

Program Documentation: ScreeningTest.py: (Medical Screening Tests)

To Do

- # TO DO
- # - Create documentation including a documentation video and deploy it
- #
- # For final submission.
- # - Do hand calculations for verification.
- # - spell check comments to get rid of gross errors.
- # - check results carefully against another calculator.
- # - create an actual test case of a specific covid screening test.

How To View This Document.

You may want to **DOWNLOAD THIS PDF** file to read it in a good PDF viewer.

This document has a convenient PDF features such as index, searching, active links which will only be available in a full featured pdf viewer.

Contacts

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Program Purpose

This program evaluates the effect of disease prevalence on the accuracy of medical screening tests.

How To Run This Program

This program is run in a web page. Enter the link below in any major web browser.

The program will then instruct you on how to proceed.

<https://share.streamlit.io/profbrockway/screeningtest/main/screeningtest.py>

Project Files: Location

This document and all the project files are hosted at GitHub: [Project ScreeningTest.py At Github](#)

Program Verification

The outputs of this program have been verified by:

- (a) Hand calculations of critical numbers.
- (b) Comparison with the output of another Screening test calculator.

https://epidemiology.sruc.ac.uk/shiny/apps/predictive_values/

Conclusion

- The program successfully models the theoretical accuracies of a screening test.
- After reading around extensively in my humble opinion:
 - Medical screening tests should be treated with a high degree of skepticism.

Inputs

- A GUI in the form of a web page:
 - The user will enter the following medical test statistics.
 - Test sensitivity.
 - Test specificity.
 - Start of population disease prevalence range of interest.
 - End of population disease prevalence range of interest.
 - Disease "Prevalence Of Interest". AKA "Prior Probability Of Infection".
 - A text annotation to label the plots.
 - Population.

Outputs

- A printable report on the input and calculated results.
- An interactive graph with:
 - x axis. The specified range of disease prevalences.
 - y axis: Any or all of the following:
 - False positive percentage.
 - False negative percentage.
 - Positive predictive value.
 - Negative predictive value.
 - False Positives (NPV)
 - False Negatives (NPV)
 - The "general" accuracy (The suspect statistic).

The program permits the user to show or hide the variables to avoid clutter.
- A display of a data grid showing the data generated from the users input and used for the plots.
 - The most interesting entries will be highlighted. The grid will be fully scrollable.
- Error messages reporting errors in user's input.
- Standard webpage links to all documentation, code, error reporting, contacts etc.
- Optional downloads to users' computer:
 - The data grid as a CSV file with the plot data.
 - The data grid as an Excel file with the plot data.
 - The plot as an image.
 - The plot as an *interactive* html web page.

COVID 19: Background

Definitions:

- **"Screening test"** means the "antigen" type of quick result, at home Covid 19 screening tests.
- **"Prevalence"**: A COVID-19 case is counted as active and part of the disease population prevalence during the 14 days after it is *confirmed*. [Covid Tracker](#)
- **"Antigen Test"**: Antigen tests look for fragments of proteins that make up the SARSCoV-2 virus to determine if the person has an active infection. [Types Of Covid Test. Nice summary](#)

The Utility Of These Screening Tests Is Difficult To Quantify.

- **The following site summarizes the many problems with the tests:** [FDA](#)
There is high consumer demand for antibody tests to detect past infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but there is a great deal of uncertainty about what a positive test means immunologically., but [antigen tests] are of limited utility for individuals.

