COVID-19 Update

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Outline

- Questions
  - Travel restrictions
  - Efficacy of wearing masks
- Evaluation of symptomatic patients with negative SARS-COV-2 PCR

Questions

What travel restrictions should there be from an area with a large number of cases to one with few cases?

Interested in a summary of clinical trials attesting to the efficacy of wearing face masks to reduce the risk of infection from COVID-19

Travel within the US

If you are thinking about traveling away from your local community, ask:

Is COVID-19 spreading where you're going? *You can get infected while traveling*

Is COVID-19 spreading in your community? *Even if you don't have symptoms, you can spread COVID-19 to others while traveling*

Will you or those you are traveling with be within 6 feet of others during or after your trip? *Being within 6 feet of others increases your chances of getting infected and infecting others*

Are you or those you are traveling with more likely to get very ill from COVID-19? *Individuals who have an increased risk of severe illness from COVID-19 should limit their travel*

Do you live with someone who is more likely to get very ill from COVID-19? *If you get infected while traveling you can spread COVID-19 to loved ones when you return, even if you don't have symptoms*

If you get sick with COVID-19, will you have to miss work? *People with COVID-19 need to stay home until they are no longer considered infectious*

Does the state or local government where you live or at your destination require you to stay home for 14 days after traveling? *Some state and local governments may require people who have recently traveled to stay home for 14 days*

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Case by Case Evaluation vs. Blanket Recommendation

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Who will travel be reported to? Before? After? Both?

How will travel be reported? Email, phone? 24/7?

What type of leave will the employee have to use?

What if employees refuse or fail to report travel?

How will the recommendation be recorded?

What is the role of HR in this process? Medical staff?

What is the follow up process after quarantine?

A rapid systematic review of the efficacy of face masks and respirators against coronaviruses and other respiratory transmissible viruses for the community, healthcare workers and sick patients

Aim: Review the evidence around the efficacy of masks and respirators for healthcare workers, sick patients and the general public

→

A systematic review of randomized controlled clinical trials on use of respiratory protection by the 3 groups

→

19 randomized controlled trials were included – 8 in community settings, 6 in healthcare settings and 5 as source control

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7191274/pdf/main.pdf

Results: Masks in community, HCW, sick patients

In the community, masks appeared to be effective with and without hand hygiene, and both together are more protective

In healthcare workers – respirators, if worn continually during a shift, were effective but not if worn intermittently: Medical masks were not effective, and cloth masks even less effective

When face masks used by sick patients, randomized controlled trials suggested protection of well contacts

Conclusion: In the community, masks may be more protective for well people. In healthcare settings continuous use of respirators, is more protective compared to the medical masks, and medical masks are more protective than cloth masks. Depending on the fabric and design, some cloth masks may not be safe for healthcare workers. The use of masks by sick patients is likely protective, and coronaviruses can be emitted in normal breathing, in fine airborne particles.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7191274/pdf/main.pdf

NYC vs. U.S.

