COVID STRATEGY

Systematic concentric circle testing methodology

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NATO CENTRE OF EXCELLENCE FOR MILITARY MEDICINE

The WHO statement "Testing, Testing Testing!!!" has crucial value in the process of defeating the infection and terminating the SARS-CoV-2 pandemic crises.

This paper is proposing an effective combination of three imperfect testing methods as a solution for a testing strategy, as a base for emerging coordinated medical, social, economic and politic measures.

When the vaccine will be available, a massive vaccination will be applied at the populational level. In the absence of the vaccination and effective treatment, the systematic testing is a decisive condition for success. As none of the testing methods proved themselves as being generally effective and applicable, a combination of them, would amplify the advantages and minimize the disadvantages.

The rationality is based on empirical assumptions, reasonably accepted.

In example:

- **The higher number of people are tested, the more asymptomatic or mild symptomatic infection carriers will be identified.**
- **Lower number of infected will produce a lower rate of infections**
- **The accuracy of the testing method will influence the effectiveness of diagnosis**
- **The number of infected will influence the loading of the medical systems**
- **The entire population cannot be tested at the same time**
- **The medical system role is crucial. Could be the problem (source of infection) or the solution (prevention, testing and identifying the infection, treatment)**
- **The logistical and economic conditions are determinant.**
- **Preserving and enlarging step by step the cleared areas will lead to cleared society**

The description of the testing methods with advantages and disadvantages are scientifically proved and there are numerous related articles published in science journals and publications.

Summary

AIM

The strategy aims to provide an effective solution to limit the amplitude and duration of the epidemy, preserving the functionality of the essential services.

DESCRIPTION

The SARS-CoV-2 pandemic is dramatically challenging the medical systems all around the word. The extremely high infectivity rate, even before the symptomatic stage and the general receptivity, in conjunction with significant number of non-symptomatic ore low and low- symptomatic patients, gives a tremendous difficulty to establish a clear situational awareness regarding the number and distribution of the infected.

The economic and social effects are without precedent, affecting the availability of necessary resources to manage the special and unique situation.

In order to prevent the development of the pandemic expansion, the identification of the infected is crucial.

The unavailability of an efficient method of testing to be applied at the populational level is the main difficulty, and many nations are experiencing several methodologies and strategies in order to understand the amplitude of the situation.

The strategy consists in introducing an objective, coherent, systematic, efficient and effective testing methodology with the purpose to trigger the additional adequate measures to limit the expansion, to reduce and to eliminate the epidemic situation.

The “door to door” populational testing strategy has low chances of success, due to the fact that there is a high risk for the tested population to be infected by the potential carriers from the untested population. Moreover, the costs, the logistic and administrative requirements of testing the entire population could be predicted as very difficult, almost impossible to be achieved.

This strategy is proposing a narrowed testing methodology, guided by precise criteria, based on population at risk, the gravity of evolution, the functionality of the essential services, and the characteristics of the transmission and virulence of the epidemy.

The testing process will follow the model of concentric circles in expansion, starting with well-defined circle centres: the medical system; the suspected voluntary isolated patients; the essential services; the population at risk for severe evolution; security and emergency systems; and the transportation of persons and mobility of goods.

As a base, the recommended method of testing is the antibody IgG/IgM Assay detection method.

The method does not imply a laboratory, can be applied on site by a technician, and requires 20 minutes for getting the results.

The rapidity, simplicity, mobility and affordability would compensate the level of accuracy which is described at around 80 to 90%. It will be possible that a certain number of the possible infected individuals will be prevented in a very short time to spread the infection, in the most sensitive parts of the society first, followed by enlarging the testing until the ending of the epidemy.

Considering the dynamics of the immune response, IgM becomes detectable at 7 days after infection.

The individuals with IgG positive reaction, will be considered as having very high chances to be infected and they will be confirmed with RT PCR.

The same confirmation with RT PCR will be applied also to all their primary contacts in the last 7 days, based on the epidemiological investigation. All the primary contacts of the confirmed infected will be tested with RT PCR.

The IgM/IgG test as the triage method, will provide a 7 days retroactive map used by the epidemiologic investigation to identify the primary (direct) contacts. Just the primary contacts will be tested using the RT PCR. This will provide a real, current, updated map of the infection.