Uneven test accuracy and statistical challenges, especially in areas of low disease prevalence, further complicate use of antibody tests for individual decision making.
At 0.1% prevalence, the PPV would only be 4%, meaning that 96 out of 100 positive results would be false positives. [FDA](#)
- **There are very few studies of the prevalence of Covid 19 which makes the tests highly suspect.**
 - Where measurement is attempted the prevalence of Covid 19 is typically between 0% and 3%. This alone puts a large question mark over the results of these tests since the efficacy of the tests depend upon population prevalence. [PMAS](#) [FDA](#)
 - Highest prevalence as of Nov 2020 in UK: 1.25% to 3.09%. [Imperial College London](#)
 - Case Prevalence in USA is 0.002 of 1 percent in March 2021 (1/489) [Covid Tracker](#)
 - Case Prevalence in USA in June 2020 peak was 0.009 of a percent (1/107) [Covid Tracker](#)
 - The "Utah" Study. Prevalence very low: 0.003 ! [Utah Study](#)
Our own randomized viral testing was conducted in Utah between May 4th and July 1st, 2020 and estimates that the prevalence of COVID-19 in Utah was 0.27%. [0.027]. At the same time, our method predicts a median viral prevalence of 0.3% [0.003]
 - However most tests were calibrated by their manufacturers at 5% prevalence thus exaggerating accuracy. [EG](#)
- **The tests are released under emergency licenses and few of the manufacturer's claims of accuracy have been independently verified.** [FDA](#)
Eg: "has not been FDA cleared or approved; but has been authorized by FDA under EUA". [FDA](#)
(Click the "HCP" link attached to any of the tests listed at the FDA site).
One evaluation by the CDC of an approved test claiming to have a sensitivity of 99% proved to have a sensitivity of 35.8% in uninfected and asymptomatic groups. [CDC](#)
- **The manufacturers published sensitivity and specificity are not necessarily "real world".** [FDA](#).
Sensitivity and specificity estimates shown may not be indicative of the real world performance of the tests.
- **The tests are not diagnostic for covid 19.**
Antibody testing does not replace virologic testing and should not be used to establish the presence or absence of acute SARS-CoV-2 infection. [CDC](#)
- **The tests should not be used to decide on quarantining.**
An antibody test should not be used to determine the need for quarantine following close contact with someone who has COVID-19. [CDC](#)

- **The tests have difficulty detecting asymptomatic and presymptomatic cases (which are very common).** [CDC](#) This lowers the theoretical sensitivity of tests.

- Rapid antigen tests have received Food and Drug Administration (FDA) Emergency Use Authorization (EUA) for use in symptomatic persons, but data are lacking on test performance in asymptomatic persons to inform expanded screening testing to rapidly identify and isolate infected persons. [CDC](#)

- The rate of asymptomatic covid or presymptomatic cases in the general population is uncertain and studies report a wide range of percentages. Even the lowest estimate undermines the claimed reliability of the tests.

17% [JAMMI](#)

35% : [PNAS](#)

25% : [Nature](#)

50%: [PNAS](#)

56% [IJBS](#)

91% [Lancet](#)

98% [Shanghai](#)

- **The tests should not be used to determine immunity.** [CDC](#)

- **The tests may be less effective against new variants of Covid 19.** [FDA](#) [FDA2](#)

A Covid 19 Test Case

Details Of The Covid 19 Test Case

- As a test case we look at a typical over the counter "Covid Instant Test" being used by (say) students.
 - The Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 [Binax](#)
 - The test is available over the counter for home use: [CVS](#)
 - Manufacture Abbot's claimed "accuracy" in its advertisement.

According to studies, Abbott's BinaxNOW COVID-19 antigen self-test has an accuracy rate of for detecting Covid-19 infections, and 98.5% for correctly identifying Covid-19 negatives.
 - Binax is one of the few "emergency" approved tests that have been tested independently.
 - CDC Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2. [CDC](#)
the BinaxNOW antigen test had a sensitivity of 64.2% for specimens from symptomatic persons and 35.8% for specimens from asymptomatic persons. (Contrast this to the manufacturer's claim of sensitivity of 84.6%).
 - A scenario for the simulation on our software:
 - Imagine all the students at a university being tested on the first day of term.
The population is young and at very little risk from Covid 19.
 - A reasonable range for population prevalence for these tests is 0% to 3%.
 - Where measurement is attempted the prevalence of Covid 19 is typically 0% to 3%.
 - There are very few studies of the prevalence of Covid 19.
This alone puts a large question mark over the results of these tests since the efficacy of the tests depend upon population prevalence. [PMAS](#)
- Eg:
- "Highest prevalence" as Nov 2020 in UK: 1.25% to 3.09%. [Imperial College London](#)
 - Case Prevalence in USA is 0.002 of 1 percent in March 2021 (1/489) [Covid Tracker](#)
 - Case Prevalence in USA in June 2020 peak was 0.009 of a percent (1/107) [Covid Tracker](#)
However most tests were calibrated by their manufacturers at 5% prevalence thus exaggerating accuracy. [EG](#)
 - The "Utah" Study. Prevalence very low: 0.003 ! [Utah Study](#)
Our own randomized viral testing was conducted in Utah between May 4th and July 1st, 2020 and estimates that the prevalence of COVID-19 in Utah was 0.27%. At the same time, our method predicts a median viral prevalence of 0.3%
- Among the subset of students in the 0% to 3% with covid anywhere between 25% and 80% will be asymptomatic. The exact number is essentially very little understood. ([DTE](#)) ([JAMA](#)). Also if students have symptoms or fell unwell most tend to not attend. Among the uninfected and asymptomatic cases sensitivity is lower.
 - So we will test with these parameters.
 - Sensitivity: 50% (Between the CDC's (35.8%) - (64.2%).
 - Specificity: 99%.
 - Prevalence range of Interest: 0% to 3%.

