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Epidemic Surveillance of Covid-19: Considering Uncertainty and Under-Ascertainment

Vasco Ricoca Peixoto[a, b] Carla Nunes[a] Alexandre Abrantes[a]

[a]Public Health Research Centre, NOVA National School of Public Health, Universidade NOVA de Lisboa, Lisbon, Portugal; [b]Public Health Unit, North Lisbon Health Centers, Lisbon, Portugal

Keywords
COVID-19 · Surveillance · Under-ascertainment · Under-reporting · Surveillance system sensitivity

Abstract
Epidemic surveillance is a fundamental part of public health practice. Addressing under-ascertainment of cases is relevant in most surveillance systems, especially in pandemics of new diseases with a large spectrum of clinical presentations as it may influence timings of policy implementation and public risk perception. From this perspective, this article presents and discusses early evidence on under-ascertainment of COVID-19 and its motifs, options for surveillance, and reflections around their importance to tailor public health measures. In the case of COVID-19, systematically addressing and estimating under-ascertainment of cases is essential to tailor timely public health measures, and communicating these findings is of the utmost importance for policy making and public perception.

Vigilância Epidemiológica do COVID-19: considerações sobre incerteza e sub-deteção

Palavras Chave
Vigilância epidemiológica COVID-19 · Sub-identificação · Sub-deteção · Sensibilidade sistemas de vigilância epidemiológica

A vigilância epidemiológica é uma parte fundamental da prática de saúde pública. Considerar e avaliar a sub-deteção de casos é relevante na maioria dos sistemas de vigilância, especialmente em pandemias de novas doenças com um amplo espectro de apresentações clínicas, porque pode influenciar os momentos e as decisões em políticas de saúde e a perceção de risco da população. Este artigo apresenta e discute evidência inicial sobre a sub-deteção do COVID-19 e os seus motivos, opções de vigilância e reflexões sobre a sua importância para informar medidas de saúde pública. No caso do COVID-19, abordar e estimar sistematicamente a sub-deteção de casos é essencial para adequar as medidas de saúde pública, e comunicar esses achados é de extrema importância para a formulação de políticas.

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Vasco Ricoca Peixoto
Public Health Research Centre
NOVA National School of Public Health, Universidade NOVA de Lisboa
Avenida Padre Cruz, PT–1600-560 Lisbon (Portugal)
vrf.peixoto@ensp.unl.pt

Introduction

Epidemic surveillance is a critical component of public health practice. It gives us pictures of reality, informs policy and decision making, gauges health service demand, and feeds forecasts and models.

However, surveillance is never perfect and diseases that present with a high proportion of mild, pauci-symptomatic, or subclinical cases can be hard to detect in most indicator-based surveillance systems and become harder to contain [1]. Surveillance pyramids can take different formats and proportions of undetected cases (often mild or asymptomatic). The scientific community is making efforts to address uncertainty about where to draw the lines separating different clinical manifestations and between ascertained and unascertained cases.

Covid-19 surveillance is challenging because mild and subclinical cases may not seek health services, cases are advised to avoid health care unless necessary, and testing capacity may be limited (Fig. 1).

In the case of COVID-19, addressing and estimating under-ascertainment of cases is essential to tailor public health measures. Communicating these findings is of the utmost importance for evidence-based policy making and community engagement.

Imported Cases, Uncertainty, and Under-Ascertainment

In Europe in late February there was a fast rise in the number of confirmed cases in Italy, and the probability of importation of cases of COVID-19 may have been high in Europe until Italy stopped movement from Northern Italy and later from the rest of the country. The rapid rise and characteristics of confirmed cases in Northern Italy indicated an earlier important undetected community transmission, especially among mild cases. As such, it is possible that in late February many cases from Northern Italy (and possibly from other European areas) were exported all over Europe. These cases may have given rise to mostly undetected transmission chains that remained active in the next months, justifying early enhanced surveillance and control measures that were taken by different governments to buy time for preparedness.

The generalized under-detection of imported cases has been confirmed in a study in Singapore, which estimated that the overall ability to detect imported cases was 38% (95% HPDI: 22–64%) of Singapore's capacity. In high-quality surveillance locations (based on the Global Health Security index) it was 40% (95% HPDI: 22–67%) [2].

In line with these findings, a report by Imperial College London estimated that 2/3 of Covid-19 cases exported from mainland China remained undetected worldwide (until February 17), resulting in several undetected transmission chains. They found countries in Europe had relatively low sensitivity for imported cases [3]. A relevant part of the fast growth in detected cases in Italy and other countries could be related to undetected transmission chains from early introduced cases and accumulated a large pool of infected cases.

