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Bayesian Approach on COVID-19 test results

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ABSTRACT

Clinical trials are very expensive and their outcomes are crucial to the target population, concerned stakeholders and, hence, there is considerable pressure to optimize them. One route of optimization is to make better use of all available information, and Bayesian statistics provides this opportunity.

Considering the current situation with Polymerase Chain Reaction (PCR) testing for COVID-19, false negative tests are particularly concerning, potentially leading to an inappropriate sense of security regarding infectivity. To accurately interpret test results, one needs to know the positive and negative predictive values of a test in the setting applied, which depend on its sensitivity and specificity, along with prevalence or pre-test probability. Bayes theorem can be applied to the interpretation of negative PCR results in patients with suspected COVID-19 infection.

Through this presentation we will understand how the Bayesian approach can enhance the design of the clinical trial and its usefulness in near future.

INTRODUCTION

Two statistical methodologies are applicable to the design and analysis of clinical trials: Frequentist and Bayesian. Most traditional clinical trial designs are based on frequentist statistics.

In frequentist statistics prior information is utilized formally only in the design of a clinical trial but not in the analysis of the data. It tests whether an event (hypothesis) occurs or not. It calculates the probability of an event in the long run of the experiment.

However, Bayesian statistics is a theory in the field of statistics based on the Bayesian interpretation of probability where probability expresses a degree of belief in an event. The degree of belief may be based on prior knowledge about the event, such as the results of previous experiments, or on personal beliefs about the event.

In other words, Bayesian statistics starts with a prior belief (expressed as a prior distribution), which is then updated with the new evidence to yield a posterior belief (also a probability distribution). It provides a mathematical method for calculating the likelihood of a future event, given the knowledge from prior events. These methods, thus, directly address the question of how new evidence should change what we currently believe. Posterior probabilities are updated via Bayes' theorem on the basis of accumulated data.

The flexibility of the Bayesian approach allows for building designs of clinical trials that have good properties of any desired sort. Examples include maximizing effective treatment of patients in the trial, maximizing information about the slope of a dose–response curve, minimizing costs, minimizing the number of patients treated, minimizing the length of the trial and combinations of these utilities.

BAYES' RULE FOR BAYESIAN INFERENCE

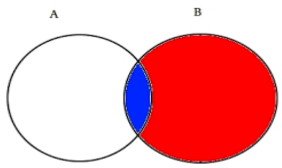
$P(\theta|D)=P(D|\theta)P(\theta)/P(D)$

Where:
$P(\theta)$ is the Prior.
$P(\theta|D)$ is the Posterior.
$P(D|\theta)$ is the Likelihood.
$P(D)$ is the Marginal Likelihood.

Bayes Rule begin by considering the concept of Conditional Probability.

P(A|B)=P(A ∩ B)/P(B)

The probability of A given B turns out to be $\frac{Blue\ Area}{Red\ Area+Blue\ Area}$



BAYESIAN APPLICATION IN COVID-19

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. We all know that Coronavirus Disease (COVID-19) outbreak as a pandemic and reiterated the call for countries to take immediate actions and scale up response to treat, detect and reduce transmission to save people's lives.

COVID-19 can provisionally be diagnosed on the basis of symptoms and confirmed using reverse transcription polymerase chain reaction (RT-PCR) or other nucleic acid testing of infected secretions. interpreting the results of PCR assays from nasal and pharyngeal swabs is crucial. With PCR testing for COVID-19, false negative tests are particularly concerning, potentially leading to an inappropriate sense of security regarding infectivity.

To accurately interpret test results, one needs to know the positive and negative predictive values of a test in the setting applied, which depend on its sensitivity and specificity, along with prevalence or pre-test probability.

No test gives a 100% accurate result; tests need to be evaluated to determine their sensitivity and specificity.
Sensitivity is the proportion of patients with the disease who have a positive test, or the true positive rate.
By true positive we mean the patient has the infection and tests have correctly detected the infection.
Specificity is the proportion of patients without the disease who have a negative test, or the true negative rate.
By true negative we mean the patient does not have the infection and tests have correctly detected no infection.

Bayes theorem can be applied to the interpretation of negative PCR results in patients with suspected COVID-19 infection.

To illustrate, we simulate two patient scenarios with differing contact history and clinical presentations.

We applied a Bayesian analysis to interpret negative and positive COVID-19 PCR assay results for two clinical scenarios. For both scenarios, we assumed a PCR assay specificity of 99.9% and varied the sensitivity from 70 to 90%.

Scenario 1 (high pre-test probability of COVID-19 infection):

- We estimated the pre-test probability among patients in hospital who presented with signs and symptoms of COVID-19, such as shortness of breath and fever. During the height of the surge in May in India, this was roughly 30%. The sensitivity and specificity of the test as 80% and 100%, respectively (the test itself has not changed, only the group of people being tested).

Of 1,000 of these patients being tested, 300 will have COVID-19 and 700 will not. Based on the sensitivity and specificity of the test, 80% of those 300 (240) with COVID-19 will have a positive test, and 100% of those 700 without COVID-19 will have a negative test:

	COVID-19: Yes	COVID-19: No	Total
Test Positive	240	0	240
Test Negative	60	700	760
Total	300	700	1000

Calculating positive and negative predictive values:

Positive predictive value = having COVID-19 if the test is positive = 240/240 = 100%
Negative predictive value = not having COVID-19 if the test is negative = 700/760 = 92%

Scenario 2 (low pre-test probability of COVID-19 infection):

- A cohort of people with subjective fevers (no temperature taken), cough, and subjective dyspnea. They have no significant exposure but live where COVID-19 infections were reported. They report frequent hand washing and practice social distancing. We estimated a pre-test probability of COVID-19 infection at 5%.

  Of 1,000 of these patients being tested, 50 will have COVID-19 and 950 will not. Based on the sensitivity and specificity of the test, 80% of those 50 (40) with COVID-19 will have a positive test, and 100% of those 950 without COVID-19 will have a negative test:

	COVID-19: Yes	COVID-19: No	Total
Test Positive	40	0	40
Test Negative	10	950	960
Total	50	950	1000

Calculating positive and negative predictive values:

Positive predictive value = having COVID-19 if the test is positive = 40/40 = 100%
Negative predictive value = not having COVID-19 if the test is negative = 950/960 = 99%

CONCLUSION

We applied a Bayesian approach to illustrate the interpretation of COVID-19 negative tests based on the clinical suspicion of disease probability. A positive test in both high pre-test and low pre-test scenarios most likely represents acute infection. Likewise, a negative test in a low pre-test probability case indicates a low likelihood of acute infection. However, when COVID-19 infection is likely, such as in a healthcare worker with significant exposure, a negative test should not rule out acute infection. In this case, as recommended 6 repeat testing or further evaluation should be considered.

REFERENCES

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CONTACT INFORMATION

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