Report 4: COVID-19: analysis of two serological tests

Francesco Donato, s259358,
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1 Introduction

Spreading of COVID-19 (COrona VIrus Disease 19) infection can be reduced with early detection of infected people, so that they can start quarantine as soon as possible. The nasopharyngeal swab test is highly reliable but it requires time and is expensive, serological tests are faster and cheaper, but less reliable. Serological tests find the presence of IgG (Immunoglobulin G) and a high level of this antibody in blood means that the person is or has been affected by COVID-19.

This work reports the results of the analysis of two serological tests, discussing the setting of the thresholds to declare a positive result.

2 Method

A group of 879 people was subjected to 3 tests: one nasopharyngeal swab test and two serological tests (Test 1 and Test 2 in the following), recording the amount of IgG; 17 cases were removed from the dataset due to an uncertain swab test result. The positive swab tests were 71, whereas the negative ones were 791.

Test 1 contained 3 outliers, which were identified using DBSCAN [1] with parameters $\epsilon = 7$ and $M = 2$, and then removed (only from Test 1). In these cases the swab test was negative for the 3 patients.

Swab test result was considered correct, and ROC curve (sensitivity versus false alarm, see Fig. 1) was measured for the two serological tests. The area under ROC was measured equal to 0.936 for Test 1 and 0.928 for Test 2.

For convenience, sensitivity and specificity versus threshold are also plotted in Fig. 2.

The following notation will be used: D means that the patient is really infected, H means that the patient is healthy, T_p means that the test is positive, T_n mean that te test is negative.

The general approach in case of a positive serological test is to check again the person using the nasopharyngeal swab. This makes acceptable a relatively large false positive prob-

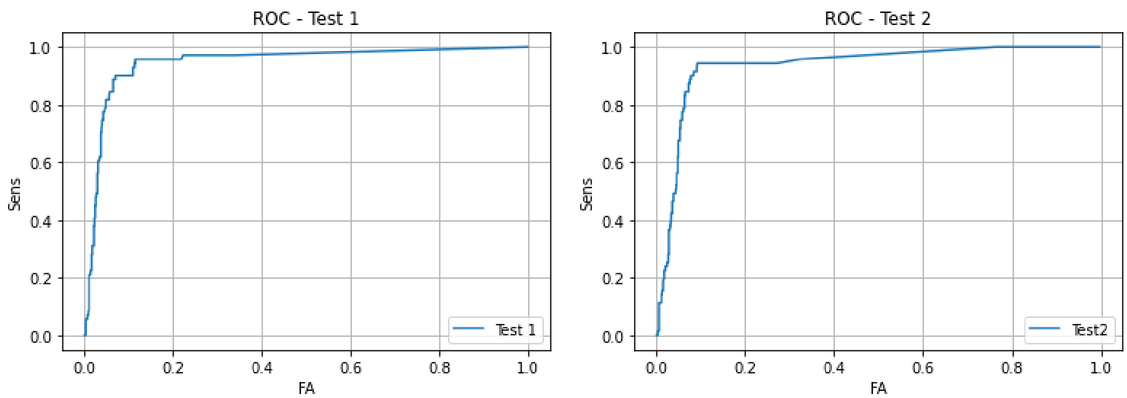

Figure 1: ROC curve for Test 1 (left) and Test 2 (right).

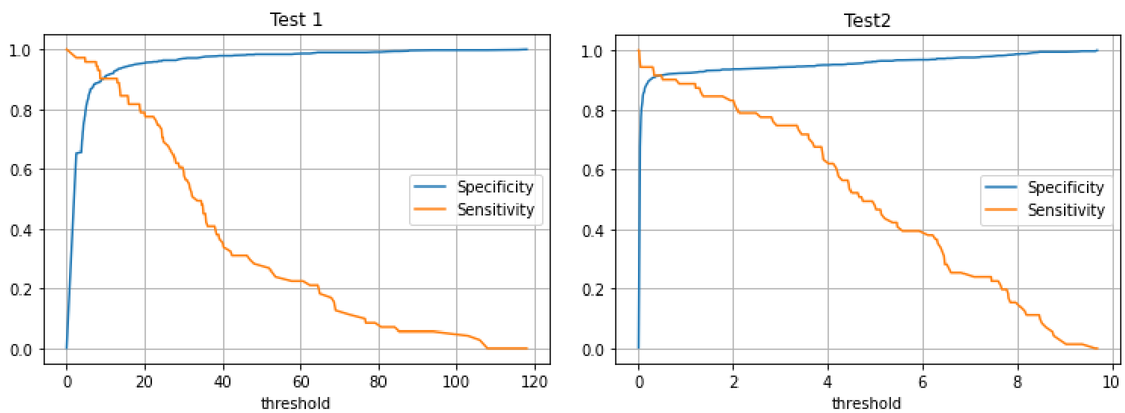

Figure 2: Sensitivity and specificity versus threshold for Test 1 (left) and Test 2 (right).

ability $P(T_p|H)$, with the only drawback that healthy people stay for a couple of days at home, maybe in an anxious state.