Each of the confirmed with RT PCR will become subject of the epidemiological investigation, narrowed exclusively to the primary contacts, in order to be tested with RT PCR.

The systematic and continuous sustained testing inside the below described circles, will eventually merge and clear the 7 days retroactive maps, and will expand untilled the circle will merge at the entire society level.

The testing strategy needs to be accompanied by the other measures in order to be effective: protective measures, social distancing, narrowed and effective quarantine and treatment.

METHODS

1.The epidemiologic investigation method alone is meant for and is effective at the beginning of the epidemic in order to identify all the possible carriers, and not in the situation when the virus is already present in the general population.

The method of epidemiologic investigation meant to identify the contacts of the confirmed infected patients, proved its limits and inefficiency, due to the fast spreading of the infection.

During the time of investigation, the secondary contact circle and then the tertiary became sources and started to spread the infection, even before the investigation reach them. Consequently, there is a high probability of missing contacts which could become the sources of new infections. Extensive epidemiological investigation is not efficient anymore in stage of pandemic were the infected are already possible present everywhere, due to the high level of infectivity and general receptivity.

Functional and economic impact of isolation measures for the suspects without the confirmation of the infection, affects the efficiency of the entities from where they belong, which, in case of medical personnel or the essential services and security or emergency intervention personnel will dramatically impact the essential services (i.e. hospitals).

Only narrowed and limited investigation triggered by the IgM/IgG testing strategy, completed by the standard RT PCR confirmation will prove the value and necessity of this method.

2.The strategy based exclusively on 100 percent of accuracy is wrong and ineffective.

The only method recognized as providing 100% accuracy is real time PCR which is not effective to be applied extensively due to the infrastructure requirements (limited number of labs), time (at least 4 hours for the method, with additional time for transportation of the samples to the lab), biosecurity during the transportation, and costs.

3. IgM/IgG antibody detection method

With a level of accuracy described at around 85% in literature, the method is fast, the rsults are available in 20 minutes on site, without special lab requirement, at significantly less costs.

IgM/IgG Assay method, based on the immune response of the infected body, reveals the presence of the virus, and the stage of infection (at the beginning, the middle or at the end).

85% accuracy would provide the possibility to identify 85% of the infected persons providing a high statistical value at strategic level, significantly reducing the infection risk and with the proper usage could maintain the functionality of essential services, with the special emphasis on the health care system.

The IgM/IgG testing method is limited not just by the level of accuracy but also by the presence of the IgG and IgM, knowing that in SARS CoVID infection the IgM is detectable after 7 days from the infection. Taking into account this disadvantage and based on the described advantages the IgG/IgM detection should be use as a triage method, revealing with 7days delay the infectivity picture at the systemic level.

Compared with nothing or with temperature screening, the advantages are huge, considering that the temperature is not specific to SARS-CoV-2 infection and the absence will not confirm the absence of infection.

METHODOLOGY

The systematic concentric circle methodology consists in simultaneous testing, using the IgG/IgM Antibody Method (Assay method) starting with special initiation points considered as the centres of the testing circles followed by enlarging the circles using the below described methodology.

The combination of the three methods should be applied simultaneously in 6 circles which will extend, until confluence.

The methods will have specific usage aiming specific processes.

Triage: IgM/IgG rapid

Expansion: Narrowed epidemiologic investigation

Confirmation: RT PCR

The strategy should be applied continuously, consistent and coordinated. It will be essential that the testing strategy will be accompanied accordingly, by medical, social, economic and political adapted measures.

1. **Hospitals**

   The medical personnel and the administrative personnel are tested before and after the shift.

   In this case, an average 85% from the infected carrying the virus in the last 7 days will be prevented to continue to spread the infection, being detected in asymptomatic phase or when they are presenting mild an unspecific symptomatology.

   Those who are tested positive will be isolated and tested with real time PCR for confirmation. The level one 7-day retroactive contact circle of these persons will be considered suspects and tested with RT PCR.

