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A Two-stage Diagnosis Strategy for COVID-19 and Similar Pandemics

COVID-19 ve Benzeri Pandemiler İçin İki-kademeli Bir Tanı Testi Stratejisi

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ABSTRACT Objective: Coronavirus disease-2019 (COVID-19) outbreak emerged in Wuhan-China in December-2019, and has covered the world by rapidly becoming a pandemic, infecting >4.5 million by mid-May 2020, killing >300,000 globally, and >90 million people tested. Several rapid test kits based on antibody response have been developed but the reverse transcription-polymerase chain reaction (RT-PCR) approach for its superior sensitivity and specificity. As rapid detection of the virus is vital, we propose a two-stage testing framework that utilizes antibody-diagnostic kits and refers to RT-PCR only when a decision cannot be made. **Material and Methods:** In this study, using the Bayes formula and independent tests assumption, we developed several "repeat-testing" strategies to increase the overall sensitivity and specificity of both tests. We compared the false negatives, false positive, burden on the testing centres, and predicted cost among strategies. **Results:** We have shown that it is possible to increase the diagnostic capabilities of poor tests, "repeat" testing strategies. The primary advantage of such approaches is the faster diagnosis of cases, which allows for timely isolation, quarantine, and affiliation work. Also such strategies reduce the burden on the RT-PCR testing laboratories, thus, allowing them to focus their efforts to individuals that are more difficult to diagnose. The cost-comparison we conducted also suggests that this proposed is more cost-effective. **Conclusion:** The two-stage diagnostic strategy for COVID-19 is more efficient regarding pandemic management as it provides the testing results more quickly for the majority of suspected cases, allowing for timely isolation and affiliation work, and more cost-effective, reducing the burden on the healthcare system.

Keywords: COVID-19; antibody test; reverse transcription-polymerase chain reaction test; sensitivity; specificity

ÖZET Amaç: Koronavirüs hastalığı-2019 (COVID-19) pandemisi, 2019 Aralık ayında Çin'in Wuhan şehrinde ortaya çıkmış ve hızla yayılım sağlayarak tüm dünyayı etkisini altına almıştır. 2020 Mayıs ayının ortasına kadar dünya genelinde 4,5 milyondan fazla kişi COVID-19 salgınından etkilenmiş, 300.000 kişi vefat etmiş ve 90 milyona yakın kişiye test yapılmıştır. COVID-19 tanısını tespit etmek amacıyla antikor tabanlı birçok hızlı tanı kiti geliştirilmiş fakat ters transkripsiyon-polimeraz zincir reaksiyonu [reverse transcription-polymerase chain reaction (RT-PCR)] testinin duyarlılığının ve özgüllüğünün daha fazla olması nedeniyle RT-PCR testleri tercih edilmiştir. COVID-19 vakalarının hızlı bir şekilde tespitinin önemi sebebiyle COVID-19 vakalarının tespitinde hızlı tanı kitlerinin kullanıldığı, sadece karar verilemediğinde RT-PCR testine başvurulan 2 aşamalı bir test stratejisi öneriyoruz. **Gereç ve Yöntemler:** Bu çalışmada, Bayes formülü ve bağımsız testler varsayımı altında, COVID-19 tanısı için kullanılan antikor ve RT-PCR testlerinin duyarlılık ve özgüllüklerini artırmak amacıyla, 2 aşamalı ve tekrarlı bir test stratejisi geliştirilmiştir. Çalışma kapsamında, yanlış negatifler, yanlış pozitifler, laboratuvarlar üzerindeki test yükü ve önerilen tanı stratejileri arasındaki tahmini maliyetler karşılaştırılmıştır. **Bulgular:** Bu çalışmada, 2 aşamalı ve tekrarlı test stratejisi önerimizle, zayıf testlerin tanısal yeteneklerinin artırılmasının mümkün olduğu gösterilmiştir. Böyle bir yaklaşımın sağladığı ilk avantaj; alandaki izolasyon, karantina ve filyasyon çalışmalarıdır. Ayrıca bu stratejinin RT-PCR laboratuvarların üzerindeki yükü azaltabileceği ve laboratuvarların çabalarını teşhis konulması daha zor olan bireylere odaklayabileceği gösterilmektedir. Çalışma kapsamında yapılan maliyet karşılaştırmasıyla, önerilen yaklaşımın sağlık sisteminde test maliyetlerini düşürdüğü gösterilmiştir. **Sonuç:** COVID-19 için 2 aşamalı tanı stratejisinin, şüpheli vakaların çoğunda test sonuçlarının daha hızlı elde edilmesini sağladığından, zamanında izolasyon ve filyasyon çalışmalarına fırsat sağladığından ve uygun maliyeti ile sağlık sistemi üzerindeki yükü azaltacağından dolayı, daha verimli olabileceği sonucuna varılmıştır.