Contrasting the trends of new infections between NYC and the United States. Daily new confirmed infections in (A) NYC and (B) the United States. The dotted lines represent linear fitting to the data between April 17 and May 9 in NYC and between April 4 and May 9 in the United States. In B, the number in NYC was subtracted from that in the United States. The vertical lines label the dates for social distancing, stay-at-home orders, and mandated face-covering.
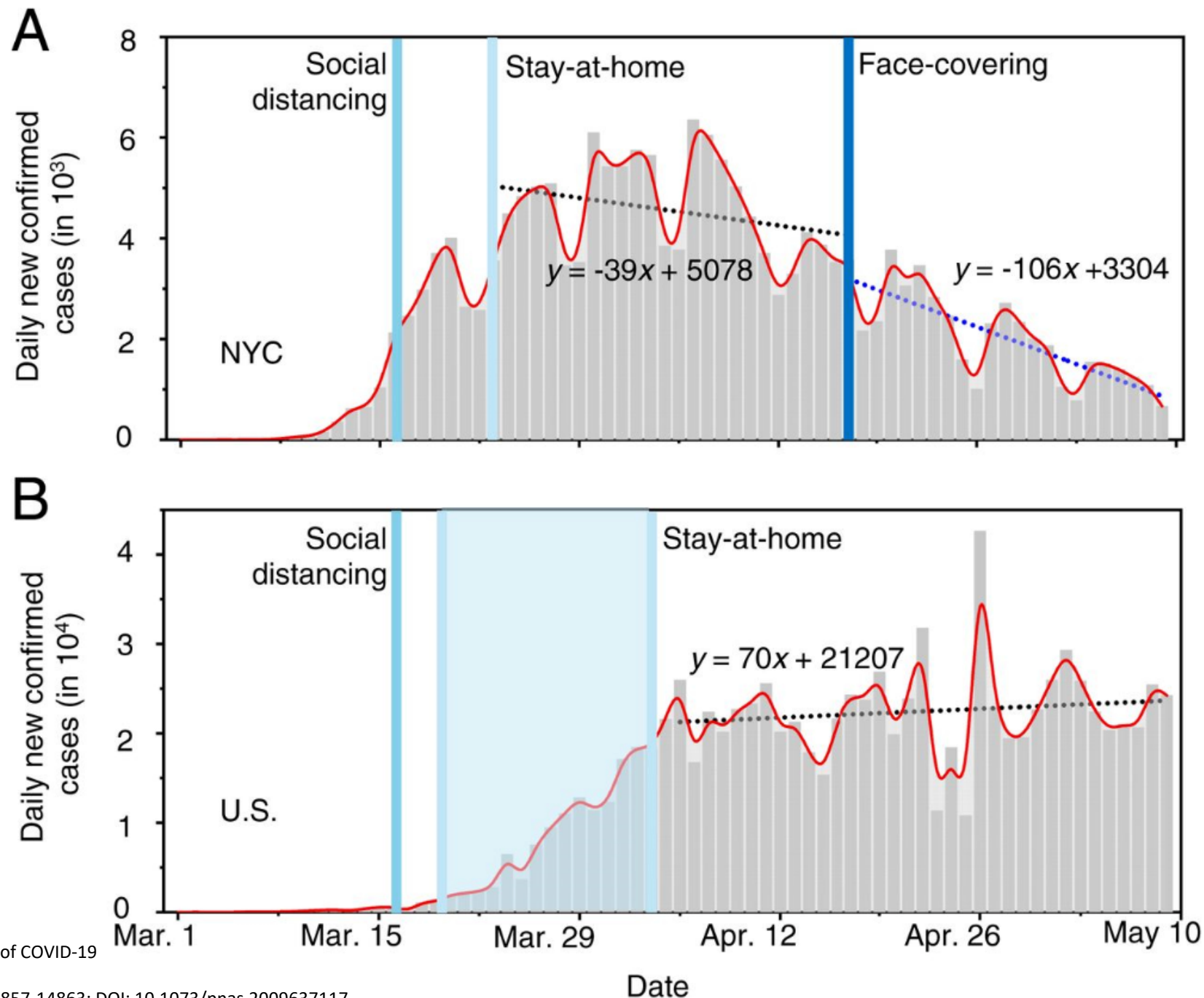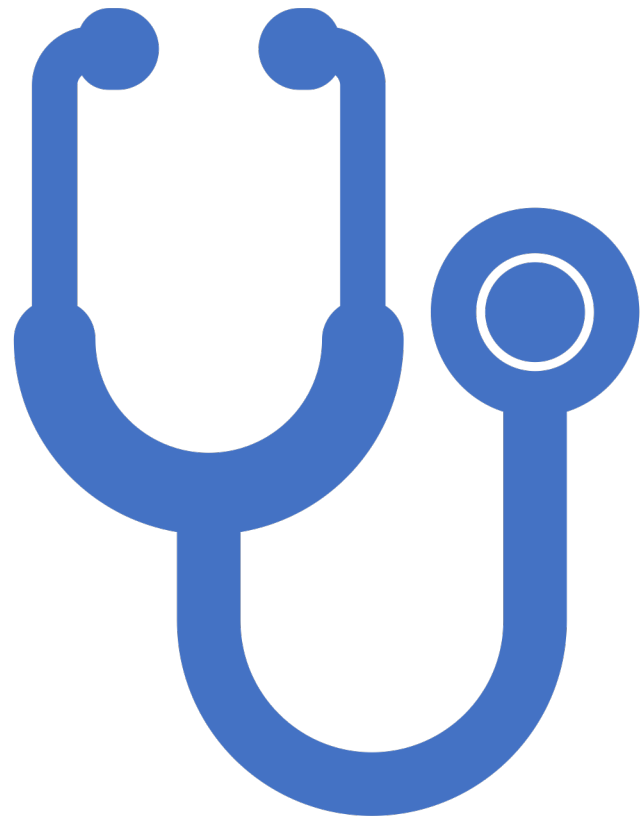
Evaluation of Symptomatic Patients with Negative SARS-COV-2 PCR

Primary Symptoms of COVID-19

Headache

Congestion or runny nose, new loss of taste or smell

Cough, sore throat

"Symptoms may appear **2-14 days after exposure** to the virus."

