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Coronavirus Pandemic

Are “cases”, “waves”, “tests” and “modeling” deceiving indicators to describe the COVID-19 pandemic?

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Abstract

This commentary elaborates on different methodological aspects complicating the interpretation of epidemiological data related to the current COVID-19 pandemic, thus preventing reliable within and across-country estimates. Firstly, an inaccuracy of epidemiological data maybe arguably be attributed to passive surveillance, a relatively long incubation period during which infected individuals can still shed high loads of virus into the surrounding environment and the very high proportion of cases not even developing signs and/or symptoms of COVID-19. The latter is also the major reason for the inappropriateness of the abused “wave” wording, which gives the idea that health system starts from scratch to respond between “peaks”. Clinical data for case-management on the other hand often requires complex technology in order to merge and clean data from health care facilities. Decision-making is often further derailed by the overuse of epidemiological modeling: precise aspects related to transmissibility, clinical course of COVID-19 and effectiveness of the public health and social measures are heavily influenced by unbeknownst and unpredictable human behaviors and modelers try to overcome missing epidemiological information by relying on poorly precise or questionable assumptions. Therefore the COVID-9 pandemic may provide a valuable opportunity to rethink how we are dealing with the very basic principles of epidemiology as well as risk communication issues related to such an unprecedented emergency situation.

Key words: COVID-19; surveillance; epidemiology.

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Introduction

The epidemiological description of the COVID-19 pandemic was initially focused on the number of confirmed positive cases and deaths. The total number of molecular tests (at real time PCR), disaggregated by age, gender and co-morbidities was mainly introduced afterwards.

The unpredictable and exponential spread of the epidemic severely burdened the healthcare systems throughout the world, prompting the enforcement of various non-pharmaceutical risk reduction measures including also country lockdowns. The spread of the disease called for immediate research actions including assessment of available health data related to clinical care, epidemiological investigations/projections, health care evaluation, assessment of public health interventions and for decision-making.

Despite the efforts of detecting, reporting, and interpreting global data around the COVID-19 pandemic, a series of methodological challenges rapidly emerged and still persist. In this commentary we tried to explore the strength and weaknesses of various aspects related to COVID-19 surveillance, which should carefully be taken into consideration when attempting within- and across-country comparison and correlation.

Cases and waves

Numbers and frequencies are reported by national health authorities and are the result of a passive surveillance [1] Specifically, notification of cases is performed at a health care facility level and, then, transmitted to regional and national bodies prior to release to the public.

Passive surveillance cannot provide a realistic picture of both size and trend of a large epidemic; such inference has become even more problematic during the COVID-19 pandemic due to incomplete coverage and to a large portion of asymptomatic (pre-symptomatic, asymptomatic and pauci-symptomatic) individuals who can still effectively transmit SARS-CoV-2 [2,3]. It is estimated that as much as 44% SARS-CoV-2 infections are caused by pre-symptomatic individuals) [4].

On the other hand, merging and cleaning hospitals data requires sophisticated software, not necessarily available in low- and middle-income settings. Moreover, patients consent and ethical statements often represent additional bureaucratic barriers to rapidly access to patients' data. The Pandemic situations require pro-active interventions to handle these issues, which should be discussed at national level [5].

Clinical data are highly time-dependent and need advanced statistical methods to adjust for typical biases like selection and misclassification. Standardization is probably one of the approaches to allow for comparability of data across different settings; however, lack of agreement and competing issues, such as excluding mortality due to other causes, often complicate the situation.

The number of deaths is often used as an indicator to quantify the severity of a disease. As rightly defined by the Institute for Health Metrics and Evaluation (IHME), daily deaths are "the best indicator of the progressions of the pandemic, although there is generally a 17- to 21- day lag between infection and deaths" [6].

At the current stage of the pandemic, where the reported confirmed COVID-19 cases are on the rise almost everywhere worldwide, a revision on the use of the current epidemiological and statistical indicators, from those adopted to describe the pandemic to those applied to monitor health system capacity to deal with severe cases, might be a pragmatic and timely decision.

In which case, focusing on bed occupancy rates in hospitals would be more important than counting the number confirmed COVID-19 cases or the number of daily diagnostic tests performed. Additionally, disaggregation by general/ICU beds and ventilators occupancy might prove accurate severity measure of the current impact of the pandemic.

However, when considering such indicators, the role of community awareness, care-seeking behaviors and hospitalization criteria cannot be neglected.

Furthermore, there is no agreed definition on the line "epidemiological wave". The fact that most of the cases are mildly or not symptomatic implies that there is no way to confirm the achievement of a zero-case scenario at country level. A wave implies a rising number of sick individuals, a defined peak, and a subsequent decline. Moreover, the word "wave" entails a natural pattern of peaks and valleys; it means that even during a lull, future outbreaks of disease are still possible. In the case of COVID-19, arguing whether a country is in a second or third wave is therefore inappropriate.