Results Of The Covid 19 Test Case:

Between prevalence of 0% to 3% the percentage of false positives ranges from 100% to 40%.

This is hardly consistent with the manufactures claim:

A positive test result means it is very likely you have COVID-19 and it is important to be under the care of your healthcare provider. [Binax Insert](#)

In my opinion under these circumstances the testing is counterproductive.

REPORT ON YOUR SCREENING TEST

- _ In this test the disease prevalence varies from 0.00000 to 1.00000 .
- _ Test Sensitivity = 0.9900.
- _ Test Specificity = 0.9900.
- _ The Prevalence Of Interest = 0.030000.
- _ About 0.25 of all positives are false at a prevalence of 0.030000
- _ About 0.00 of all negatives are false at a prevalence of 0.030000.
- _ Positive Predictive Value (PPV) = 0.7538.
- _ Negative Predictive Value (NPV) = 0.9997.
- _ Plot Prevalence Start = 0.00000.
- _ Plot Prevalence End = 1.00000.
- _ Population = 100.

Active Plot Of The Test Case

(Double click to open)



activeplot2 (2).html

Data Table of the Test Case

(Double click to open)



Microsoft Excel
97-2003 Worksheet

- Most of the tests have not been tested on emerging variants. [Lucira Example](#)
The performance of this test was established based on the evaluation of a limited number of clinical specimens. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation.
- Sensitivity of tests drops dramatically with asymptomatic subjects. [CDC](#)
 - So, for example, testing large groups of apparently healthy students at schools would probably produce more hysteria and hypochondria than usable information.

FDA description of how to calculate the tests stats

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/statistical-guidance-reporting-results-studies-evaluating-diagnostic-tests-guidance-industry-and-fda>

- Screening Tests For Covid are "Rapid antigen tests".

Health care providers typically rely on molecular tests, particularly when people have COVID-19 symptoms, whereas antigen testing is often used when quick results are needed or for general screening and surveillance.

<https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html#:~:text=The%20U.S.%20Food%20and%20Drug,which%20indicates%20current%20viral%20infection.>

- antigen tests perform best when subject is positive.

FDS BIAS in sens and spec

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/statistical-guidance-reporting-results-studies-evaluating-diagnostic-tests-guidance-industry-and-fda>

Simply increasing the overall number of subjects in the study will do nothing to reduce bias.

approved at home tests

https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/home-otc-covid-19-diagnostic-tests?utm_medium=email&utm_source=govdelivery#list

<https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/covid-19-test-uses-faqs-testing-sars-cov-2>

Screening for COVID-19 is looking for occurrence at the individual level even if there is no individual reason to suspect infection such as a known exposure. This includes broad screening of asymptomatic individuals without known exposure with the intent of making individual decisions based on the test results. Screening tests are intended to identify infected individuals prior to development of symptoms or those infected individuals without signs or symptoms who may be contagious, so that measures can be taken to prevent those individuals from infecting others. FDA regulates screening tests as in vitro diagnostic devices and has provided recommendations and information regarding EUA requests for COVID-19 screening tests in the EUA templates referenced in the Policy for Coronavirus Disease-2019 Tests. Examples of screening include testing plans developed by a workplace to test all employees returning to the workplace regardless of exposure or signs and symptoms and testing plans developed by a school to test all students and faculty returning to the school regardless of exposure or signs and symptoms, with the intent of using those results to determine who may return or what protective measures to take on an individual basis.

Should SARS-CoV-2 antibody test results be used to assess whether or not a person is protected from COVID-19? (02/24/22)

A: No, antibody testing should not be used to assess immunity to COVID-19. More research is needed to understand what antibody test results can tell us, both in people who have been infected with SARS-CoV-2 and in people who have received a COVID-19 vaccination. While a positive antibody test result can be used to identify SARS-CoV-2 antibodies in a person's body, it should not be used to evaluate a person's level of immunity or protection from COVID-19 at this time.

CDC guidance on screening tests for covid

<https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html>

Antibody testing is not currently recommended to assess for immunity to SARS-CoV-2 following COVID-19 vaccination, to assess the need for vaccination in an unvaccinated person, or to determine the need to quarantine after a close contact with someone who has COVID-19.

CDC about screening tests ALSO LIST OF TESTS WITH THEIR SENS AND SPEC

they state the ppv and npv at prev = 5% unrealistically high.

<https://open.fda.gov/apis/device/covid19serology/>

Important caveats

Sensitivity and specificity estimates shown may not be indicative of the real world performance of the tests.