Anahtar kelimeler: COVID-19; antikor testi; ters transkripsiyon-polimeraz zincir reaksiyon testi; duyarlılık; özgüllük

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The coronavirus disease-2019 (COVID-19) outbreak emerged in Wuhan, China in December 2019, and has covered the world under its influence by rapidly becoming a pandemic infecting more than 4.5 million by mid-May 2020, killing more than 300,000 globally, and more than 90 million people tested, While United States is leading in terms of total cases and deaths, new epicenters of the pandemic such as Russia, Brasil, India are emerging and it is highly likely that other epicenters will emerge as well.

In fighting with this pandemic, chest-computed tomography (CT) is one of the first-line COVID-19 testing modalities for patients who present to the healthcare system with symptoms, especially respiratory symptoms.[1] On the other hand, the World Health Organization (WHO) provided guidelines for COVID-19 genetic-based testing within nucleic acid amplification tests (NAAT) framework such as reverse transcription-polymerase chain reaction (RT-PCR).[2] RT-PCR tests are conducted in designated laboratories with trained personnel and its accuracy is affected by the sample quality, whether or not the sampling is oropharyngeal and nasopharyngeal, and RNA degradation.[3-5] Antibody test-kits are also used mainly as supplemental tools to the RT-PCR approach to diagnose past infections using body fluids such as blood; however, these tests have less favorable diagnostic measures, and the timing of these tests is highly critical and the repeat tests are needed.[5,6] In the COVID-19 diagnostics report published by the National University of Singapore, Saw Swee Hock School of Public Health, they describe many commercial and non-commercial COVID-19 diagnostic tests.[7] However, almost all of these tests are not presented with their corresponding sensitivity and specificity measures, or unrealistic characteristics such as 100% sensitivity and 100% specificity are reported.[8] Chan et al. reports that RT-PCR has 95% sensitivity.[9] Therefore, we will use the conservative sensitivity and specificity measures for the antibody tests and 95% sensitivity and a hypothetical 95% specificity for RT-PCR in our computations.[9]

Following the work of Kocak, which discusses the advantages of repeat RT-PCRT tests to manage the spread of COVID-19 pandemic, in this paper, we propose a two-stage testing strategy to reduce the false positives and false negatives in COVID-19 pandemic control efforts, where an antibody test is conducted in the first phase, and an RT-PCR test is conducted in the second phase only if it is deemed necessary at the first stage so that the medical team can move faster on the ground in terms of quarantine, self-quarantine, isolation, and treatment efforts.[10] We also compute the lessened burden on the RT-PCR labs as well as compare this new testing strategies in terms of costs to the healthcare system.

MATERIAL AND METHODS

We describe the two-stage COVID-19 diagnosis strategy using the following algorithm:

Stage-1: Conduct even numbers of antibody tests, say 4 replicates, for each patient.

1. If there are more positive tests, the case is declared to be “positive” and no RT-PCR test is needed; for example, if 4 test replicates are conducted and at least 3 are positive, then the final decision is that the patient is COVID-19 positive;

2. If there are more negative tests, the case is declared to be “negative” and no RT-PCR test is needed; for example, if 4 test replicates are conducted and at least 3 are negative, then the final decision is that the patient is COVID-19 negative;

3. If there is a tie, then we go to Stage-2 and conduct a single RT-PCR test.

Stage-2: Conduct a single RT-PCR test:

1. If the RT-PCR test is positive, then the patient will be declared COVID-10 positive.

2. If the RT-PCR test is negative, then the patient will be declared COVID-10 negative.

COVID-19 tests are conducted free of charge in Turkey; therefore, it is not easy to get a unit price; therefore, our cost estimation and comparison should be considered as an example, not necessarily the real cost. From what we can obtain from the Ministry of Health of Turkey and its General Directorate of Public Health, the unit cost of antibody tests is around 75-80 TL based on the amounts announced by the Ministry

of Health.[11] Similarly, based on the amounts announced by the Ministry of Health and General Directorate of Public Health, the unit cost of RT-PCR test per test is around 1,200-1,250 TL. In this study, we used 80 TL per antibody test and 1,250 TL per RT-PCR test.

We compared the two-stage testing strategies scenarios:

- No. of antibody tests: 2, 4, 6
- Sensitivity/specificity combination for the antibody tests: 0.80/0.70 (Scenario-1), 0.90/0.80 (Scenario-2).

The final sensitivity and specificity measures for the entire testing algorithm are computed through Bayes formula as a combination of the sensitivity and specificity measures of the antibody and RT-PCR tests.

All computations are performed using SAS 9.4® (Cary, USA). Computational SAS codes have been provided in the Appendix 1.

RESULTS

We provide the final sensitivity and specificity measures of different scenarios under consideration in Table 1 below.

TABLE 1: Examples of two-stage COVID-19 testing final sensitivity and specificity calculations.

Sensitivity specificity scenarios	Antibody test sensitivity	Antibody test specificity	No. of antibody replicates per patient	RT-PCR sensitivity	RT-PCR specificity	Final sensitivity	Final specificity
Scenario-1	0.80	0.70	2	0.95	0.95	0.944	0.889
			4			0.9651	0.9031
			6			0.9789	0.9203
Scenario-2	0.90	0.80	2	0.95	0.95	0.981	0.944
			4			0.9939	0.9651
			6			0.9980	0.9789

RT-PCR: Reverse transcription-polymerase chain reaction.

We observe that even with two repeats of the antibody tests, we improved the diagnostic ability of our two-stage testing algorithm with sensitivity from 0.80 to 0.944 (first scenario), or from 0.90 to 0.981 (second scenario), and similarly specificity from 0.70 to 0.889, or from 0.80 to 0.944. It is seen that repeating antibody tests evenly in Scenario-1 and Scenario-2 and applying an RT-PCR test once, reduces the test costs. Namely, 1 an RT-PCR test corresponds to the unit cost of approximately 15 antibody tests. In this case, when antibody test is used instead of RT-PCR test, it enables more patients to test and reduces costs.

In Table 2 below, we present the hypothetical situation if we were to conduct another antibody test rather than an RT-PCR. Here, we conclude that the testing accuracy can be improved even without the help of RT-PCR while this improvement falls short as expected. For example, in Scenario-1, doing the antibody tests three times and taking the majority call in decision improves sensitivity from 0.80 to 0.896, about 5% less than the two-stage approach, and specificity from 0.70 to 0.784, about 10% less than the two-stage approach. It is intuitively clear that the two-stage approach is more favorable only when the sensitivity and specificity of RT-PCR are higher than its antibody counterparts. In such a case In this part, the total test costs of patients who underwent RT-PCR test according to their false positive and false negative status are included. Even in such a scenario, it is seen that the total test cost is below the test cost only when RT-PCR

is performed. In any case, repeating antibody tests and applying RT-PCR test only when necessary seems to reduce the test cost burden on the health system., it is seen that when the antibody test is repeated with odd numbers, it decreases the cost per patient and the cost of the tests, although the number of tests increases, does not exceed the unit cost of the an RT-PCR test.

TABLE 2: Examples of two-stage COVID-19 testing only using antibody tests.

	Antibody test sensitivity	Antibody test specificity	No. of antibody replicates per patient	No. of RT-PCR replicates per patient	Final sensitivity	Final specificity
Scenario-1	0.80	0.70	3	0	0.8960	0.7840
			5	0	0.9421	0.8369
			7	0	0.9667	0.8740
Scenario-2	0.90	0.80	3	0	0.9720	0.8960
			5	0	0.9914	0.9421
			7	0	0.9973	0.9667

RT-PCR: Reverse transcription-polymerase chain reaction.

