

Testing for SARS-CoV-2 Portuguese experience: Clinical, ethical and economical perspectives

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ABSTRACT

Portugal, unlike its neighbours, Spain and Italy, has so far managed to maintain the flattening of the epidemiological curve of Infections by SARS-CoV 2. The pandemic response strategy in this country included the implementation of measures commonly referred to as non-pharmacological, as well as the rapid growth of responsiveness to perform RT-PCR tests for the diagnosis of COVID-19. The clinical and epidemiological reflection of the measures adopted, political and economic considerations, is made, and ends with a bioethical analysis of the methodologies implemented.

Keywords: Epidemiological; Pandemic; Non-pharmacological; Bioethical

Introduction

The disease that was designated COVID-19 by the WHO in February 2020, was declared a pandemic on the 12th of March. The SARS-COV2 spread across the world very rapidly, demonstrating an infectivity much superior to that of previously known human coronaviruses and proving to be responsible for a variety of uncommon symptoms in the affected patients. The pandemic is currently not only a sanitary emergency but also an economic and social one that challenges each and every one of us. It is time to accept that Human Rights also imply duties and the renouncing of individual rights to protect the rights of all. It is the moment to challenge assertive leaderships and to demand a careful and efficient communication. It is the challenge to the rationalization of means, to stimulate scientific progress and to protect the most vulnerable as well as to ensure the protection of the healthcare professionals and of other professional groups indispensable in this context [1-3].

As in other pathologies, to establish a diagnostic is the first step to project a therapeutic strategy. In the context of the pandemic, to diagnose and objectify the number of infected

people adds epidemiologic value that is crucial. The available tests are scarce and their performance requires a certain technical complexity, making it fundamental to prioritize their performance. This article states the Portuguese experience perceived by a doctor, a bioethicist and an economist.

Clinical and Epidemiologic Perspective

The first doctor to declare the appearance of several pneumonia cases was Li Wenliang, who worked at the hospital in Wuhan. He was arrested under the accusation of spreading "rumours" and eventually died by contracting the

disease himself. Besides his bravery, it is also to be emphasised that only the third test performed on him tested positive. This is one of the downsides of the test, the occurrence of false negatives. The tests are done by detection reaction). The thermic inactivation of the virus at 56° is part

of the virus RNA via RT- PCR (real-time polymerase chain of the lab process, which with low viral loads may contribute to the occurrence of false negatives. The incorrect collection of the sample with a swab may also favour false negatives. It is

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also to be emphasized that this is a new disease and as such it is not perfectly established in which moment the collection of the sample should be done after appearance of the symptoms, nor is it established the acuity of the test in asymptomatic people who have been in contact with infected patients. The serological tests may be a way to reduce the high percentage of false negatives in the future via the use of com RT-PCR. Furthermore, the further consolidated knowledge regarding serologic response to this infection may favour the adoption of other measures of public health to reduce the risk of contagion. In this respect, a group of German investigators are elaborating a study with 100 thousand volunteers with the purpose of creating "Immunity passports" which allow the citizens who are already immunized to resume professional activity. However, the measures of public health which we currently dispose of include solely the measures of isolation to prevent new contagions and the performance of tests with RT-PCR of the virus [5-9].

On the 16th of March, the general secretary of the WHO emphasized that in spite of the social distancing measures implemented in numerous countries, there was still a rapid growth in the number of infected patients, proving it necessary to perform a larger number of tests [10].