   The medical personnel is tested also after finishing their work. Inside of the hospital a source will infect his/her contacts in consecutive moments, so the IGM will be detectible in consecutive moments. As the IgM/IgG method is a retroactive triage for mapping the infection, the repetitive tests will increase the accuracy of the method and will increase the chances to detect the infection as soon as possible.

The patients

All the new patients arriving to the hospital will be tested in a triage area before entering the hospitals. Any patient with a positive test result will follow the pathway and protocol for the infected patients.

Consequently, the first contact circle of these identified carriers/infected patients will be tested as well (family, friends...). This measure will decrease dramatically the chance to infect the hospital and will increase the chances to identify the existence of the infection in a part of society.

The hospitals should be considered the priority centre of systematic concentric testing strategy because:

- The medical personnel are the most exposed at risk
- The infected medical personnel could be the most effective source of infection for the most endangered population (patients with comorbidities)
- The risk of infection is higher than in general population

Results: **Cleared hospitals, cleared contact circles**

- Effective reducing the risk of infection of the hospitals
- Effective early detection of infection of the hospitals
- Effective early diagnostic of the incoming patients
- Effective detection/clearing of the infection inside the contacts circles
- Effective motivation of the medical personnel. Ensuring the continuity of testing among medical personnel will exponentially rise the morale and the sense of security of this very vulnerable group

2. Isolated suspects

Current situation: As the voluntary isolated suspects are tested with real time PCR just in case of specific symptoms, if they do not develop symptoms during the isolation period, they have freedom to move as the general population. In case of asymptomatic or low symptomatic infection they could still be carriers, even after the isolation. As a result, there is a high probability for spreading the infection even after the isolation, for example during shopping, or other permitted activities.

Systematic testing of the isolated population with the Assay Method will identify 85 % of the infected, which persons will be confirmed by PCR testing, quarantined and treated.

The patients with negative results will be tested again at the end of the isolation period, before being considered as the general population.

This measure will decrease the chances of infection from this highly potential source of infection with another 85%

3. **Population at risk of severe disease**

As known, there is a population at risk defined as the candidates for the ICU and for death caused by COVID19.

The elders above 65 years old are subject to special restrictions and measures in many countries.

A weekly systematic testing program could be feasible for this special population category, due to:

- Early diagnostic and more effective therapy
- The elders are living in pairs of two in family, or in nursing homes with many possible cohabitants, having as a consequence a multiplying risk of infection. The early detection would decrease the risk of overloading the hospitals and most important will decrease the pressure over the ICU capabilities
- Predictability of the number of severe evolutions will support a proper readiness of the system to face and solve the situation

4. **Essential services: water, power, gas, communication, food, administration**

The employees running the essential services are exposed to the risk of infection as the general population is, leaving in their families. Added to this, they are in permanent contact with their colleagues and other persons during the job execution. As a consequence, they can import or export the infection from and to their families and also from and to their institution or general population.

The rapid IgM/IgG test will decrease the risk of infection and will increase the chances of effectiveness of the essential services on a long term.

Daily tests will increase the accuracy, by repetition.

On the other hand, a positive test will allow an early detection of the risk and effective measures to coup the bridge in bio security of the services.

Furthermore, a positive result will trigger the testing in the primary contact circle of contacts, enlarging the circles of clearing process in general population.

The same combination with epidemiological investigation and RT PCR will be applied.

5. **Security and emergency services: police, gendarmery, firefighters, military**

The principle is identical with the previous category.

Moreover, the risk of receiving or spreading the infections is higher, due to the specificity of their mission, interacting randomly with general population (many of them are those who are not obeying the rules of isolation or escaping from the quarantine with high risk of positive infection)

6. **Mobility of persons and goods:**

Systematic testing of all the travellers and transporters: ground, air or maritime, at origin and at destination and at the borders. This measure will prevent the import-export of the infection.

The testing should be also applied at all the borders.

The positive tests will initiate the circles of testing, accelerating the efficiency of this strategy.

Furthermore, the measure will add a sense of security to the mobility of goods.