It is likely that a high proportion of imported cases all around Europe have not been found, and isolation, contact tracing, and quarantine could not be applied considering the WHO suspect case definition (as of February 27, 2020).

Although many countries advised travellers returning from certain areas to report (call a health line or medical doctor) if they had symptoms, it is possible that people with mild symptoms may not have followed this advice. Consequently, many cases that might have followed from this would not be tested because they lacked a clear epidemiological link (Fig. 2).

In fact, several articles suggest a major under-ascertainment/under-reporting of total cases in different countries.

One study modelled the real dimension of the epidemic in Italy from international case exportations and estimated a real size of 3,971 cases (95% CI: 2,907–5,297), compared to a case count of 1,128 on February 29, 2020, suggesting an under-ascertainment of 72% (61–79%) of cases. In sensitivity analyses, the range of variation was from 1,552 to 4,533 cases (implying the identification of 27–75% of cases) [4].

Publicly available epidemiological data for Hubei, from January 11 to February 10, 2020, revealed a significant decline in the fatality rate with time. As testing becomes widespread, the detection of milder cases that would not seek health care in the early stages will result in a lower case fatality rate [5].

Another study used data from air travel and cases imported from Iran in other Middle Eastern countries and estimated that there were 16,533 (95% CI: 5,925–35,538) COVID-19 cases in Iran as of February 25, which meant only 0.6% of all cases had been reported [6].

Other models used reported infection within China, in conjunction with mobility data, a networked dynamic metapopulation model, and Bayesian inference, and estimated that 86% of all infections were undocumented

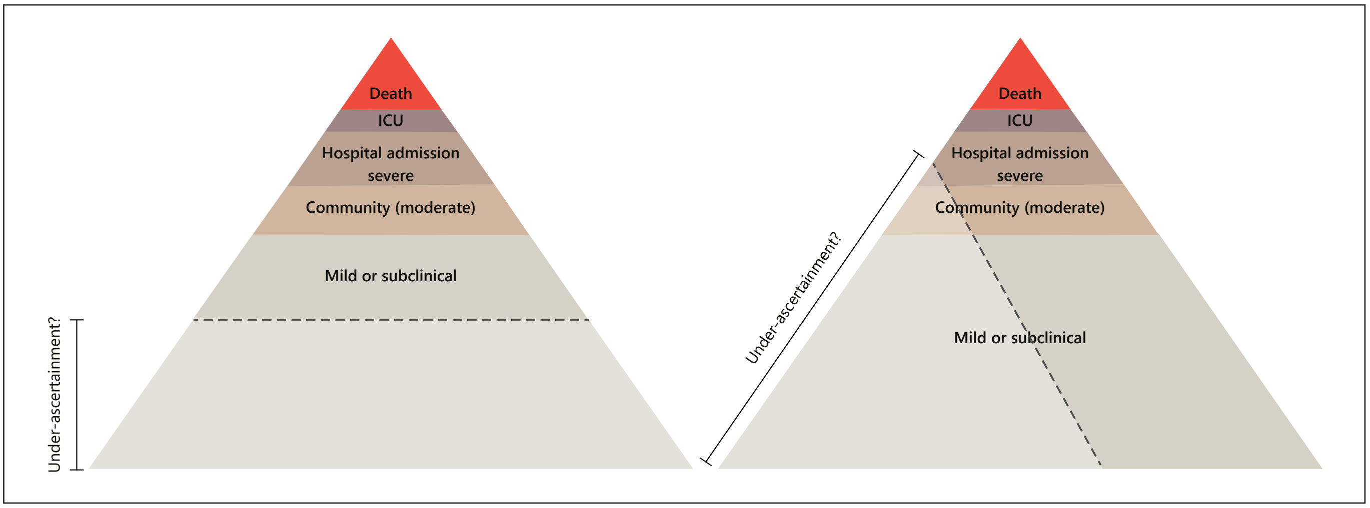

Fig. 1. Hypothetical examples of surveillance pyramids for COVID-19 with two of many possible under-ascertainment lines.

