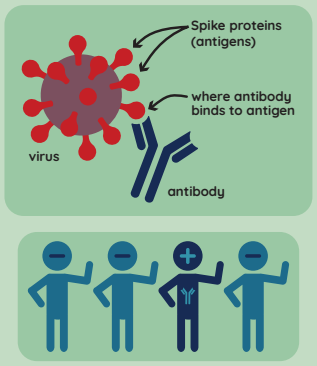
Stanford Medicine
COVID-19 Journal Club

Evaluating COVID-19 seroprevalence studies.

What is seroprevalence?

When a person is infected by a virus, their body makes **antibodies** that specifically recognize the virus's **antigens**. Antibodies persist after infection subsides and often protect a person against re-infection, but not always.

A **seropositive** person has a particular antibody, which indicates previous infection with that virus. Seropositivity can take days to weeks to develop after an infection starts. **Seroprevalence** is the % of seropositive people in a population.



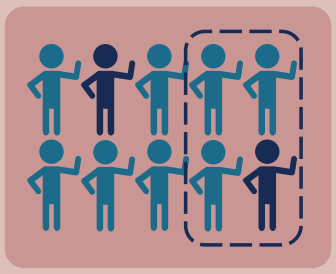
Why is determining seroprevalence useful?

Experts believe many people have been infected with SARS-CoV-2 but were not tested. Seroprevalence helps us estimate the number of people who have **ever** been infected, even if they no longer have the virus. This helps us answer:

- When & where did the pandemic spread?
- What percent of infected people die?
- How many people might be immune against re-infection?

Remember, antibodies don't always protect against re-infection. Scientists don't yet know if SARS-CoV-2 antibodies are protective.

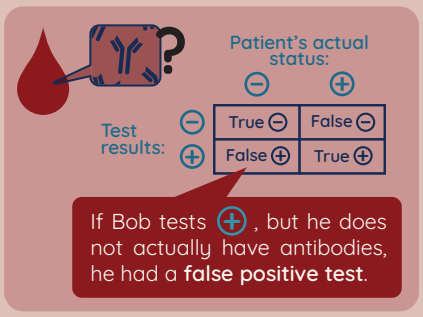
How are seroprevalence studies performed?



Recruit subjects...

...by selecting people from population databases, using existing blood bank donations, placing ads on websites, or recruiting passers-by in public.

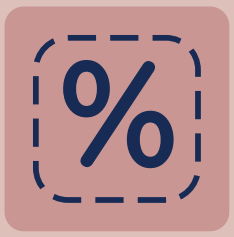
Ideally, different characteristics (i.e. age, gender, race, risk of COVID-19 exposure) are proportionally represented.



Detect antibodies in blood...

...using commercially available tests or custom laboratory methods.

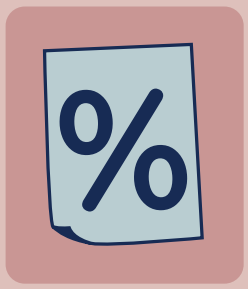
A reliable test should have low false-positive and false-negative rates.



Make statistical adjustments...

...on the % of apparently seropositive subjects to account for unequal representation of population characteristics, and/or the test's false-negative & false-positive rate.

If the representation is very unequal or the test is unreliable, it may not be possible to do this accurately.



Report results...

...ideally as a research publication, with method details and data that have been review by other experts. Due to urgency, many results are being reported via press release, press conference, or unreviewed preprints.

How can we assess a seroprevalence study's reliability and usefulness?

- ☐ Who was tested? Where? When? How many?
- ☐ Do the subjects represent the general population?
- ☐ Which test was used? Did the manufacturer report its reliability? Did the researchers themselves check the test's reliability?
- ☐ Which statistical corrections were applied?
  - ☐ For recruitment bias
  - ☐ For false negatives & positives
- ☐ How do the results compare to other numbers on the pandemic in that area?
  - ☐ # known deaths
  - ☐ # known cases

The goal is to use a recruitment method that will recruit a mix of people who accurately represent the general population in the study area.

People with recent symptoms or travel to certain countries are excluded from blood banks, so recruitment at a blood bank may **underestimate** seroprevalence.

Internet ads may attract people who know they are high-risk due to their occupation or other exposures, causing **overestimation**.

The false positive rate is especially important if the seroprevalence is low. A test with a high false positive rate could lead experts to think more people are seropositive than actually are, or that the virus isn't as deadly as it is.

Remember that seroprevalence estimates in the particular area where a study was done may not reflect the seroprevalence in a different city or state.

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