In Portugal, the first patient was diagnosed on the 2nd of March and on the 6th of April the statistics showed 11278 cases and 298 deaths. The test capacity in Portugal in the beginning of March was of roughly 900 tests in the public sector, shared solely by 3 hospitals of reference which until then were the ones designated, and of roughly 750 tests in private laboratories. On the 16th of March, the first Drive-Through structure was assembled in the city of Porto by private initiative, which then was replicated throughout the country. At the same time, it was necessary to quickly extend the number of reference hospitals for COVID-19, which became 20, and with the capacity to perform tests. Some University Institutes have followed this need, and have also begun to carry out a few hundred tests a day. The private capacity also exponentiated to approximately three thousand and five hundred per day. Currently, there is a capacity of approximately ten thousand tests per day in Portugal, and it is estimated that this number may grow up to twelve thousand tests per day. The number of performed tests until this moment is of roughly 9 thousand per million inhabitants. If we analyse the numbers of sample collections performed at the Drive-Through in the city of Porto, we verify that since the 16th of March until now, there has been an increase of 200 tests per day, at around 750 per day. The percentage of positivity in the tests initially presented a sustained rise, stabilizing close to 20%, and posteriorly a tendency to fall to 12% was verified. This progression will also be the consequence of the transition of an enlarged suppression stage to a mitigation stage [11].

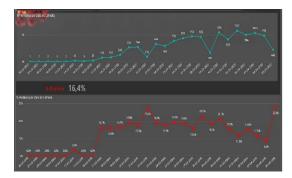


Figure1: Percentage of Positive Cases

Proceeding to the evaluation of the national data in Portugal since 20/03, immediately after the declaration of a state of national emergency with the implication of the reduced circulation of people, prohibition of events with agglomerations of people, promotion of closure of all commercial entities and shows, with the exception of pharmacies and establishments selling food, it was verified that with the impact of these non-pharmacological interventions and the increment of the tests it was possible to achieve the diminishing of the speed of the progression of the disease.

With this slower progression it has been possible for the Healthcare Service to gain a new fighting chance and also to gain time to readjust hospitals, namely by enlarging the availability of beds in intensive care units. To avoid the humanitarian catastrophes of China, Iran, Spain and Italy, what is to be learnt is that the most important is to firstly implement and ensure the following of the measures of social isolation. Secondly, it is to prevent the collapse of the response by the healthcare services and that collapse occurs mostly when the capacity of invasive ventilatory support runs out. For the patients whose therapy may be done without the use of significant technical resources, there is the possibility to improvise campaign hospitals. It is also important to predict the need for campaign hospitals with negative pressure capacity. The collapse occurs when the capacity of the intensive care units is exhausted. The flattening of the curve of the progression of the pandemic having been achieved, time is gained to increase the capacity of response with the acquisition of ventilators and other technical resources. Thirdly, the number of healthcare professionals that were infected and of those who died oblige us to guarantee the sufficing and adequate provision with equipment for individual protection for these professionals, as well as others such as firemen and security forces. Fourthly, in spite of the limitations of the tests, namely the high percentage of false negatives, it is necessary to test the largest possible number of the population and the criterion regarding the necessity to prioritize this scarce and expensive resource are well defined by the CDC, by the WHO, and by the sanitary authorities of each country [12-14]. It is important to guarantee and know how to inform the testes individuals that a single negative test does not remove the necessity of social isolation. Still in this context and foreseeing the introduction and validation of serological tests as well as of "immunity passports" in the near future, it is of

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primordial relevance to ensure the technical capacity and laboratorial provision to execute the serologies. The fifth lesson to be drawn is the necessity to anticipate the needs of the most vulnerable, namely residents of nursing homes and of institutionalized people (convicts, mental health patients, etc), who require the disposal of an anticipated evacuation planning and of a timely and adequate reorganization of isolation measures. The reports that arrive not only from Spain and Italy but also from the rest of Europe regarding the dramas experienced by these populations are enlightening [15-17].

In sixth place, the implications of the pandemic in general and in clinical activity are emphasized. On the one hand, the need for leadership with the capacity to organize; besides the COVID-19 patients, the remaining pathologies also require medical assistance and therefore the reorganization of the services and prioritization of clinical activity must be done in timely manner and communicated effectively. In Portugal, the National Health Service has articulated with the private institutions to optimize the sanitary response. On the other hand, it is vital to facilitate to doctors the access to scientific information and to means of diagnostic. I tis known that, for example, when a test is negative but there is strong clinical suspicion, the performance of a thoracic TAC may be crucial to support the clinical orientation the patient is to be provided with. However, the performance of a TAC in a patient under suspicion of COVID-19 implies a slow process of disinfection of the equipment, which severely undermines the remaining hospital activity. In the present moment, there are some private groups that do perform imageology exams solely to COVID-19 patients for larger operationalization of the healthcare. Also, in a time of pandemic, all patients subject to any anaesthetic or surgical procedure, patients in chemotherapy or radiotherapy, will ideally be tested previously for SARS CoV-2 with the intent to ensure the adequate protection of the professionals. In other words, all the possible restraints of clinical practice in the pandemic context must be predicted and minimized [18,19].

