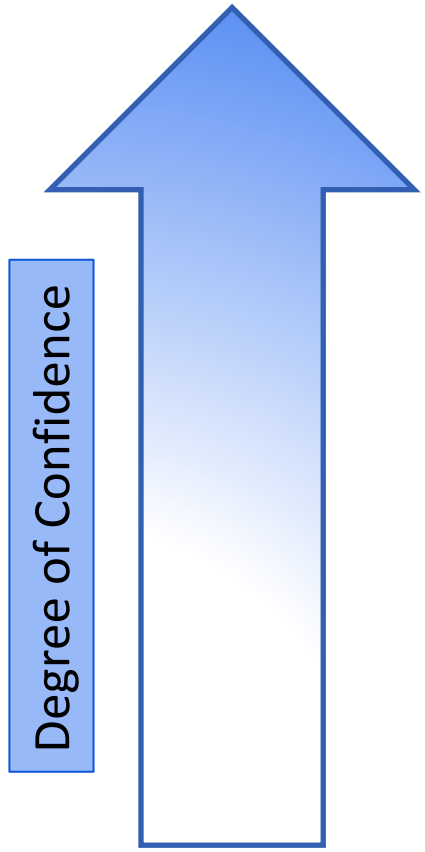
Ct Values and Estimating Genome Copies

- A standard can be used to improve the correlation between Ct and genome copies
  - NIBSC* manufactures an international standard
  - Can be utilized to calibrate assays Ct values to each other
  - Standard curves should be run regularly
  - Prospectively
  - Does not eliminate all caveats
  - Cannot be linked to infectiousness or transmissibility without additional data (e.g., culture)

*NIBSC: National Institute for Biological Standards and Control

How can Ct values be Used?

- Prospectively in quantitative assay
  - Use of molecular standard, standard curve
  - Monitoring of reproducibility, etc.
  - Sequencing
- When associated with other confirmatory lab data (i.e., culture)
- In groups as an estimate of viral load
  - Same assay should be used (or comparison standard)
  - Standardization of populations improves the correlation (sample type, symptom onset, symptomatic/ asymptomatic)