The "wave" thinking can be misleading as it gives the impression that health system starts from a scratch to respond. Building the analysis on this assumption without incorporating knowledge and experiences may give false expectations and wrong interpretations on the trend of the epidemic, thus leading to wrong public health decisions.

Tests

Molecular assays to diagnose COVID-19 were quickly developed once the genetic sequence of SAR-CoV-2 was published in January, 2020 [7].

The number of tests performed is usually part of the passive surveillance system and, hence cannot describe the response to an epidemic or assess the spread of a virus in a community. Even testing strategies targeting vulnerable groups cannot be considered appropriate.

As SARS-CoV-2 infected individuals may be contagious without or before showing symptoms, tracing is inevitably challenging; while asymptomatic individuals appear to account for only 15% of infections [8] pre-symptomatic individuals are estimated to regard 50% of total infections [9].

Large-scale testing programs were conducted to address the above challenge and allow an earlier identification of asymptomatic and pre-symptomatic carriers in several sites around the world [10]. City-wide testing programs have for instance been reported in various cities in China, including Wuhan (May 2020) and Qingdao (October 2020) [11]. Again, while this strategy may be applied in high-resourced settings, it can be a major bottleneck for the majority of countries in Sub-Saharan Africa as well as in other developing world regions.

Also, to note the increase rate of false negatives tests with the dilution of samples due to group testing, which is not often taken into consideration [12].

On the other hand, delays in obtaining molecular testing results inevitably increase the risk of SARS-CoV-2 transmission. The longer patients wait, the more likely they will not self-isolate at the time that they are most infectious and will resume daily activities before receiving test results. The global competition for

reagents and supplies, which has severely slowed down the testing capacity, particularly in resource-constrained settings represents another limitation of molecular testing. The consequences of these limitations include continued restrictions and delays in confirming or excluding SARS-CoV-2 infection at the individual-level for case management or isolation, and at population-level for surveillance and response purposes [13]. The introduction of saliva COVID-19 testing to screen the prevalence of SARS-CoV-2 variants in the genral population has further aggravated the situation [14].

Antigen-detection rapid diagnostic tests (Ag-RDTs) are a valid alternative in various settings. Ag-RDTs can be visually read or processed and read using a small portable device, can be done outside the laboratory and provide a result within 15–20 min. These rapid tests can be produced much faster and cheaper in larger quantities for large scale deployment. Although these tests can be highly specific, they are generally not as sensitive as molecular tests [13].

Epidemiological modeling

Epidemiological modeling is complicated, and paucity of inputs required to inform models represents a major issue. Precise aspects related to transmissibility, clinical course, and effectiveness of the public health and social measures (PHSM) are influenced by unbeknownst and unpredictable human behaviors and modelers try to overcome missing epidemiological information by relying on poorly precise or questionable assumptions [15].

There is a dearth of evidence on the actual usefulness and accuracy on epidemiological models. A good example is provided by a 2020 Cochrane systematic review on the assumptions related to the "stay-at-home" public health policy [16]. One of the major problematic factors resulting from the latter systematic review was that the policy was analyzed as binary indicator and the number of new cases could have been easily undocumented, causing potentially significant biases in intepreting results. The "stay-at-home" policy therefore might not have been that effective as riks reduction measure against SARS-CoV-2 transmission.

Subsequent mathematical models showed that the combination of "staying at home" together with the use of face masks, hand washing, early-case detection (PCR test), and the use of goves as well as hand sanitizers for at least 50 days could have reduced the number of new cases. The simulations that drove the world to lockdown was eventually questioned [17].

As previously mentioned, all the available studies applied relatively complex epidemiological models with unrealistic parameters that were either chosen or accommodated "*ad-hoc*". Also, it is important to note that the temporal delay between the introduction of a certain intervention and the actual measurable variation in the number of cases and death rates prevented by such interventions is often not properly be taken into account.

International scientific societies and international bodies could provide focused guidance to adequately assess the burden of the infection, appropirately comparing the effectiveness of public health interventions at national and international level.

Conclusions

As suggested by Ibrahim, applying active surveillance, use of more innovative methods for data collection, and crowdsourced tasks will add important values for controlling the COVID-19 pandemic. However, this goal can be achieved by designing surveillance systems tailored to a national context, in terms of epidemiological burden of the disease and healthcare system characteristics [18].

The COVID-9 pandemic provides a valuable opportunity to rethink how we are dealing with the very basic principles of epidemiology as well as risk communication issues related to such an unprecedented emergency situation.

Authors' Contributions

CMPN, SB and OAM conceived the overall concept and wrote the first draft of the manuscript. LC, GP, GS and GF helped in the literature review and contributed to the first version of the manuscript. CMPN, SB, GS and OAM revised the manuscript and prepared the final version.

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