Fatigue, muscle or body aches, fever or chills

Shortness of breath or difficulty breathing

Nausea or vomiting, diarrhea
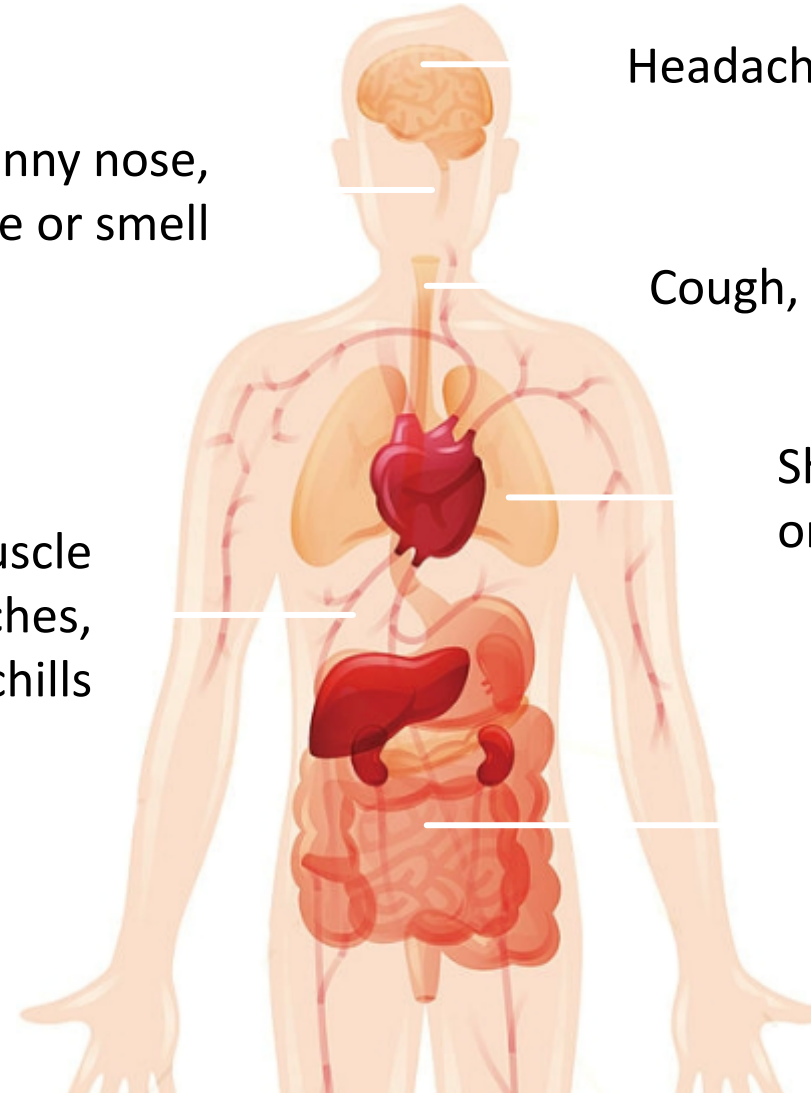
Which One of These Patients Is SARS-COV-2 PCR Positive?

Patient # 1, 44-year-old female
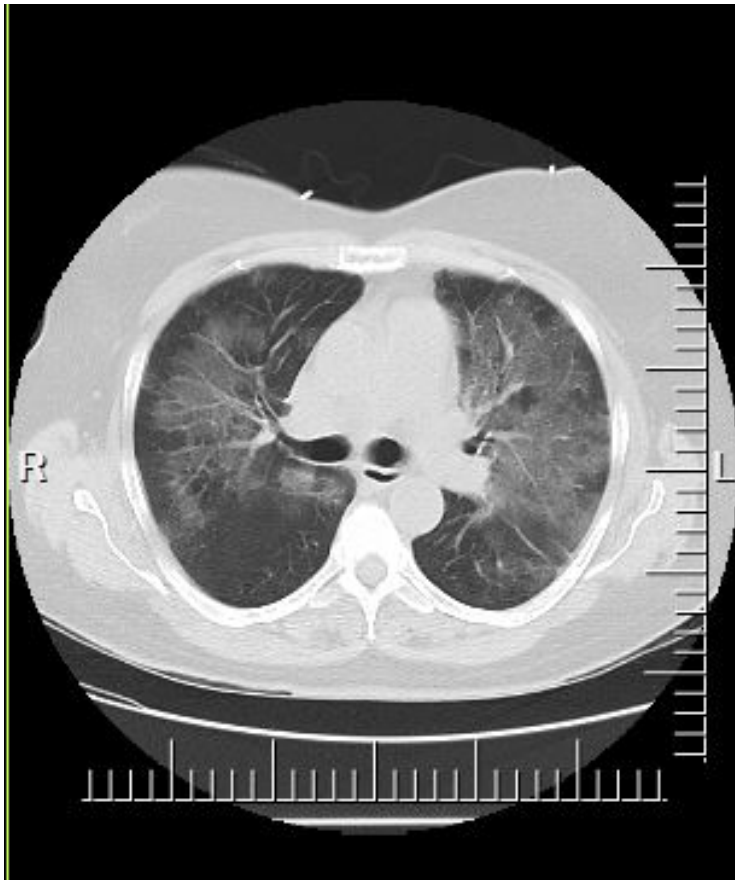
- One-day hx of SOB, cough, myalgias,
- DM, COPD
- Co-worker COVID positive
- Labs
  - Lymphopenia
  - D dimer: normal
  - PCT normal
  - CRP 77
  - CAP workup negative