In Table 3, we present the probability that a given patient would move to Stage-2 in the above scenarios, which indicates the reduction of the overall burden on the RT-PCR testing laboratories based on this two-stage testing approach. As we see, the move to Stage-2 of any patient is dependent upon the antibody diagnostic characteristics and the number of tests conducted. For example, with 4-repeat approach, only 15% of the truly COVID-19 positive patients move to Stage-2 and only 26% of the truly COVID-19 negative patients move to Stage-2 while these proportions are around 5% and 15% for Scenario-2. Regardless, it is clear that no more than 40% of the patients will move to Stage-2 under any of these scenarios. In this part, the total test costs of patients who underwent RT-PCR test according to their false positive and false negative status are included. Even in such a scenario, it is seen that the total test cost is below the test cost only when RT-PCR is performed. In any case, repeating antibody tests and applying RT-PCR test only when necessary seems to reduce the test cost burden on the health system.

TABLE 3: Percentage of patients who would move to Stage-2 (RT-PCR sensitivity and specificity are 0.95 and 0.95, respectively).

	Antibody test sensitivity	Antibody test specificity	No. of antibody replicates per patient	No. of RT-PCR replicates per patient	% of Truly COVID-19 positive patients	% of Truly COVID-19 negative patients
Scenario-1	0.80	0.70	2	1	0.3200	0.4200
			4	1	0.1536	0.2646
			6	1	0.0819	0.1852
Scenario-2	0.90	0.80	2	1	0.1800	0.3200
			4	1	0.0486	0.1536
			6	1	0.0146	0.0819

RT-PCR: Reverse transcription-polymerase chain reaction.

As of May 15, 2020, around 10% of the total COVID-19 tests in Turkey are reported to be positive. Considering that RT-PCR approach is used in all these tests and assuming that there is no difference in nasal/throat sampling handling and testing procedures, with 95% sensitivity and 95% specificity, in order to

get around 10% positive tests, i.e., 1,000 positive cases in every 10,000 tests, the disease prevalence must be 5.56%. Now, using this prevalence value, we compare the two-stage testing scenarios described above in terms of false positives and false negatives in Table 4.

TABLE 4: Comparison of false positives and false negatives under each scenario for every 10,000 tests.

Comparison Metric	Scenario-1 (Sensitivity=0.80, Specificity 0.70)			Scenario-2 (Sensitivity=0.90, Specificity 0.80)			Just RT-PCR
	Repeats=2	Repeats=4	Repeats=6	Repeats=2	Repeats=4	Repeats=6	
P (T+)	0.1576	0.1455	0.1301	0.1078	0.0886	0.0758	0.1004
P (D+|T+), i.e., NPV	0.3354	0.3714	0.4214	0.5096	0.6282	0.7373	0.5299
P (D-|T-), i.e., NPV	0.9962	0.9977	0.9987	0.9988	0.9996	0.9999	0.9969
N (T+)	1576	1455	1301	1078	886	758	1004
n (True positives)	529	540	548	549	557	559	532
n (False positives)	1047	915	753	529	329	199	472
n (True negatives)	8392	8525	8688	8911	9110	9241	8968
n (False negatives)	32	20	11	11	4	1	28
No. of antibody tests	20000	40000	60000	20000	40000	60000	0
No. of RT-PCR tests	4144	2584	1794	3122	1477	781	10000
Total cost (TL in million)	5.18 M	6.43 M	8.70 M	5.50 M	5.05 M	5.78 M	12.5 M

RT-PCR: Reverse transcription-polymerase chain reaction.

We see that even under Scenario-1, where we apply two antibody test and apply RT-PCR only when undecided, we conduct 4,144 RT-PCR (around 41%) for 10,000 patients. As we increase the number of antibody test repeats, we reduce the burden on the RT-PCR testing facilities. Looking at the scenarios for every 10,000 tests in Table 4, when two antibody tests under the scope of scenario-1 and an RT-PCR test are applied only in unstable situations, the total cost is 5,180.000 TL, whereas only RT-PCR tests are applied, this cost rises to 12,500.00 TL. As the repeat numbers of antibody tests increase, it is possible to reduce the cost by reducing the load in the laboratories where RT-PCR tests are performed.