Lastly, the seventh lesson is that although not directly within the realm of clinical activity, implications of ethical and socioeconomic nature that must be considered in the pandemic context are innumerous. It is the regard of these implications that the co-authors of this paper shall address, it being certain that the result of these implications has a direct impact on the daily medical practice.

Economical Analysis and Political

Perspective

The analysis of this pandemic must start from two premises that are evident and thus essential to define at the start of this analysis. Firstly, there were no macroeconomic developments that could have led to predict an event of this magnitude. According to the bulletin of Eurostat of the 31st of January of 2020, the rapid estimate of growth of the gross domestic product in the euro zone and of the European Union in the Q4 of 2019 was of solely +0,1%, compared do the previous quarter, growth which had been falling since Q4 of 2017. There were signs of deacceleration at a European level, but nothing that could foresee the current scenario [20].

This brings us to the second premise of this analysis. The economic crisis at hand is totally unexpected and abrupt. Therefore, it does not fit in the traditional economical prediction models which are based on past data to predict future scenarios, which in the present context are meaningless.

Besides the traditional economic variables, we must include in these models the variables of the pathologic agents as variables of definition of the final obtained result.

An example of this is the approach adopted by the European Committee in 2006, a model based approach to pandemic events which included diverse clinical variables such as morbidity rates, rates of death by the disease, duration of incapacity to work, presenting several diverse scenarios for each of these variables.

To these variables we can and should add others which, tough elevating the complexity of the modelling process, are relevant to make the results of diverse scenarios more complete. Examples of such variables are:

Velocity of transmission of the pandemic, Levels of regional dispersion, Levels of immunization of at each stage of the epidemic, The appearance of the vaccine as a "show-stopper".

These variables are crucial to understand what measures or non-pharmacologic policies such as lockdown measures are relevant at what stages.

The levels of immunization are vital to grasp what kind of return to normal economical activity may be established, as well as how many "aftershocks" (or waves) the pandemic may have, thus defining the presence or absence of the need of further lockdown measures for the duration of each "aftershock" [21].

At the end of the day, solely comprehending science and introducing it in our modelling assumptions in a dynamic approach, will we be able to obtain models with acceptable degrees of reliability that may offer degrees of certainty to the economic agents that allow them to use these results for decision making.

On the 23rd of March, several sources published a study by the NECEP of the Portuguese Catholic University pointing to a recession in 2020 in Portugal between 4% and 20%, with the existence of 3 scenarios based on the duration of the "critical stage" of the epidemic. On the pessimistic scenario, the pandemic has a period of "critical stage" of 6 months. In accordance with the readiness of this study, the dimension of the uncertainty gap is natural. However, with more variables regarding the pathogenic agent, we could offer to the economic agents the possibility to adjust the scenarios to their own data and interpretations of the scientific production taking course, adding a higher degree of trust and confidence to each decision made, even in initial stages of this type of pandemic context [22].

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A variable of extreme economic importance and of enormous political repercussions at a national and transnational level is the implementation of lockdowns – complete or moderated – in the affected countries.

If from the point of view of controlling the pandemic these measures are objectively those of greater effectivity, from the economic and political point of view these are measures of tremendous consequences because they aggravate the supply and demand shocks that the pandemic itself, by its own nature, has created.

But what is the real consequence of this measure for the economy?