RESULTS

All the described circles of this concentric testing strategy would merge at some point, having as a result, due to a coherent and narrowed mass testing strategy:

- Early diagnosis
- Functional hospitals
- Functional essential services
- Effective security and emergency response system
- Effective isolation of the infected persons
- Decreased pressure on the medical system and ICU
- Efficient and more predictable epidemic limitation in time and amplitude

The graphic representation of the testing strategy in evolution

The dark red represents the uncertain presence of the infection

The lightening evolution of the dark red, represents the increasing level of the cleaning in the target circle

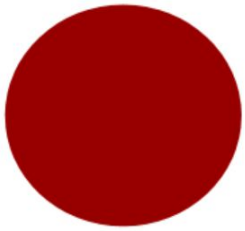


Fig.1 Target circle (i.e. Hospital) before Testing

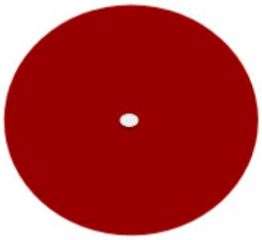


Fig.2 Systematic test beginning (white spot)

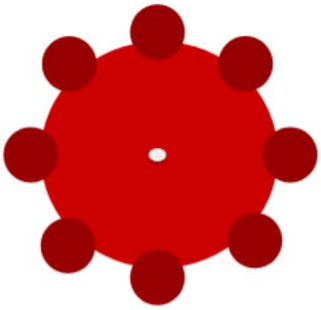


Fig.3. Measures for clearing the infection (lighter red colour), identifying the primary contact circles (small dark red circles)

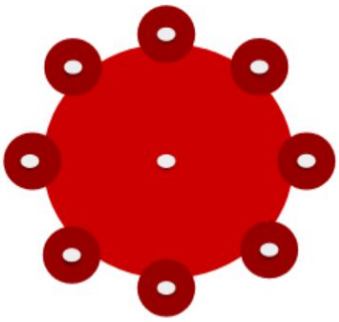


Fig.4 Continuing the testing process in the hospitals, testing the contact circles (white spot in the small dark circles

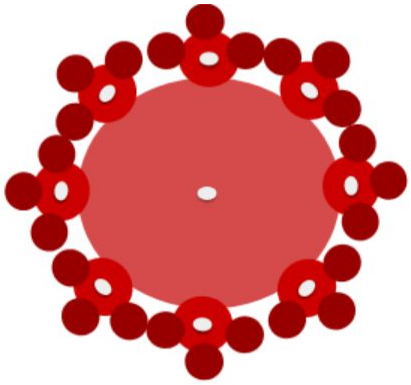


Fig.5 Continuing the testing process in the hospital identifying the extended contact circle (smallest, peripheric dark red spots)

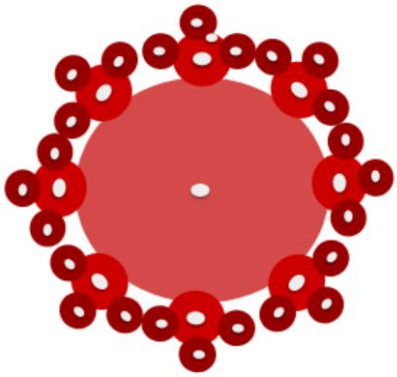


Fig.6 Continuing the testing the in the hospital, testing the extended contact circles

Fig.7,8,9,10 Expansion- Sustaining the expansion of testing (in the target circle and the peripheric contact circles)