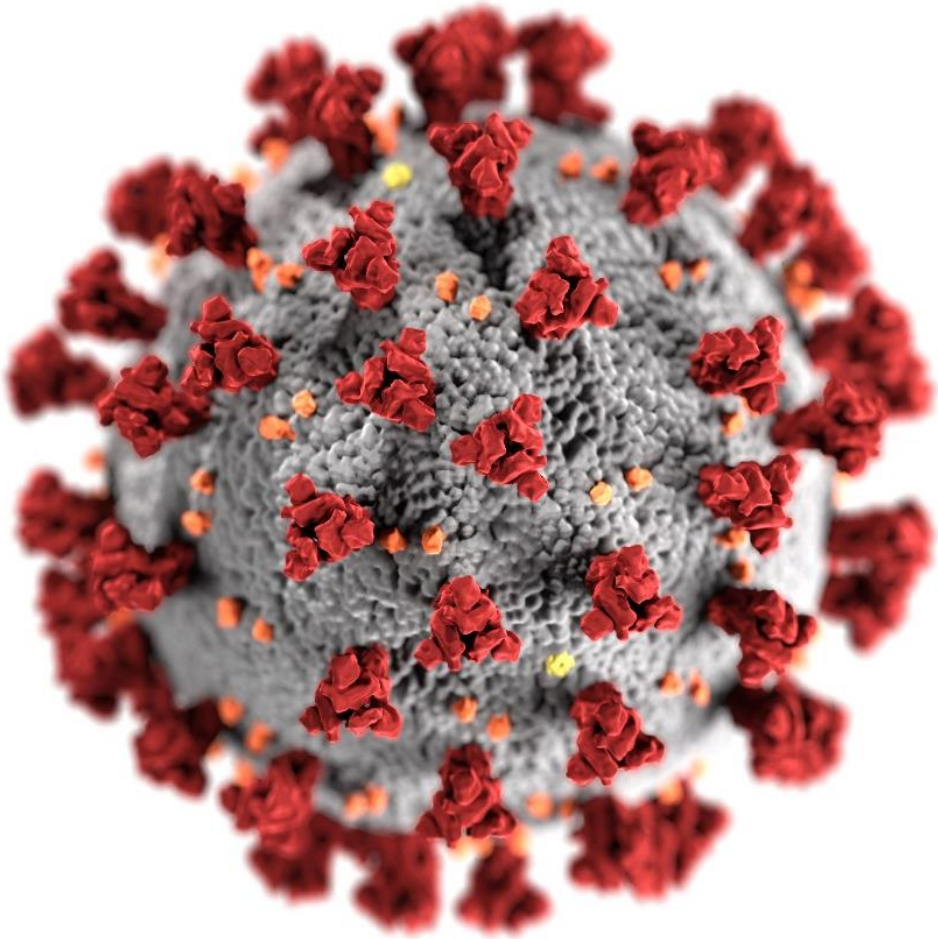


Ct values should not be used to estimate infectiousness without additional supporting data

Takeaways

- **Ct values are not a definitive measure of infectiousness**
- **Ct values can correlate with genome copy**
  - Study designed prospectively to minimize variability
  - Inferences can be strengthened by applying a standard/ standard curve especially at smaller sample sizes
- **Ct values can be used to compare data from populations or groups to infer general assumptions on viral load**
  - Ct values compared from the same test or standardized by a reference
  - Language used should be more suggestive not definitive
- **Typical diagnostic/clinical reporting of Ct values are difficult to administer and interpret**
  - Substantial technical barriers in diagnostic labs
    - Assay result capture is positive, negative, inconclusive, or invalid
    - Multiple assays are used which can introduce significant variability
  - Values generated can be greatly overinterpreted

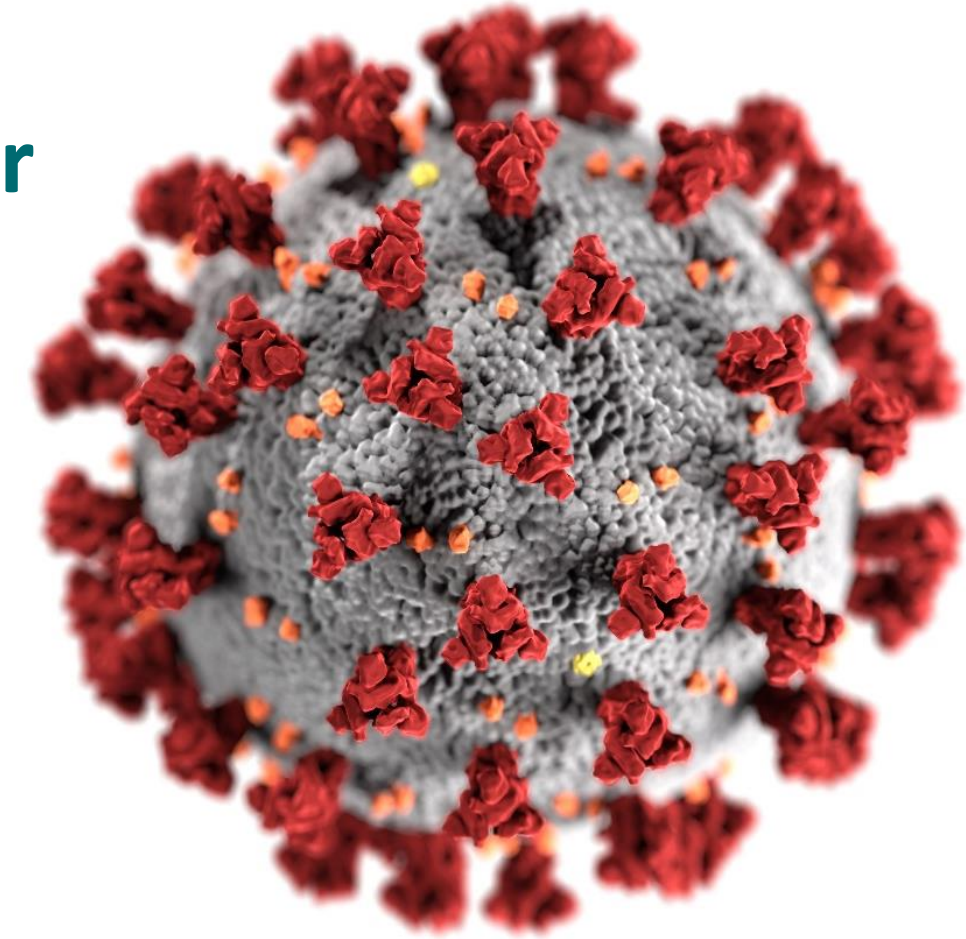
Thank you



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.