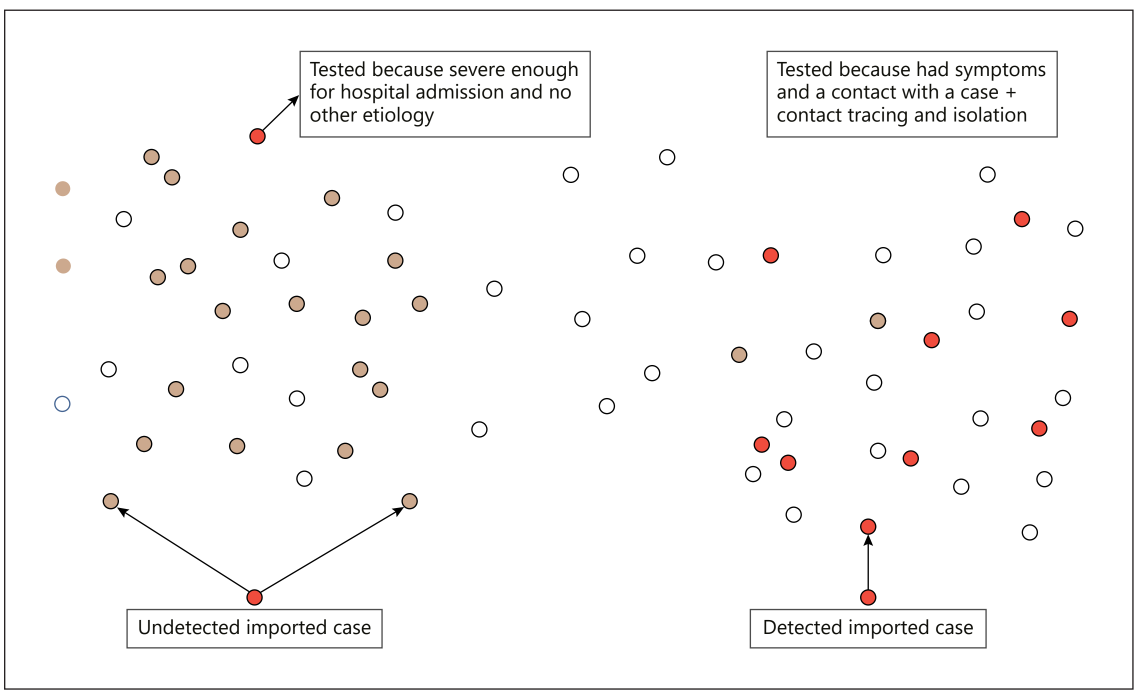

Fig. 2. Schematic representation of undetected transmission chains started in undetected imported cases (left) and detected and controlled transmission chains started in a detected imported case (right) if only the WHO suspect case definition from September 27, 2019, is considered (as of March 20, 2020).

(95% CI: 82–90%) prior to 23 January, 2020, travel restrictions and that undocumented infections were the infection source for 79% of documented cases [7].

Adding to this we should consider specific surveillance system delays from infection and symptom onset to reporting. We should ask ourselves whether different choices at different timings would be made at an individual and policy level if we only looked to the confirmed cases. Modelled estimations of total infected and counts of suspect/possible cases that were not laboratory confirmed should be considered and communicated together with uncertainty in model assumptions (Fig. 3).

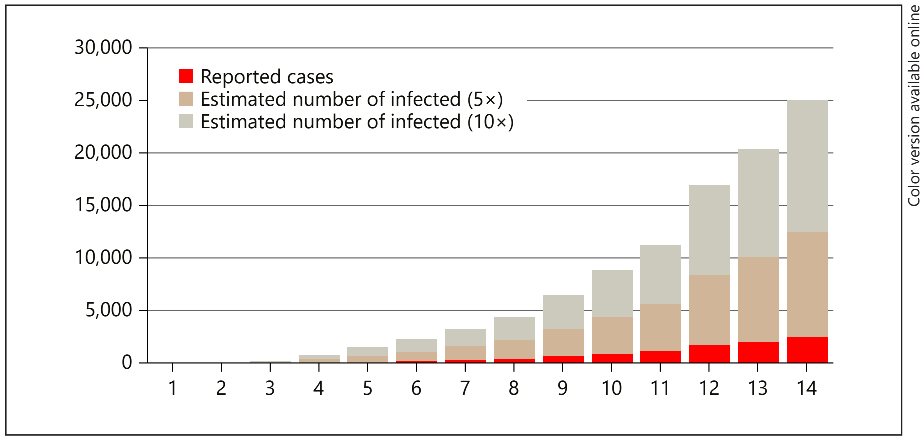

Fig. 3. A hypothetical graph showing reported cases (assumed case evolution in Italy by day) and estimated number of infections considering 5× and 10× higher incidence [4–7].