On the study of the Federal Reserve Board - version of 30th of March of 2020- where there we have and analyisis of the consequences of the pandemic of 1918 in 30 states and 43 cities - the authors are clear starting from the title of the study: "Pandemics Depress the Economy, Public Health Interventions do not". The authors conclude that the pandemic is the cause of the "abrupt and persistent decrease in the economic activity with negative effects on the industrial production, the stock of durable goods and bank assets, suggesting that the pandemic places the economy in recession". What the study shows is that "the cities that implemented more rapidly the most severe non pharmacologic interventions (NFI) - such as social distancing and lockdown - did not show worse levels of economic recovery. The data also shows that the cities with the most aggressive NFI measures recovered more rapidly. Professor Emil Verner, co-author of the study mentioned above, adds that "We did not find evidence that the cities that acted with more aggressive INF's showed worse economic performance. If anything, the cities that acted more aggressively showed an improved economic performance". Several examples can be seen in the study of different cities comparisons [23,24]

This study brings to light a potentially relevant conclusion at a clinical and economic regard: there is no trade-off between the necessary public health measures and economic activity: "the locations most strongly affected by the pandemic are less capable of reconstructing their economy as swiftly when compared to areas less affected by the same effects". Cities that invested more rapidly in social distancing measures, closures of schools and others measures obtained a better clinical performance but also an quicker economic recovery.

This study shows several other NFI measures adopted in 1918 which are being taken today by several countries throughout the world. Groudning our reasoning in the study mentioned above, it is possible and likely that countries, states and cities which have taken NFI measures more promptly and aggressively not only contained the pandemic to a better degree but in doing so, also created conditions for an improved and faster control of the return to the normal prepandemic economic levels.

This conclusion is, by itself, solely partial. The economic support measures taken by the countries, states or cities, central banks and other entities are essential for the determination of the impact of the pandemic on the capacity of economic recovery.

The IMF made a compilation of economic measures taken worldwide by the different governments as a response to COVID-19. The IMF also stated that on the regard of macrofinancial measures to fight the supply and demand shocks that arise from the pandemic, should be designed and implemented in "no regret" mode, in order to shorten and reduce the economic impact on the crisis. The measures should be implemented in a timely manner and directed to economic and population segments that will be more severely affected, in addition to liquidity measures to mitigate risks of financial instability [25,26].

These measures, as it is said in the NECEP study for the Portuguese case, are of major importance. The study says "the governmental decisions and those of the central banks will significantly influence the economic activity in the short term". The reaction of the economic agents in Portugal was also very quick in response to the crisis with over 33 thousand companies in Lay-off, representing a total of 556.000 workers, in order to protect companies and workers [22,27].

The government placed a collection of measures in motion, firstly of safekeeping of public health, mentioned on the first part of this article, followed by macro-financial measures at the disposal of the companies and of the individuals and in support of liquidation, in agreement with the guidelines of response to the crisis advised by the IMF. The economic agents in diverse sectors were themselves quick in their individual responses to this crisis. Several companies changed their productions to devices or materials needed to fight this crisis. Companies selling alcoholic beverages engaged in the production of alcoholic solutions for disinfection companies in the textile field developed production capacity of masks and other individual protection equipment and companies linked to plastics designed several utensils for the collection of samples such as swabs or protective masks [26,28-30].

In conclusion to this point, from an economic analysis point of view regarding the response to the crisis:

The Portuguese government acted well in the prioritization of the public health toward the crisis as a primordial weapon to fight the economic consequences of the crisis, tackling morbidity and mortality rates, The Portuguese government took the correct and required measures on the implementation of social distancing measures and other NFI measures, particularly the closure of schools – against the advice of the National Council of Public Health– in anticipation of various European countries, as well as in the lockdown measure taken on the 20th of March [31]

The NFI measures taken to mitigate the pandemic from a healthcare perspective, are also those that better protect the certainty of the economic agents and allow for the management of a better and swifter recovery, taking into consideration the analysis of the 1918-1919pandemic [23].

The government presented financial and economic measures of in support of the economic and entrepreneurial system, in line with the other European countries. In this component, it is yet early to evaluate the capacity of these measures to support the economy in it's reaction to this double shock of supply and demand, in a logic of "no regret" policies, as advised by the IMF.

This point has been criticized by economic agents in Portugal, but the balance between the measures to take and the financing capacity of the country must be taken into account given the lack of European solidarity demonstrated on several occasions throughout this crisis, so far.