SARS-COV-2 PCR NEGATIVE
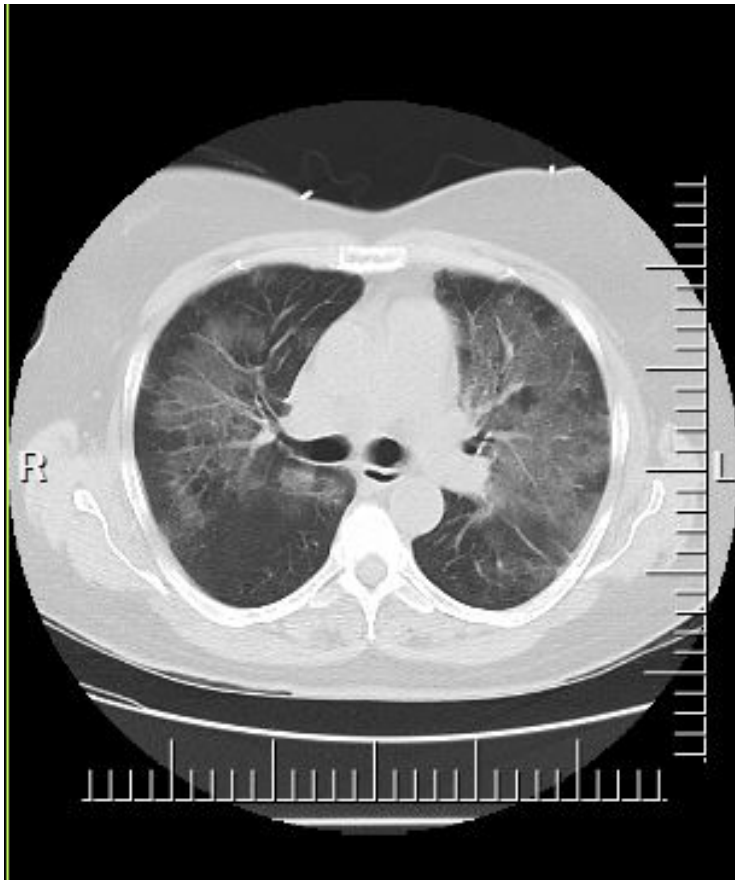
Patient # 2, 23-year-old male

- Four-day hx of SOB, cough, N/V/D and headache
- DM, Asthma
- Mother COVID positive
- Labs
  - No lymphopenia
  - D dimer: Elevated
  - PCT normal
  - CRP 82
  - CAP workup negative

SARS-COV-2 PCR POSITIVE

Which of These Patients has COVID-19?

Patient # 1, 54-year-old female

- One-day hx of SOB, cough, myalgias,
- DM, COPD
- Co-worker COVID positive
- Labs
  - Lymphopenia
  - D dimer: normal
  - PCT normal
  - CRP 77
  - CAP workup negative

Patient # 2, 18-year-old male

- Four-day hx of SOB, cough, N/V/D and headache
- DM, Asthma
- Mother COVID positive
- Labs
  - No lymphopenia
  - D dimer: Elevated
  - PCT normal
  - CRP 82
  - CAP workup negative

BY CASE DEFINITION BOTH PATIENTS HAVE COVID-19

WHO: Suspect Case Definition

A patient with acute respiratory illness (fever and at least 1 sign/symptom of respiratory disease, eg, cough, shortness of breath)

And 1 of the following:

A history of travel to or *residence in a location reporting community transmission* of SARS-CoV-2/ COVID-19 during 14 days prior to symptom onset	Contact with a confirmed or probable SARS-CoV-2–infected/ COVID-19 person in the 14 days prior to symptom onset	Requires hospitalization, with no alternative diagnosis that fully explains the clinical presentation

Usual FDA requirements for Diagnostics

Clinical Test Performance

Analytical test performance

- "Natural clinical specimens"
  - Entail patients undergoing an index test and a "reference standard" test that determines their true state.

- Analytic sensitivity indicates the likelihood that the test will be positive for material containing any virus strains and the minimum concentration the test can detect.

- Analytic specificity is the likelihood that the test will be negative for material containing pathogens other than the target virus.