What cannot be accepted is instead a large false negative probability: in this case nasopharygeal swab is not tested, and the person can spread the virus to many others. Thus, it is important to have a large sensitivity $P(T_p|D)$ (probability that the test is positive given that the person has the disease), but even more important is the probability $P(D|T_n)$ that the person has the disease given the test is negative. This last probability should be kept as small as possible.

Having assumed COVID-19 prevalence equal to 2 %, Figs. 3 and 4 respectively show versus the threshold:

1. The probability $P(D|T_p)$ that the patient is truly infected given that the test is positive and the probability $P(D|T_n)$ that the patient is infected given that the test is negative.

2. The probability $P(H|T_p)$ that the patient is healthy given that the test is positive and the probability $P(H|T_n)$ that the patient is healthy given that the test is negative.

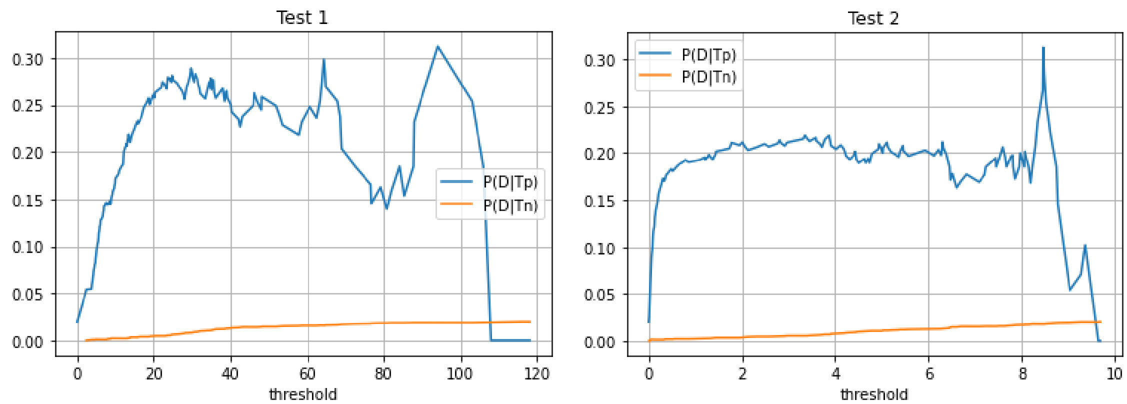

Figure 3: $P(D|T_p)$ and $P(D|T_n)$ versus threshold for Test 1 (left) and Test 2 (right).

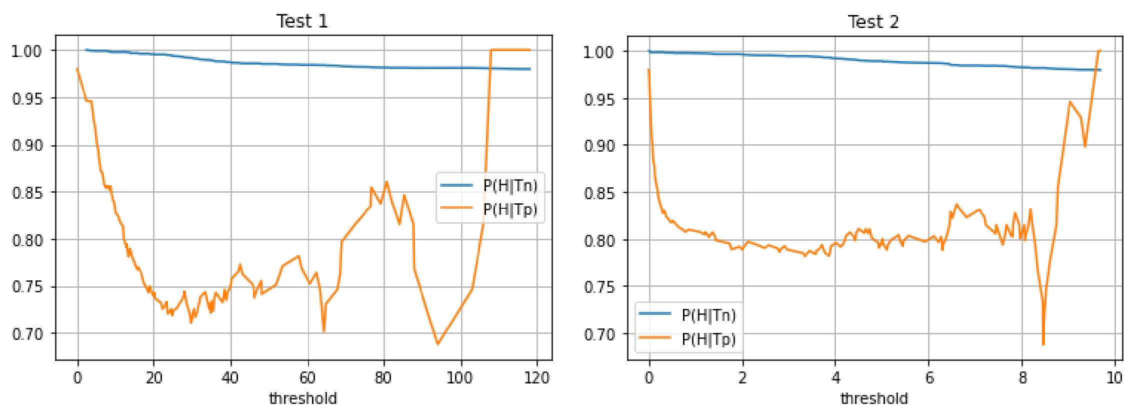

Figure 4: $P(H|T_p)$ and $P(H|T_n)$ versus threshold for Test 1 (left) and Test 2 (right).