DISCUSSION

The COVID-19 pandemic has challenged health systems even in the most powerful countries of the world. While many countries could not prevent the number of cases and deaths while struggling with the pandemic, at the same time, due to the insufficient hospitals, they established emergency tent hospitals on the streets and parks. In some countries, the insufficiency of hospital staff and medical devices affected their population much worse. Many sports or exhibition halls were converted to health centers due to insufficient hospital capacities, and the number of patient admissions was tried to be increased.[12] Due to the pandemic, it is likely that there will be an increase in unemployment, a decrease in economic growth rate, an increase in inflation rate, a deterioration in the budget balance and difficulties in foreign financing and a deep contraction in the economy. However, besides this, preventive and complementary medicine measures, making the use of masks and gloves widespread and compulsory, social distance rules, disinfection and flexible production systems will help minimize the economic losses by preventing the production to stop. Considering the long-term effects of pandemic, measures such as debt deferral, tax/credit facilities and direct funding will be increased.[13]

We see that COVID-19 pandemic has been a trauma in the lives of individuals and one of the unprecedented challenges for governments by forcing their healthcare resources to its limits to manage the public health aspect of the pandemic; the pandemic caused fear for individuals that they would get the virus and transmit it to their family, and caused insecurity that nowhere is safe.[14-16] At the same time, in potential quarantine and isolation periods, individuals' separation from their loved ones, their restricted freedom of movement cause anger, behavioral problems and healthy communication difficulties. Increased duration of quarantine, isolation and lock-down may also lead to depression, widespread anxiety disorder, and panic disorder as well as causing an increased likelihood of alcohol, substance and drug abuse as a method of healing themselves and looking for comfort.[17]

All potential negative impact of the pandemic forces us to come up with better pandemic management systems, in which COVID-19 diagnosis presents itself among the first areas to manage. To help address that challenge, in this study, we proposed a two-stage diagnostic operation to speed up the decision-making process as much as possible with the resources at hand. As part of this effort, we calculated the final sensitivity and specificity measures of several testing strategies which involve repeats of the antibody and RT-PCR test with their sensitivity and specificity rates determined in the literature as much as possible. We then compared the false positive and false negative calls in every 10,000 hypothetical individuals tested. The primary problem with false-negative cases is that although they have COVID-19, they are told that they are not COVID-19 patients. This can cause them to be more comfortable in their social interactions and spread the virus to others without realizing. Similarly, the main problem with false positives is that these cases are individuals thought to have the disease and are quarantined with their access to their families and work limited, also increasing the burden on the healthcare infrastructure, which may already be overwhelmed due to the pandemic. Therefore any testing strategy should be developed without sacrificing in any of these error types as well as the timeliness of the test results. Although RT-PCR tests are more accurate tests, and thus indispensable in the containment of the COVID-19 pandemic, their main limitation is that their results are not obtained immediately, and patients are kept isolated in their homes or in hospitals or quarantine locations until their test results are obtained within a day, or two, or even much later.

For these reasons, there should be a practical balance between the number of tests performed, the duration in which the test results are obtained, and the cost of the tests to the healthcare system. As we were not able to obtain a reliable diagnostic measure for the antibody test, we used sensitivity and specificity measures as 80% and 70%, respectively in one scenario, and 90% and 80%, respectively in another scenario as representative, perhaps too optimistic, measures. For RT-PCR test, we used the sensitivity of 95% and specificity of 95%. Our testing strategy consisted of two stages: In the first stage, even number of antibody tests are performed for each patient, and RT-PCR is conducted as a tie-breaker only when the number of positive and negative results from the antibody test repeats are equal (e.g., 2 out of 4 repeats are positive, or 3 out of 6 repeats are positive, etc.); if there is no tie in the antibody testing, then, RT-PCR testing is not carried out.