Natural Test-Performance Studies

- **For a sick person**, the reference standard should be a clinical diagnosis, established by an independent panel unaware of the index-test results

  Clinical sensitivity = Positive index tests/ Positive "reference standard"

- **BUT**, under the EUAs, the FDA does allow clinical test performance by establishing the new test's agreement with an authorized RT-PCR test in known positive material from symptomatic people or "contrived specimens".*

- **Problems**

  – Use of either known positive or contrived samples may lead to overestimates of test sensitivity, since swabs may miss infected material in practice

  – Assessment of clinical sensitivity in asymptomatic people had not been reported for any commercial test as of June 1, 2020.

  * "Contrived specimens": produced by adding viral RNA or inactivated virus to leftover clinical material.

Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure

Methods

- 7 Studies reviewed
  - Data on RT-PCR by time since symptom onset or exposure among patients tested for SARS-CoV-2
  - 1263 Tests reviewed

- **Reference Standard**
  - Most studies did serial testing and required at least 1 positive RT-PCR result to consider a case confirmed.
  - Some studies also included probable cases as determined by a set of clinical criteria and most confirmed by positive for IgM or IgG SARS-CoV-2 antibodies

Probability of having a negative RT-PCR result given SARS-COV-2 Infection
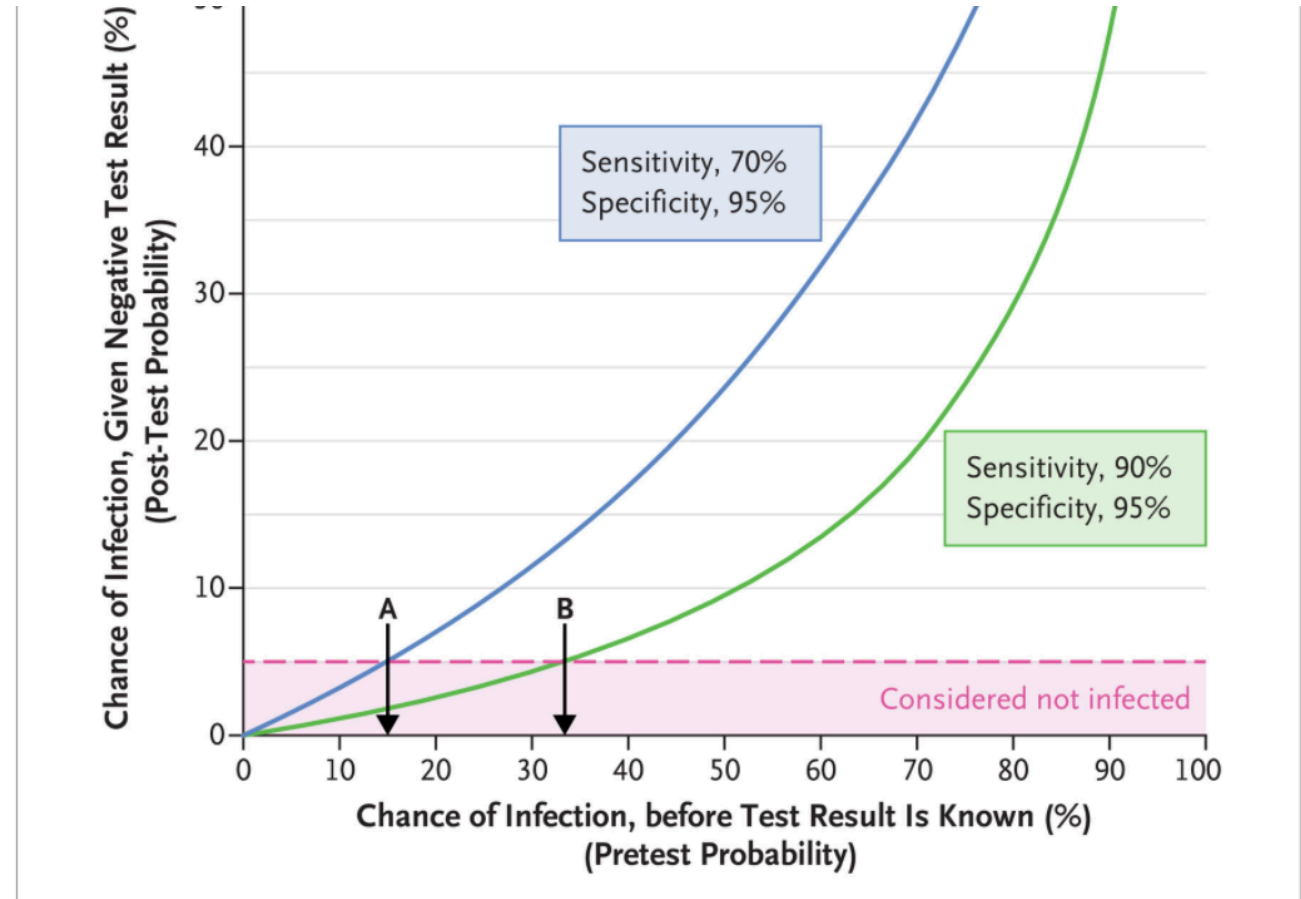