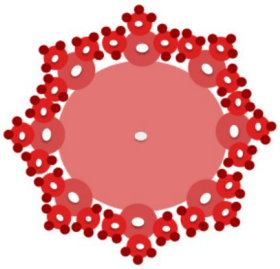


Fig.7

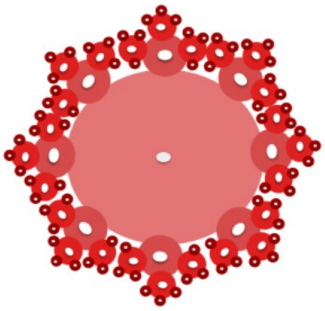


Fig.8

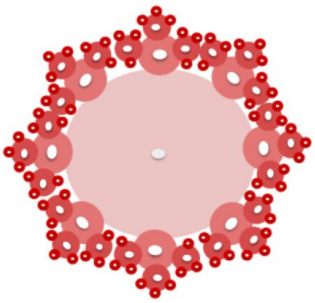


Fig.9

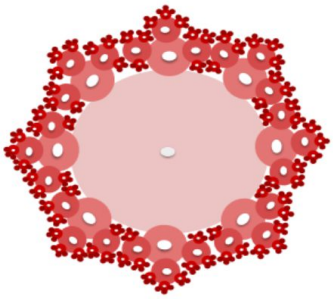


Fig.10

Fig.11 Populational picture of the 6 circles before testing

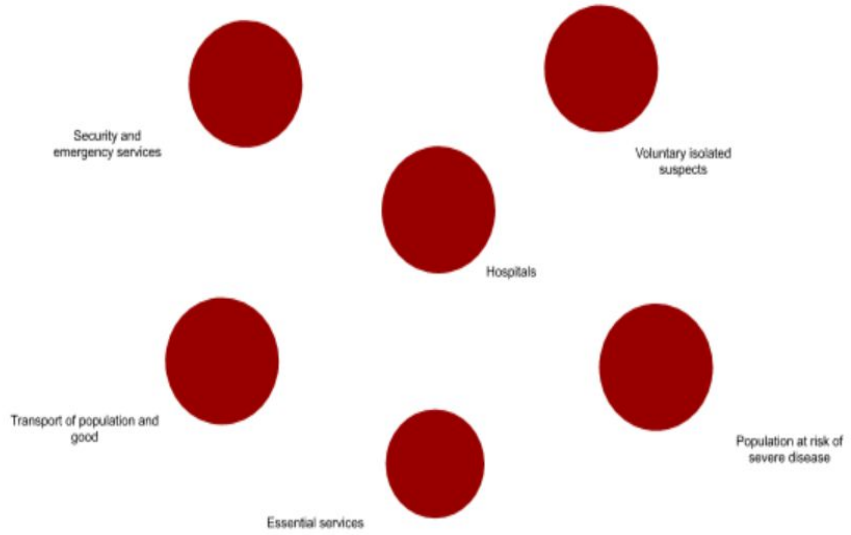
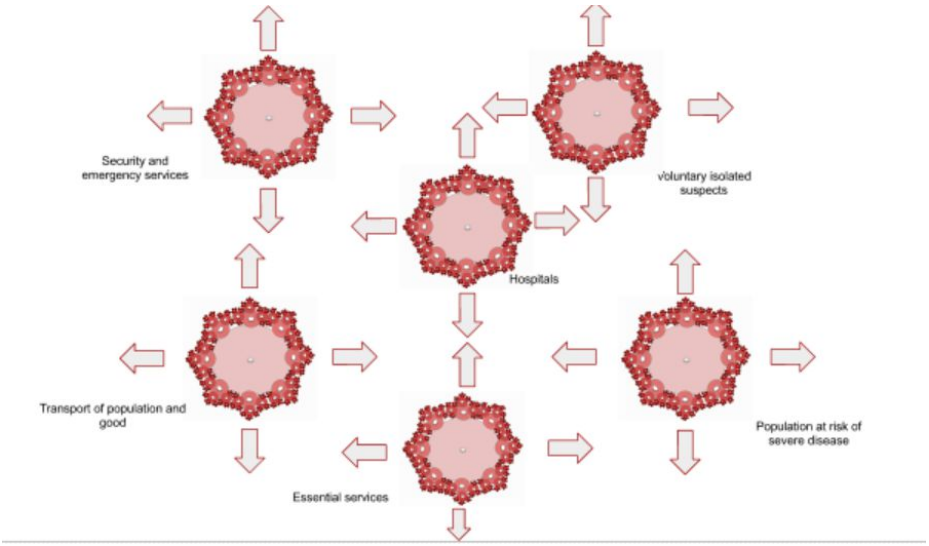


Fig.12 Populational effect of expanding of the 6 testing circles (with the concentric circle testing strategy)