Utility of Genomic Sequencing for Public Health and Clinical Care



CDR Alison Laufer Halpin
December 9, 2021
Clinician Outreach and Communication Activity (COCA) Call

cdc.gov/coronavirus

Genomic Sequencing: Public Health

- A critical public heath activity to track SARS-CoV-2, the virus that causes COVID-19, and inform policy
- Ideally both representative and sensitive
  - A high probability that national genomic surveillance system will detect a variant circulating at very low levels

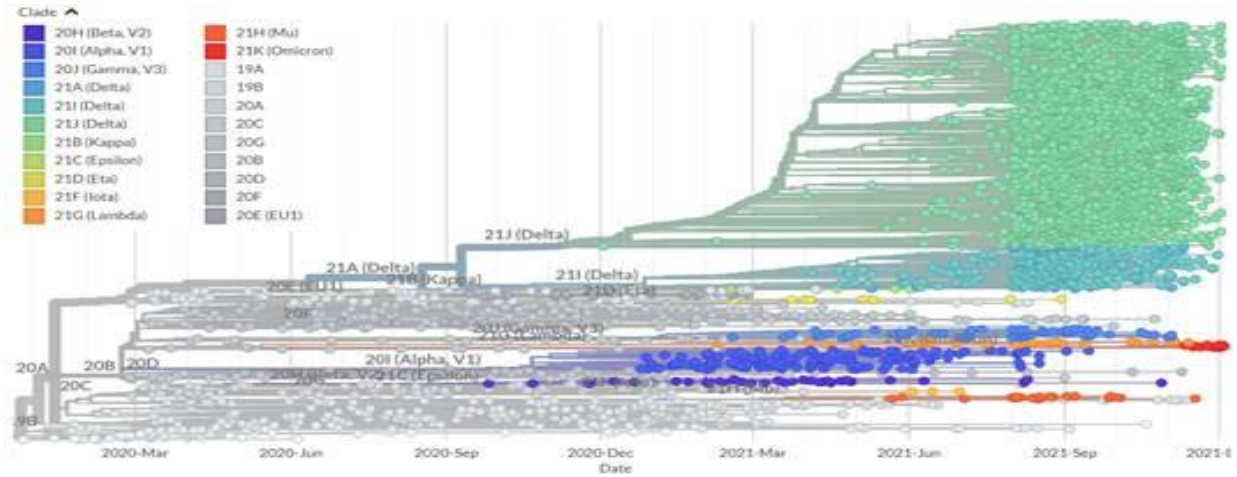


Figure from: https://nextstrain.org/ncov/gisaid/global

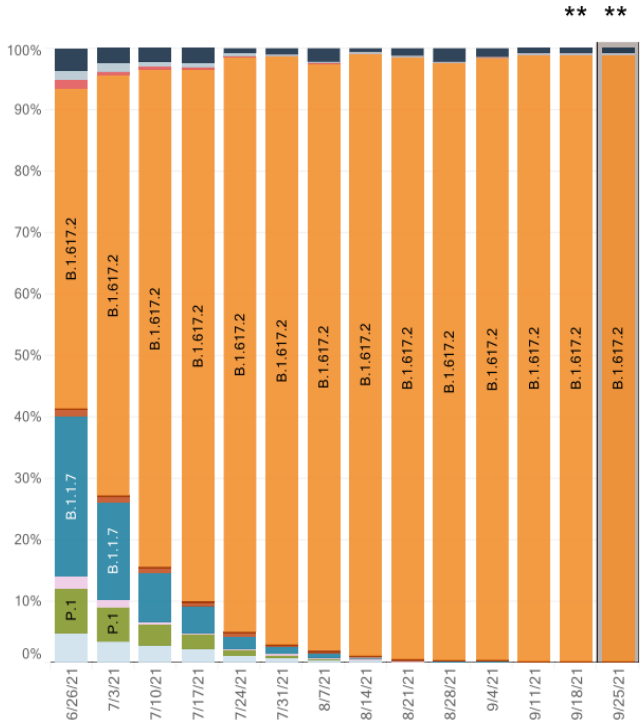
Genomic Sequencing: Public Health

- Surveillance using genomic sequencing supports:
  - Population-level molecular epidemiology
  - Detection of the introduction or evolution of new variants
  - Monitoring of:
    - Variant prevalences
    - Genomic mutations associated with resistance to therapeutics used for treatment and prevention of COVID-19
  - Building a repository of cultured viruses for sharing with partners and phenotypic characterization