Ann Int Med, May 2020
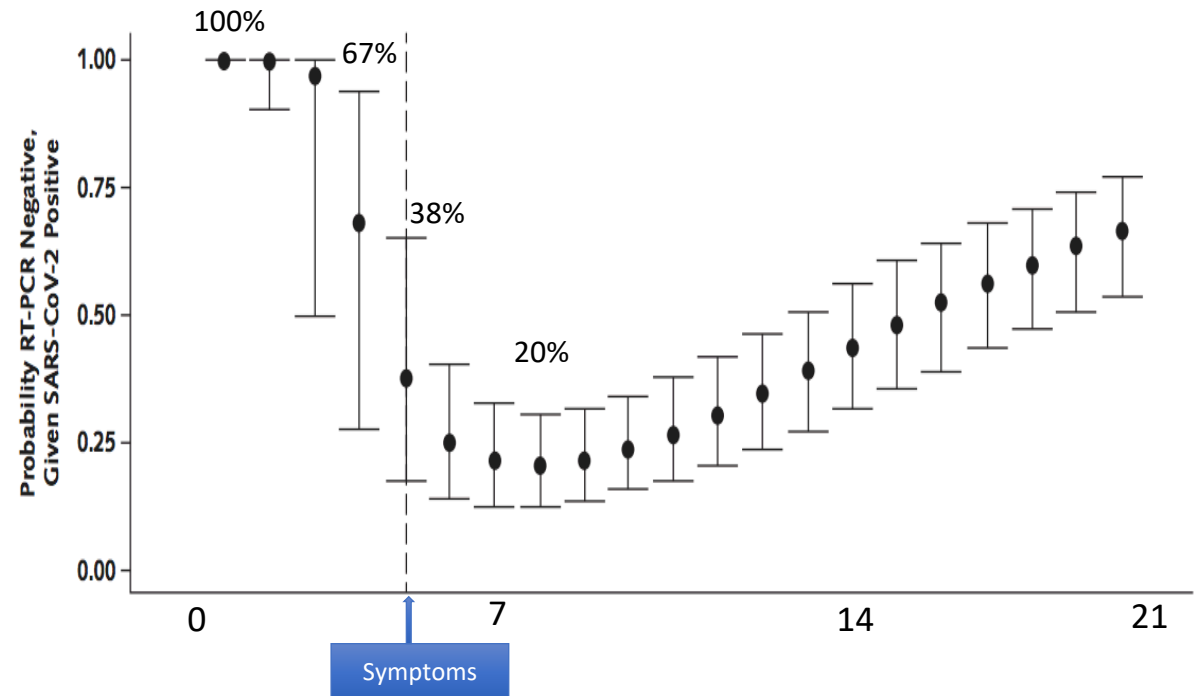
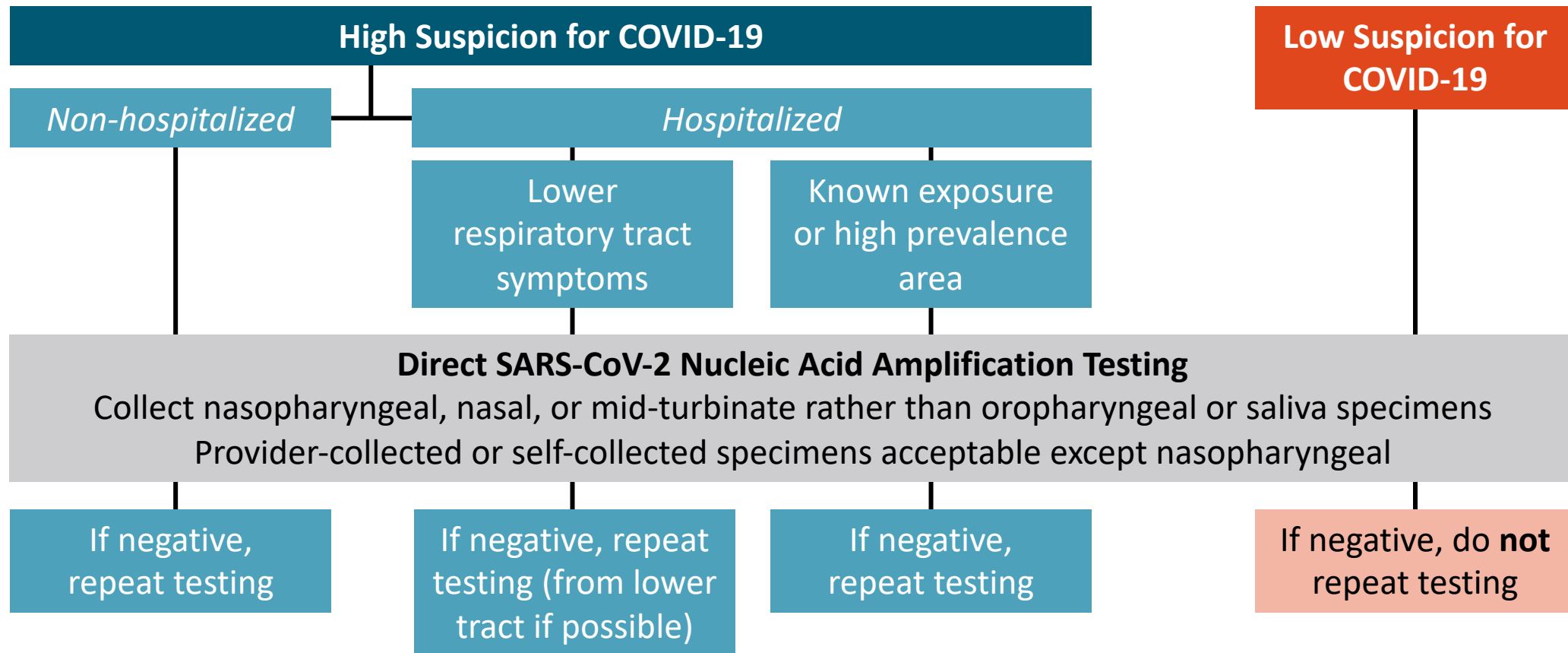# With imperfect tests, a negative result means only that a person is less likely to be infected.