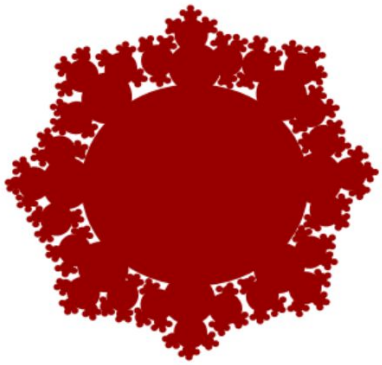
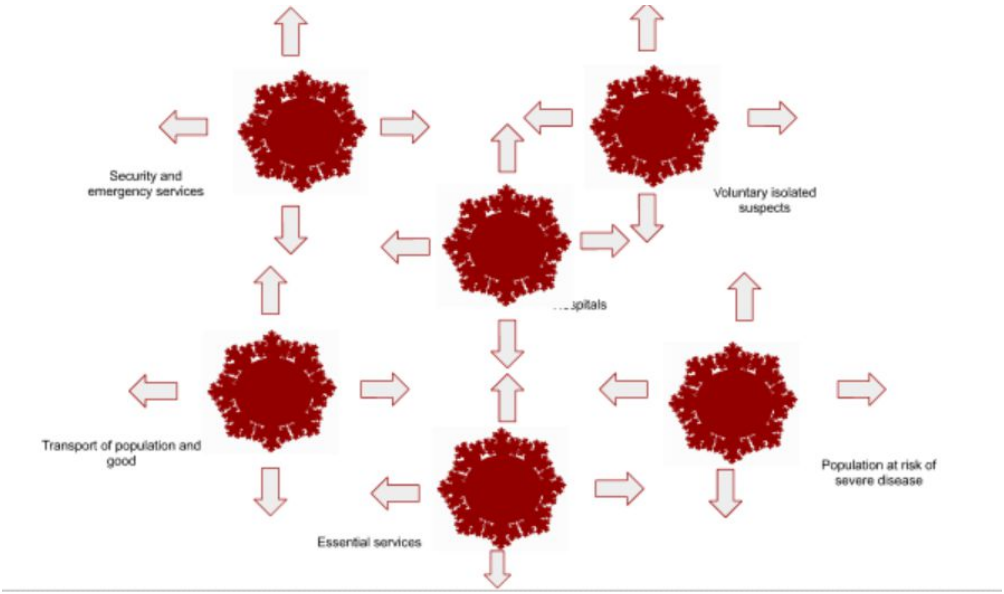


Fig.12 Infection spreading from 1 circle without testing

Fig.13 Populational effect of the infection spreading without testing strategy



Systematic testing process will progressively clear the defined circles.

The expansion of the circles will increase the cleared areas and eventually the circles will reach each other and overlap, until the infection is eliminated at the society level.

All the new infected out of the circles will enter the circles since they will become symptomatic, opening new contact circles.

Without the systematic testing strategy, the infection will follow the same pathway as the clearing without testing.

COST EFFECTIVENES

Medical cost: How many tests could be bought by the 1 ICU patient less per day, multiplying with the number of the patients which would not need ICU anymore as a result of this strategy.

Social and security costs: How much money would be spent for unfunctional essential and security systems

Economical costs How much money would be saved by the national economies for every day of shortening the medical emergency special crisis

CONDITIONS FOR SUCCESS

In order to be efficient, the concentric systematic testing strategy should be applied strictly coordinated in the entire community. The testing process should start at the same time in all the defined circle centres.

The rapidity of testing, the mobility of the testing materials, the relative acceptable costs of the testing method, and the acceptable accuracy, are the main arguments in favour of the concentric systematic testing strategy.

This strategy would be effective combined with all the other measures, objectivising the epidemiologic investigations, and providing objective criterium for the narrowed and effective actions.

NOTE: The Strategy is based on usage of low level of specificity (80%) and sensitivity (90%) of the method compensated by the rapidity, mobility and affordability.

As is stated in the methodology, the lack of accuracy is assumed and repeated tests (twice a day, daily and weekly) will increase the chances to capture the misdiagnosed. However, they will continue to infect their contacts, medical personnel or patients. Corelating the positive testing from this new group of infected (85% will become positive) with the narrowed epidemiologic investigation, the undetected source will be identified with very high probability. However, the RT PCR should remain the standard method, and used only for confirmation of positive rapid tests.

DISCUSSION

Because the infection is spreading so fast and so easy, being present in society everywhere, it is not without sense to assume that everybody could be considered as potential infected.