POP PREV NOT KNOWN !!!

<https://www.pnas.org/doi/10.1073/pnas.2026412118>

In epidemiology, "prevalence" is the fraction of a population **currently** infected, and "incidence" is the fraction of susceptible people infected in a unit of time. Prevalence tells us the size of the infected group and, in some circumstances, gives us information about the size of the susceptible group. Incidence describes the rate of spread.

InteliSwab COVID-19 Rapid Test - Instructions for Use Healthcare Provider

approved by fda

<https://www.fda.gov/media/149911/download>

- The product has not been FDA cleared or approved; but has been authorized by FDA under EUA.

list of quick at home tests

<https://www.nytimes.com/wirecutter/reviews/at-home-covid-test-kits/>

BINAX rapid test THIS IS OUR TEST CASE

It's a big selling rapid at home test. It's one of the few that the CDC has tested (Emergency FDA licenses have mostly not been evaluated by the government). It's claimed stats are massively more than the CDC found. CDC found spec ranging between .642 and .358. really low. Even this was with a very high prev= 0.087 !!!!

Claimed: ??

evaluation:

<https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e3.htm>

BinaxNOW antigen test had a sensitivity 52.5% https://www.cdc.gov/mmwr/volumes/70/wr/mm7003e3.htm#T2_down

The results of the current evaluation differ from those of an evaluation of the BinaxNOW antigen test in a community screening setting in San Francisco (7), which found a BinaxNOW antigen test overall sensitivity of 89.0% among specimens from all 3,302 participants, regardless of the Ct value of the real-time RT-PCR-positive specimens.

The prevalence of having SARS-CoV-2 real-time RT-PCR positive test results in this population was moderate (**8.7% overall; 4.7% for asymptomatic participants**); administering the test in a lower prevalence setting will likely result in a lower PPV.

SCREENING TESTS NOT WORKING

<https://www.sciencedirect.com/science/article/pii/S0966842X20302808>

Antibody tests should not be used for individual decision making at this time. This paper describes why this is the case: (i) antibody test results may be inaccurate without multiple sequential testing due to low disease prevalence and statistical limitations; (ii) many tests on the market are not of good quality, leading to inaccurate results; (iii) it is unknown whether past exposure to SARS-CoV-2 leads to durable immunity or if reinfection is possible; and (iv) it is unknown whether transmission is possible even if reinfection does not lead to clinical symptoms.

if the disease is of low prevalence. This has to do with the predictive value, also referred to as the 'base rate fallacy,' which takes into account both test performance and the background population prevalence of disease.

list of tests with their sens/spec

<https://www.centerforhealthsecurity.org/covid-19TestingToolkit/serology/Serology-based-tests-for-COVID-19.html>

CDC recommended quick tests

<https://www.cdc.gov/coronavirus/2019-ncov/testing/self-testing.html>

Nice summary

<https://medical.mit.edu/faqs/faq-testing-covid-19>

<https://www.verywellhealth.com/coronavirus-antibody-test-uses-4844950>

A LOW DISEASE PREVALENCE

https://bfi.uchicago.edu/wp-content/uploads/2020/07/BFI_WP_202054_Revised2.pdf

We use recent Covid-19 serology studies in the US, and show that the parameter confidence set is generally wide, and cannot support definite conclusions. Specifically, recent serology studies from California suggest a prevalence anywhere in the range 0%-2% (at the time of study), and are therefore inconclusive. However, this range could be narrowed down to 0.7%-1.5% if the actual false positive rate of the antibody test was indeed near its empirical estimate (~0.5%).

FDA Approving crap tests

https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2020/200618-serosurvey-strategy.pdf

The FDA, NIH, CDC, and NCI should release the results of their antibody test validation study. Validation of serological tests is critical to ensuring that the tests perform as they are intended, and a lack of validation has led to a patchwork of false positives and false negatives across the country, interfering with estimates of seroprevalence. Currently, tests need to be internally validated for EUA submission. Upon EUA submission, the manufacturer now must also submit the test for independent validation through institutes such as the NCI. Currently approved tests must also submit their kits for independent validation. Outside studies, typically in academic settings, have found discrepancies between the accuracy claimed by the manufacturer and their independent tests.