Genomic Sequencing: Public Health

See: covid.cdc.gov/covid-data-tracker/#variant-proportions

United States: 6/20/2021 – 9/25/2021



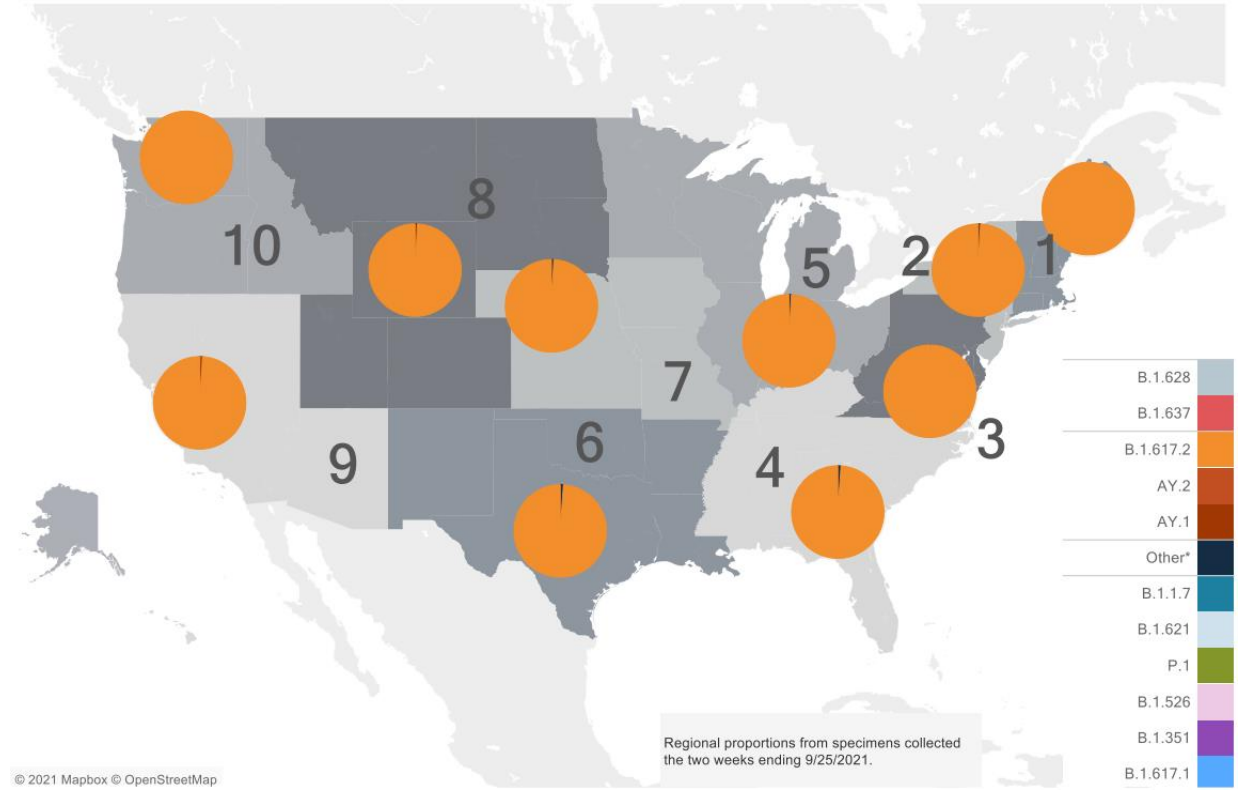
United States: 9/19/2021 – 9/25/2021 NOWCAST