All the existing strategies are developed and applied in stages, based on the extension of the infection, measured by the number of infected, the rate of infected and the fatality rate.

For example, considering that the medical systems as being at the front line of the effort, the availability of the medical personnel is essential. Preserving the limited human resources in the health systems is essential especially under the continuous increasing pressure in the pandemic situation. Based on the real data provided by this strategy, the managing process of the human resources will be adapted in line with situation. If the situation requires, the medical personnel could be kept implicated, even if they are affected by the infection (asymptomatic infected, low symptomatic infected, uninfected). Special protocols should be developed for each situation. The effectiveness of the medical human resources strategy depends on the accuracy of the data.

A reliable situational awareness is fundamental for the effectiveness of all plans and measures.

There are several theories which are meant to consider the necessity and reliability of objectivising the real expansion of the infection, in different manners. For exemplification to opposed theories are described below:

The blind theory.

A rational theory would be to assume, without testing anybody, considering everybody as being possible infected, so everybody should be responsible to act as an asymptomatic infected person and be responsible to apply the protective measures against spreading the infection. In this case the infection propagation would be blocked or significantly limited and after a certain time the epidemy would be terminated.

The weakness of this theory is given by the fact that is relaying on individual responsibility of all the members of society, which has a very low chances to succeed. We could witness the numbers of penalties applied to those who does not comply to the rules imposed by the authorities.

Appling the blind theory would make impossible to objectivise a dimensional measurement of the phenomena and the real effects would be revealed by the number of severe pathology and fatality.

Being unable to predict, the system will be unable for proper preparation and proper reaction.

The flash theory:

The attempt to find all the infected with 100% accuracy testing methods.

This theory would be successful if the 100% accurate methods would be available, affordable and time effective. In reality, the only available 100% accurate method is the RT PCR which requires special infrastructure (specialized laboratories) and is inefficient in time, which requires strict isolation of the subjects from the moment of testing to the moment of finding the results. Even in case of availability of the necessary tests, the method is impossible to be applied at populational scale.

Due to the length of the process, the proved uninfected subjects are at risk to become infected at any moment. This will compromise the situational awareness about the real situation. Those who are confirmed uninfected, might become infected afterwards, acting as a "Trojan horse", inside of the presumed cleared systems, blinding the assessment, and alternating the image and the quality of the emergent strategies and actions

The concentric circle testing strategy

Based on the advantages of three imperfect methods and taking in to account the imperfections of all of them, the strategy is amplifying the combined benefits and minimizing the limitations.

	Method	Advantages	Limitations	Application
1	**IgM/IgG**	**Fast, affordable, mobile, repeatable**	**Low level of accuracy (sensibility sensitivity) Late reliability (after 7 days from the infection)**	**Large scale triage Marking 85 % of the infected**
2	**Epidemiological investigation**	**Identification of the possible infected (contacts of the confirmed infected)**	**High rate of subjectivity, Needs Lab confirmation Time consuming**	**Narrowed to define the primary contacts of the positive finding from the IgM/IgG triage and the confirmed infected**
3	**RT PCR**	**100% accurate**	**Time consuming, low affordability, special infrastructure**	**Narrowed and precise confirmation of the suspects identified by the previous methods.**

Triage-confirm-investigate-confirm, systematic inside the circles.

Social distance and protective measures will reduce the primary contact circles.

Special and adequate protective measures for the medical professionals will reduce the primary contact circles.

CONCLUSION

At the moment, the only objective markers of the evolution of the pandemic are the curves of the severe case rate and the mortality rate curve.

The total number of infected and the rate of the new infections are subjective criteria highly dependent on the number of tests.

The actions are reactive and adapted to these curves.

This strategy provides the possibility of realistic prediction and anticipation, adding additional objective criteria to define the evolution.

The systematic application of the three imperfect method's combination in the inside of the expanding circles described in this strategy, would provide a clear and objective picture as a base for the efficiency of the adapted medical, social, economic and politic emerging strategies.

Nevertheless the strategy provides an extensive immunity map based on the IgG positive results which would add extra value and benefits (immune personnel does not need so much protection, the vaccine prioritisation and they could become active social and professional).

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