Very low prevalences

<http://www.nathanseegert.com/papers/Yang2020a.pdf>

Our own randomized viral testing was conducted in Utah between May 4th and July 1st, 2020 and estimates that the prevalence of COVID-19 in Utah was 0.27%

At the same time, our method predicts a median viral prevalence of 0.3%

VERY LOW PREVALENCES> This could be my source

<https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1009374>

As of December 31, 2020, we estimate nation-wide a prevalence of 1.4% [Credible Interval (CrI): 1.0%-1.9%] and a seroprevalence of 13.2% [CrI: 12.3%-14.2%], with state-level prevalence ranging from 0.2% [CrI: 0.1%-0.3%] in Hawaii to 2.8% [CrI: 1.8%-4.1%] in Tennessee, and seroprevalence from 1.5% [CrI: 1.2%-2.0%] in Vermont to 23% [CrI: 20%-28%] in New York. Cumulatively, reported

cases correspond to only one third of actual infections. The use of this simple and easy-to-communicate approach to estimating COVID-19 prevalence and seroprevalence will improve the ability to make public health decisions that effectively respond to the ongoing COVID-19 pandemic.

(But remember that what matters is not the prevalence of a disease in the population,
but the proportion among tested people who actually have the disease.)

ALARMIST STATEMENTS ABOUT TESTING

<https://finance.yahoo.com/news/omicron-testing-failure-134504476.html>

#####

ScreeningTest: TESTING

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#

- You can verify the results of this program at

<https://epitools.ausvet.com.au/predictivevalues>

#

- This file has a built in driver so we can test without a separate driver

file.

#

#####

ScreeningTest: SPECIFIC TEST CASE USING REAL DATA

#####

#

THE EFFECT OF DISEASE PREVALENCE ON THE EFFICACY OF SCREENING TESTS

Medical screening Tests vaunted with very high 'Overall accuracy' can give

staggering levels of false results when the prevalence of a disease is low.

This program explores the effect the prevalence of an infection in a

population on the usefulness of screening tests. The goal is to

demonstrate that screening tests are complex and less reliable

than commonly supposed.

#

NIH report on Spec and Sens of screening tests.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8220942/>

Screening tests are 2 types

Lateral flow antigen" test or "rapid antigen" test

#

THE "OVERALL ACCURACY OF A SCREENING TEST

The "Overall Accuracy" is the measure sometimes (IMHO) creates a

impression that a screening test is useful when

in fact it is dangerously misleading.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1492250/>

CASE PREVALENCE

Case prevalence measures the number of active COVID-19 cases in a

state as a percentage of the state's population.

A COVID-19 case is counted as active during the 14 days after it

is confirmed.

Case Prevalence in USA is 0.002 of 1 percent in March 2021 (1/489)

Case Prevalence in USA in June 2020 peak was 0.009 of a percent (1/107)

<https://covid-tracker.mckinsey.com/prevalence>

THE PREMISE OF MY PROJECT CONFIRMED BY THE FDA.

"At 0.1% prevalence, the PPV would only be 4%, meaning that 96 out

of 100 positive results would be false positives. the following link confirms the above tracker link.

<https://www.fda.gov/medical-devices/letters-health-care-providers/potential-false-positive-results-antigen-tests-rapid-detection-sars-cov-2-letter-clinical-laboratory>

Google

fda medical devices letters health care providers potential false positive results
#

PREVALENCE NOT KNOWN

<https://academic.oup.com/ectj/article/25/1/1/6325165>

Prevalence of a novel infection like SARS-CoV-2 (the virus causing COVID-19 disease) **is a quintessential missing data problem**. Only a small subset of the population has been tested, this subset is almost certainly selective; we do not even know the accuracy of tests, and our understanding of the pandemic is vague enough so that we might not want to overly rely on heavily parameterized models.

PREVALENCE 1.9 FROM SERO STUDIES.

<https://www.sciencedirect.com/science/article/pii/S1047279722000369>

Prevalence Studies Rare

Measuring Prevalence of the Coronavirus

February 24, 2021 <https://www.pnas.org/doi/10.1073/pnas.2026412118#sec-2>

At the time of this writing there are few published, population-representative COVID-19 prevalence studies. In a recent review Franceschi et al. list 37 (5). Two in North America are the state of Indiana (6) and the state of Connecticut (7) in the United States. In addition to these, the state of Ohio Department of Health released results from a prevalence study conducted in that state during July 2020 (8, 9). Two important challenges affected many of these studies.

Highest prevalence yet November 2020 (2021 1.25% to 3.09%

<https://www.imperial.ac.uk/news/231715/react-study-records-highest-coronavirus-prevalence/>

For this latest round of the REACT study, 67,208 people swabbed themselves at home and their samples were analysed by PCR testing. 1,021 of these were positive, giving an overall weighted prevalence of 1.72%. Weighting is where the researchers make adjustments to their calculations to ensure the sample reflects England's population.