- Bayes' theorem: To determine the likelihood of a person being infected you need information about both the person and the accuracy of the test .

    1. **Pretest probability**: Estimate of the person's chance of being infected

        Local Covid-19 prevalence

        SARS-CoV-2 exposure history

        Symptoms

    2. **Test sensitivity and specificity:**

        Measured in various clinically relevant real-life situations (e.g., varied specimen sources, timing, and illness severity).

False Negative Tests for SARS-CoV-2 Infection Challenges and Implications

- **Chance of SARS-CoV-2 Infection, Given a Negative Test Result, According to Pretest Probability.**The blue line represents a test with sensitivity of 70% and specificity of 95%. The green line represents a test with sensitivity of 90% and specificity of 95%. The shading is the threshold for considering a person not to be infected (asserted to be 5%). Arrow A indicates that with the lower-sensitivity test, this threshold cannot be reached if the pretest probability exceeds about 15%. Arrow B indicates that for the higher-sensitivity test, the threshold can be reached up to a pretest probability of about 33%. An interactive version of this graph is available at NEJM.org.

IDSA: SARS-CoV-2 Nucleic Acid Testing of Symptomatic Individuals

High Suspicion for COVID-19

Non-hospitalized

Hospitalized

Lower respiratory tract symptoms

Known exposure or high prevalence area

Low Suspicion for COVID-19

Direct SARS-CoV-2 Nucleic Acid Amplification Testing
Collect nasopharyngeal, nasal, or mid-turbinate rather than oropharyngeal or saliva specimens
Provider-collected or self-collected specimens acceptable except nasopharyngeal

If negative, repeat testing

If negative, repeat testing (from lower tract if possible)

If negative, repeat testing

If negative, do **not** repeat testing

Prioritize testing for symptomatic patients. If resources adequate, consider testing select asymptomatic individuals
(eg, exposed, immunosuppressive procedure, major time-sensitive surgery, aerosol-generating procedure with limited PPE).

Conclusions

- Diagnostic testing will help in safely opening the country, but only if the tests are highly sensitive and validated under realistic conditions against a clinically meaningful reference standard.

- FDA should ensure that manufacturers provide details of tests' clinical sensitivity and specificity.

- Test sensitivity in asymptomatic people is an urgent priority.

- Developing methods for estimating the pretest probability of infection for asymptomatic and symptomatic people is crucial.

- Negative results even on a highly sensitive test cannot rule out infection if the pretest probability is high, so clinicians should not trust unexpected negative results (i.e., assume a negative result is a "false negative" in a person with typical symptoms and known exposure).