3 Choice of the threshold

3.1 Test 1

- Sensitivity and specificity are both equal to 0.90 when the threshold is equal to 9.28, in which case $P(D|T_n) = 0.002$ and $P(D|T_p) = 0.157$.
- Being this sensitivity not large enough, it is convenient to decrease the threshold; we suggest a threshold equal to 7.59 for which:
  - Sensitivity $P(T_p|D) = 0.958$, false negative probability $P(T_n|D) = 0.042$.
  - Specificity $P(T_n|H) = 0.886$, false positive probability $P(T_p|H) = 0.114$.
  - $P(D|T_n) = 0.001$, $P(H|T_n) = 0.999$.
  - $P(D|T_p) = 0.146$, $P(H|T_p) = 0.854$.

3.2 Test 2

- Sensitivity and specificity are both equal to 0.91 when the threshold is equal to 0.44, in which case $P(D|T_n) = 0.002$ and $P(D|T_p) = 0.181$.
- Since this sensitivity cannot be considered sufficient, the lower threshold 0.3 is recommended, for which:
  - Sensitivity $P(T_p|D) = 0.944$, false negative probability $P(T_n|D) = 0.056$.
  - Specificity $P(T_n|H) = 0.908$, false positive probability $P(T_p|H) = 0.092$.
  - $P(D|T_n) = 0.001$, $P(H|T_n) = 0.999$.
  - $P(D|T_p) = 0.173$, $P(H|T_p) = 0.827$.

4 Conclusions

Coronaviruses (CoV) are a large family of viruses that cause illnesses ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). A novel coronavirus (nCoV) is a new strain that has not been previously identified in humans. SARS-CoV-2 (the virus that causes coronavirus disease) spreads from an infected person to others through respiratory droplets and aerosols when an infected person breathes, coughs, sneezes, shouts, or talks. The droplets vary in size, from large droplets that fall to the ground rapidly (within seconds or minutes) near the infected person to smaller droplets, sometimes called "aerosols", which linger in the air, especially in indoor spaces. Infectious droplets or aerosols may come into direct contact with the mucous membranes of another person's nose, mouth, or eyes, or they may be inhaled into their nose, mouth, airways, and lungs. The virus may also spread when a person touches another person (i.e., a handshake), a surface, or an object (also referred to as a fomite) that has the virus on it, and then touches their mouth, nose, or eyes with unwashed hands [2].

Testing of all people for SARS-CoV-2, including those who have no symptoms, who show symptoms of infection such as trouble breathing, fever, sore throat, or loss of the sense of smell and taste, and who may have been exposed to the virus will help prevent the spread of COVID-19 by identifying people who are in need of care in a timely fashion. A positive test early in the course of the illness enables individuals to isolate themselves - reducing the chances that they will infect others and allowing them to seek treatment earlier, likely reducing disease severity and the risk of long-term disability or death [3].

For the two serological tests analyzed, two different specific thresholds have been chosen, in particular, a threshold of 7.59 for Test 1 and a threshold of 0.3 for Test 2. The reason behind this threshold setting is that, in both cases, the chosen value permitted to have a low false negative probability as well as a small probability of having the disease given that the test is negative ($P(D|T_n)$) (which should be kept as small as possible), but still reaching a reasonable value for the probability of having the disease given that the test is positive ($P(D|T_p)$). In fact, observing the plots shown in Fig. 3, choosing a threshold that minimizes to zero the $P(D|T_n)$ is not a good choice as $P(D|T_p)$ would reach a very small and unreasonable value. Comparing the two analyzed tests, the results are quite similar, being Test 1 a slightly better choice because the area under the ROC curve (Figure 1), that has an ideal value of 1, is equal to 0.936, while for Test 2 is around 0.928. Moreover, with the chosen threshold, the sensitivity for Test 1 is about 0.958 and the false negative probability is equal to around 0.042, while for Test 2 the sensitivity is equal to 0.944 and the false negative probability is around 0.056. It must be highlighted that it is suggested to have a high sensitivity and a low false negative probability.

In conclusion, it is acceptable in both tests to have a slightly higher false positive probability, with the only drawback that healthy people stay for a couple of days at home, maybe in an anxious state.

References

[1] Ester M., Kriegel H-P., Sander J., Xu X. *A density-based algorithm for discovering clusters in large spatial databases with noise*. Proceedings of the Second International Conference on Knowledge Discovery and Data Mining 1996 (KDD-96), pp. 226-231. AAAI Press.

[2] `https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals/main-modes-transmission.html`

[3] `https://www.nia.nih.gov/news/why-covid-19-testing-key-getting-back-normal`