Our computations showed how the diagnostic ability of the antibody tests can be increased to the desired levels with repeats. As RT-PCR has more favorable diagnostic ability, it significantly adds to the gained accuracy in testing beyond what the repeats of antibody tests achieve. For example, with 4 repeats of the antibody test, we can increase the sensitivity from 80% to beyond 96% and specificity from 70% to 90%. We have also presented the results where another antibody test is used as a tie-breaker; as expected, the final sensitivity and specificity falls short compared to using RT-PCR as a tie-breaker (Table 2).

To assess the reduction of the burden on the RT-PCR laboratories, we computed the probability of ties in Stage-1 of our testing strategy (Table 3). For example, if we apply only two antibody tests in Stage-1, a tie occurs requiring an RT-PCR tie-breaker test with 32% chance if the patient is COVID-19 positive, and 42% change if the patient is COVID-19 negative. In 10,000 patients, this corresponds to 4144 patients having a tie, thus requiring an RT-PCR time-breaker (Table 4). As the number of antibody tests increase, the need for

RT-PCR goes down rather quickly as expected. This will allow for more COVID-19 screening tests to be conducted on the field and the gained availability in the RT-PCR labs through our two-stage testing strategy can be utilized to meet the demands for this potential screening tests. the RT-PCR labs.

As the RT-PCR labs are generally working full capacity, the repeat RT-PCR test in the field may not be feasible; however, the use of our two-stage testing strategy in COVID-19 will achieve such an aim, produce test results faster for majority of COVID-19 suspected individuals, and lessen the burden on the health system and overall economy.

Another added benefit of our testing strategy is the reduction in the total testing cost. Based on the per-test cost estimate we were able to obtain, for 10,000 individuals, the cost of conducting only RT-PCR is around 12 million TL; with our testing strategy, even with a poor selection of an antibody test with 6 repeats the cost remains below 9 million TL. In countries or regions that do not have direct access to an RT-PCR lab, our two-stage testing algorithm can still be used with another antibody test as a tie-breaker. Thus, a fight with COVID-19 can still be given successfully in remote areas, even at homes, with these repeat testing strategies, which is still a much more cost-effective strategy. It is clear that more simulation studies should be carried out covering different realistic cost components and resource needs in pandemic management.[17]

CONCLUSION

We conclude that two-stage diagnostic strategy for COVID-19 can be both more efficient in terms of testing accuracy and the management of the pandemic as it provides the testing results more quickly for the majority of suspected cases, allowing for timely isolation and affiliation (i.e., case-relatedness) work in the field, and it is more cost-effective, reducing the burden on individuals and the healthcare system.

APPENDIX 1

We provide below examples of the SAS codes we used so that other users can implement similar computations in SAS as well as other statistical packages such as R, SPSS, Stata, Minitab, etc.

```
*** Two-Stage Diagnostic Tests***;
%macro twostage_diagnosis(se1=0.90, sp1=0.80, se2=0.96, sp2=0.91, tsize1=5, tsize2=1);
data stage1;
se1=&se1; sp1=&sp1; se2=&se2; sp2=&sp2;
do npos=0 to &tsize1; nneg=&tsize1-npos;
p_pos=pdf('binomial', npos, se1, &tsize1);
p_neg=pdf('binomial', nneg, sp1, &tsize1);
output; end; run;
data stage1; set stage1; p_pos1=pdf('binomial', 1, se2, 1); p_neg1=pdf('binomial', 1, sp2, 1);
pposlag=lag(p_pos); p_pos_final=p_pos; p_neg_cum+p_neg;
if npos=%sysevalf(&tsize1/2) then p_pos_final=p_pos*(1-p_pos1);
else if npos=%sysevalf(&tsize1/2+1) then p_pos_final=p_pos+pposlag*p_pos1; run;
proc sort data=stage1; by nneg; run;
data stage1; set stage1; pneglag=lag(p_neg); p_pos_cum+p_pos;
if nneg=%sysevalf(&tsize1/2) then p_neg_final=p_neg*(1-p_neg1);
else if nneg=%sysevalf(&tsize1/2+1) then p_neg_final=p_neg+pneglag*p_neg1;
else p_neg_final=p_neg;
if npos>%sysevalf(&tsize1/2) then positiveside=1; else positiveside=0;
if nneg>%sysevalf(&tsize1/2) then negativeside=1; else negativeside=0;run;
/*proc sql; select distinct sum(p_pos_final), sum(p_neg_final) from stage1; quit;*/
proc print data=stage1; run;
proc sql; select distinct sum(p_pos_final) as newse label='Final Sensitivity' from stage1 where positiveside=1; quit;
proc sql; select distinct sum(p_neg_final) as newsp label='Final Specificity' from stage1 where negativeside=1; quit;
%mend;
```

```
*** Sample Run ***;
%twostagedx_diagnosis(se1=0.80, sp1=0.70, se2=0.95, sp2=0.95, tsize1=2, tsize2=1);
```