USA

WHO Label	Lineage	US Class	%Total	95%PI
Alpha	B.1.1.7	VBM	0.0%	0.0-0.2%
Beta	B.1.351	VBM	0.0%	0.0-0.2%
Gamma	P.1	VBM	0.0%	0.0-0.2%
Delta	B.1.617.2	VOC	99.0%	97.9-99.8%
	AY.1	VOC	0.1%	0.0-0.5%
	AY.2	VOC	0.0%	0.0-0.2%
Iota	B.1.526	VBM	0.0%	0.0-0.2%
Kappa	B.1.617.1	VBM	0.0%	0.0-0.2%
Mu	B.1.621	VBM	0.0%	0.0-0.2%
N/A	B.1.628		0.0%	0.0-0.2%
	B.1.637		0.0%	0.0-0.2%
Other	Other*		0.9%	0.0-1.9%

* Enumerated lineages are VOI/VOC or are circulating >1% in at least one HHS region during at least one two week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.
** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates
# Sublineages of P.1, B.1.351 and B.1.621 are aggregated with the parent lineage and included in parent lineage's proportion. Q.1-Q.8 are aggregated with B.1.1.7. AY.3-AY.32 and their sublineages are aggregated with B.1.617.2.

United States: 9/19/2021 – 9/25/2021 NOWCAST



Genomic Sequencing: Public Health

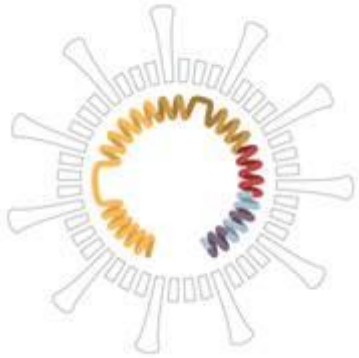
- Genomic sequencing requires days to weeks to complete and with present technology results are not available rapidly enough to direct therapeutic choices at the bedside
- However, monitoring genomic mutations is instrumental for informing *empiric recommendations* for treatment and prevention:
  - Monoclonal antibodies
  - Small molecule antivirals
- At present, available therapeutics* are distributed through the U.S. government based on prevalence of resistance mutations
  - See www.phe.gov/emergency/events/COVID19/therapeutics

* See https://www.phe.gov/emergency/events/COVID19/investigation-MCM/Documents/USG-COVID19-Tx-Playbook.pdf for details regarding ordering and administration of monoclonal antibodies for COVID-19 treatment and prevention

Genomic Sequencing: Self-knowledge Test

Genomic sequencing should be ordered for persons diagnosed with SARS-CoV-2 infection for the following reasons:

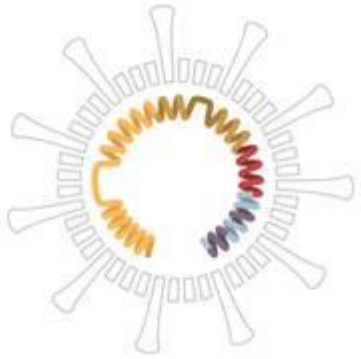
A. To determine which monoclonal antibody might be appropriate
B. To determine which small molecule antiviral might be appropriate
C. To inform recommendations for the length of isolation
D. To assess the need for higher level care
E. A, B, and D
F. None of the above



Genomic Sequencing: Self-knowledge Test

Genomic sequencing should be ordered for persons diagnosed with SARS-CoV-2 infection for the following reasons:

A. To determine which monoclonal antibody might be appropriate
B. To determine which small molecule antiviral might be appropriate
C. To inform recommendations for the length of isolation
D. To assess the need for higher level care
E. A, B, and D
F. **None of the above**