NEJM, June 5

Management of a Symptomatic Patient with SARS-COV-2 Negative Test in the outpatient setting

HIGH PROBABILITY

- Known exposure to a confirmed COVID-19 case OR
- History/signs/symptoms consistent with COVID-19 with no alternative diagnosis
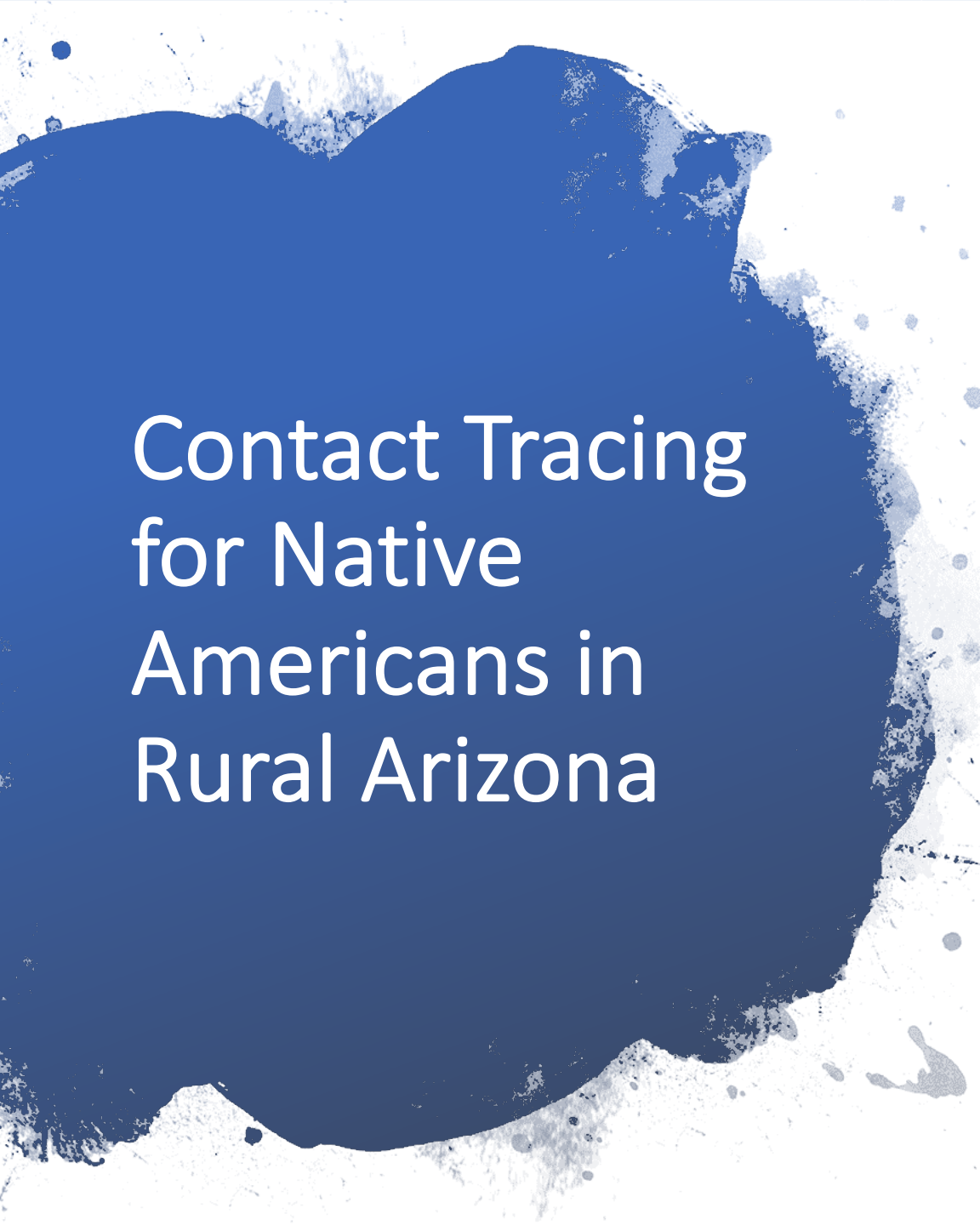- Isolation for 10 days is warranted

MODERATE PROBABILTY

- No known exposure
- History/signs/symptoms not clearly high or low probability.
- Consult Infectious Diseases, if not available consider as high probability

LOW PROBABILITY

- Alternative diagnosis much more likely than COVID-19 and
- No known exposure to confirmed case.
- Patient may return to work after symptoms resolve

Patients with asthma/COPD exacerbation, SOB, or abnormal chest imaging should **never** be coded as LOW PROBABILITY

Contact Tracing for Native Americans in Rural Arizona

"Covid-19 is a novel disease in need of novel approaches. But our experience has shown that there is no substitute for providing services according to the most basic principles of medicine and public health. In our current health care system, knocking on doors and talking to patients may be the most novel approach of all"

Ryan M. Close, M.D., M.P.H. Myles J. Stone, M.D., M.P.H.

Indian Health Service

Whiteriver, AZ