An example of this are the coments made by the dutch minister of finance to the countries of southern Europe, refuted publicly by the portuguese prime minister in vehement manner as "repugnant and anti-EU" [32].

The theme of European solidarity and of financial European solidarity – for instance, via mutualized debt (Corona Bonds) – will not be a target point of this article, but is, in our view, an issue of necessary reflexion in the logic of "no regret" policies to face a crisis with economic, social and political consequences that have never been seen nor felt by this generation, nor by its poticians and decision-makers.

Ethical Perspective and Conclusions

Making an analysis under the prism of Medicine, a calamity is characterized by an acute and sudden situation where the demand of resources is insufficient to guarantee the medical support to all. The aspects of screening and service to the population affected by a calamity must follow the principles of the Medical Code of Ethics.

The principles of bioethics must be respected: autonomy, beneficence, non-maleficence and justice. If in daily clinical practice one privileges the autonomy principle, in situations of medical emergency it is the principle of beneficence that guides the medical practice. For example, in a situation of cardiorespiratory arrest, the decision to initiate reanimation manoeuvres is not subject to previous assessment of individual options, the decision is thus essentially a clinical one [33].

In a pandemic situation which occurs in our profoundly globalized society with intense circulation of people, the virus SARS CoV-2 has found ground for rapid dissemination. In countries as Italy and Spain, the dissemination occurred in uncontrolled manner, having taken the dimensions of a real humanitarian catastrophe . The scarcity of human resources and the collapse of the healthcare services obliged the doctors to decide which patients had a greater chance of survival and to only those was applied invasive ventilation. In other words, the principle of Distributive Justice acquired chief relevance in the taking of these difficult clinical decisions [34,35].

It is known that political decisions in this context of a pandemic must respect ethical principles. Firstly, there is the principle of necessity: social isolation measures are implemented because they are necessary to contain the

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dissemination of the virus in the population. Secondly, there is the principle of precaution which aims to ensure that there will not be unnecessary risks for public health. Thirdly, we have the principle of proportionality, meaning, to avoid legislative excesses, namely regarding the limitation of individual freedom if such a measure does not result in obvious benefit to all. Fourthly, the principle of transparency according to which all the measures must be accompanied by clear and effective communication. The fifth principle is that of solidarity which aims to ensure cooperation between all social actors so that there is the protection of those who are most vulnerable. The last principle is that of subsidiarity. Subsidiarity and cooperation promote the sharing of public policies and strategies of intervention in healthcare, contributing to the establishment of equative and proportional measures [36].

As the clinical and epidemiologic perspective explicated, the aim is the flattening of the curve of the progression of the epidemic. The deacceleration of that progression would avoid the rupture of the healthcare services and would ensure, to a certain extent, the existence of therapeutic resources to all. However, i tis also true that measures usually referred to as non-pharmacologic, such as social isolation and domestic confinement, cannot be imposed indefinitely until the obtainment of an effective cure or vaccine for the disease. For this matter, realistically speaking, the implicit overburdening of the healthcare system would end up undermining the care for the other pathologies.

In the economic and political perspective, the nonpharmacologic measures will necessarily cause a severe economic recession with a supply and demand shock in the entire world, and Portugal will be no exception, as Portugal shows, at the present moment, a high degree of uncertainty regarding the extent of this economic recession. However, those measures and the rigor in their implementation are the best attempt to guarantee an economic recovery, taking as grounds the measures taken by different location in the pandemic of 1918-19. This means that the NFI measures are the best choice to safeguard public health and mitigating economic effects and enabling and quicker economic recovery.

Following this line of reasoning, the implementation of serological studies which enable the creation of an immunological passport may constitute a rational way to facilitate the gradual relief of the domestic confinement measures and the gradual return to entrepreneurial activities.

The authors also suggest that whilst there is no vaccine, the use of individual protection masks on a daily basis, which contributes to the prevention of contagion, may constitute an important resource to allow the resuming of a certain extent of normality in people's lives, while the pandemic is not totally defeated [37,38].

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