We also share a SAS macro which provides different diagnostic measures from a combination of prevalence, sensitivity and specificity.

```
%macro diagnosticsummary(dp=0.056, se=0.95, sp=0.95, tsize=10000);
data dxsummary; targettp=0.10; se=&se; sp=&sp; do dp=&dp;
tp=round(se*dp+(1-sp)*(1-dp),0.0001); dptp=round(se*dp/tp,0.0001); dntp=1-dptp; dntn=round(sp*(1-dp)/(1-tp),0.0001); dptn=1-dntn;
n=&tsize; ntp=round(n*tp,1); true_p=round(ntp*dptp,1); false_p=round(ntp*dntp,1); true_n=round((n-ntp)*dntn,1);
false_n=round((n-ntp)*dptn,1); ndecision=true_p+true_n+false_p+false_n; output;
end;
label se='Sensitivity, i.e., P(T+|D+)' sp='Specificity, i.e., P(T-|D-)' dp='Prevelance, i.e., P(D+)'
tp='P(T+)' dptp='P(D+|T+)' dntp='P(D-|T+)' dntn='P(D-|T-)' dptn='P(D+|T-)'
n='Sample Size' ntp='n(T+)' true_p='n(True Positives)' false_p='n(False Positives)'
true_n='n(True Negatives)' false_n='n(False Negatives)'; ndecision=true_p+true_n+false_p+false_n;
run;
proc sql outobs=1 noprint; select *, abs(targettp-tp) as tp_diff from dxsummary order by tp_diff; quit;
proc sql outobs=1 noprint; select tp, dptp, dntn, ntp, true_p, false_p, true_n, false_n into :v1, :v2, :v3, :v4,:v5, :v6, :v7, :v8
from findprevelance; quit;
proc sql; select distinct 0, "P(D+)", "&dp" from dxsummary union
select distinct 1.1, "P(T+|D+), i.e., Sensitivity", "&se" from dxsummary union
select distinct 1.2, "P(T-|D-), i.e., Specificity", "&sp" from dxsummary union
select distinct 2, "P(T+)", "&v1" from findprevelance union
select distinct 2.1, "P(D+|T+), i.e., NPV", "&v2" from dxsummary union
select distinct 2.2, "P(D-|T-), i.e., NPV", "&v3" from dxsummary union
select distinct 3, "n, i.e., Total Number of Tests", "&tsize" from dxsummary union
select distinct 3.1, "n(T+)", "&v4" from findprevelance union
select distinct 3.2, "n(True Positives)", "&v5" from dxsummary union
select distinct 3.3, "n(False Positives)", "&v6" from dxsummary union
select distinct 3.4, "n(True Negatives)", "&v7" from dxsummary union
select distinct 3.5, "n(False Negatives)", "&v8" from dxsummary; quit;
%mend;
*** Sample Run ***;
%diagnosticsummary(dp=0.10, se=0.95, sp=0.90);
```


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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Mehmet Koçak;* ***Design:*** *Mehmet Koçak;* ***Control/Supervision:*** *Mehmet Koçak;* ***Data Collection and/or Processing:*** *Mehmet Koçak;* ***Analysis and/or Interpretation:*** *Mehmet Koçak, Sinem Cece, Tuğçe Türkay;* ***Literature Review:*** *Mehmet Koçak, Sinem Cece, Tuğçe Türkay;* ***Writing the Article:*** *Mehmet Koçak, Sinem Cece, Tuğçe Türkay;* ***Critical Review:*** *Mehmet Koçak, Sinem Cece, Tuğçe Türkay.*

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