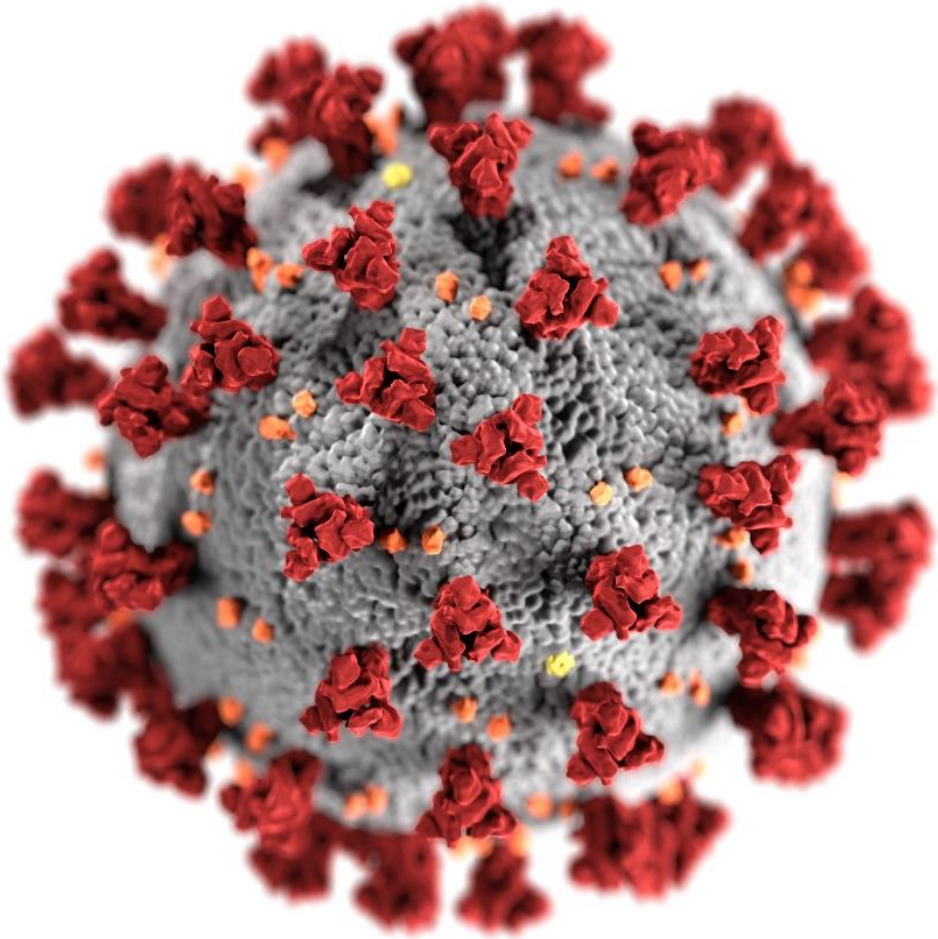


Genomic Sequencing: Clinical Care

- The time required between specimen collection and availability of genomic sequence data obviates the benefit of genomic sequencing for diagnostic purposes or for clinical management at the individual patient level
- The results of genomic sequencing of SARS-CoV-2 are not typically CLIA-validated or authorized by FDA*
- CDC and other public health laboratories only perform genomic sequencing for the following purposes:
  - Surveillance, investigations (e.g., outbreaks), research purposes
- Methods for near-real-time characterization of variants are under investigation

* In the US, *in vitro* diagnostic devices (including Laboratory Developed Tests) are regulated by two federal agencies: the Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS). The FDA regulates the safety and effectiveness of the diagnostic test, as well as the quality of the design and manufacture (under Food Drug and Cosmetics Act). CMS regulates the quality of clinical laboratories and the clinical testing processes under the Clinical Laboratory Improvement Amendments (CLIA). The CLIA regulations are intended to ensure that laboratory tests performed on human samples to diagnose, prevent, treat disease, or assess human health are accurate and reliable.

Thank you



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.

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Continuing Education

- All continuing education for COCA Calls is issued online through the CDC Training & Continuing Education Online system at https://tceols.cdc.gov/.

- Those who participate in today's COCA Call and wish to receive continuing education please complete the online evaluation by **January 10, 2022,** with the course code **WC2922-120921**. The access code is **COCA120921.**

- Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **January 11, 2022,** and **January 11, 2024,** and use course code **WD2922-120921**. The access code is **COCA120921.**

- Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CEs obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

Today's COCA Call Will Be Available to View On-Demand

- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage https://emergency.cdc.gov/coca/calls/2021/callinfo_120921.asp

**A transcript and closed-captioned video will be available after the original video recording posts at the above link.*

Upcoming COCA Calls & Additional COVID-19 Resources

- Continue to visit emergency.cdc.gov/coca to get more details about upcoming COCA Calls, as COCA intends to host more COCA Calls to keep you informed of the latest guidance and updates on COVID-19.

- Subscribe to receive notifications about upcoming COCA calls and other COCA products and services at emergency.cdc.gov/coca/subscribe.asp.

- Share call announcements with colleagues.

- Sign up to receive weekly ***COVID-19 Science Updates*** by visiting cdc.gov/library/covid19/scienceupdates.html?Sort=Date%3A%3Adesc.

Join Us On Facebook at

Thank you for joining us today!

emergency.cdc.gov/coca