Surveillance Strategies Used to Ascertain Cases and Inform Planning

Some countries initiated earlier and wider testing than others [8]. Some started earlier to test admitted cases of bilateral pneumonia without other aetiology (allowing for earlier consideration of community transmission), and some tested contacts even if asymptomatic. Criteria for testing in earlier stages was variable and resulted in very different testing rates [8]. The different testing strategies and consequent different levels of under-ascertainment may account for some of the differences in the fatality rate found in different countries in Europe such as Italy and Germany (9 and 0.2%, respectively) [9], though we should also consider the impact of overload of the health systems, characteristics of the specific surveillance system, and population demographics and behaviour. There are various options for surveillance to improve case detection or make estimations (Table 1).

Limited capacity for testing may play a role in testing strategies, forcing some countries to prioritize testing, but it makes discussion and research around under-ascertainment even more relevant in those contexts. Under-ascertainment in surveillance should make us consider an under-ascertained need for specific early measures (for example of social distancing) but also, in later stages, that a much larger part of the population could be immune and social distancing strategies could change, which also raises the importance of serologic surveys in those circumstances to confirm these estimates.

One document of the European Centre of Disease Control (ECDC) [10] reports that "the detection of COVID-19 cases and/or deaths outside of known chains of transmission is a strong signal that social distancing measures should be considered." However, with restrictive testing strategies, these signals may be missed. The document states that "the early, decisive, rapid, coordinated and comprehensive implementation of closures and quarantines is likely to be more effective in slowing the spread of the virus than a delayed implementation" and that decisions "will very rarely be purely evidence-based" as social and political considerations will also need to be taken into account. Evidence is always incomplete, especially in new pandemics.

Different Triggers, Different Measures, Different Outcomes

There is evidence of the effectiveness of public health measures such as travel bans, movement restrictions, and social distancing. A study used a SEIR (susceptible-exposed-infectious-removed) model to estimate epidemiological parameters before the implementation of measures in Wuhan. If these measures had been initiated 1, 2, or 3 weeks earlier in China, cases could have been reduced by 66, 86, and 95%, respectively, together with a significant reduction in the number of affected areas [11].

Another study reports that the effective reproduction number in Wuhan fell from 2.35 (95% CI: 1.15–4.77) 1 week before the introduction of restrictions on January 23, 2020, to 1.55 (0.41–2.39) 1 week later and calculated that in sites with Wuhan-like transmission potential in early January, when there were only 4 cases introduced, there is more than a 50% chance of the infection settling in this population [12].

Other simulation [13] suggests that to control most outbreaks, for R0 (number of cases directly generated by

Table 1. Surveillance strategies to identify and estimate community cases and inform planning (beyond the WHO suspect case definition from February 27, 2020, as of March 20, 2020)

Surveillance and estimation strategies	Description
Sentinel surveillance (for example in primary care)	At regular intervals, a representative batch of specimens are sent to a reference/referral laboratory for confirmation and further characterization
Syndromic surveillance – collection of syndromic data through health lines and mobile apps	Some countries have different platforms where people or clinicians report symptoms and situations and are forwarded as adequate; clinicians may have platforms to report suspect/possible/probable cases (even if testing is not available); this allows for syndromic surveillance, registration of cases as well as directing suspect cases for testing
Estimate imported cases through modelling	Estimate imported cases from travel information and the number of imported cases in countries with higher detection rates and other methods
Detect imported cases	Quarantine of cases coming from affected areas; entrance screening (low effectiveness); communication campaigns for engagement to call health lines at first symptoms (even if mild)
Estimate undetected cases	Estimations based on models: using international case exportations, mobility data, SEIR models (dynamic transmission), other methods considering number of deaths, case fatality rates, and others
Sample testing	Probabilistic sampling in a determined population to estimate infection
Serologic surveys	Probabilistic sampling in a determined population to estimate exposure
Mass testing	Testing of a large proportion of the population; may be difficult considering testing capacity but may be done in smaller settings

one case in a population where all individuals are susceptible to infection) of 3–5, more than 70% of contacts had to be identified. In most scenarios, highly effective case identification and isolation of contacts could control a new outbreak of COVID-19 within 3 months. However, importantly, the probability of control decreases with delays in the identification of cases and contacts, increased time from onset of symptoms to isolation, fewer cases identified, and increased transmission before symptoms.

The Oxford COVID-19 Government Response Tracker [14] describes variation in government responses and explores whether rising stringency of response affects the rate of infection. They calculate a stringency-risk ratio but warn that recorded cases partly depend on how much testing is done, which is likely to co-vary with the stringency of the government's response. Regular updated results will be available for anyone.

A recent study by the Imperial College COVID-19 Response Team shows that in the UK and US context, suppression requires a combination of social distancing of the entire population, home isolation of cases, and household quarantine of their family members, that may need school and university closures and reports other strategies that may involve social distancing of those >70 years old. However, the study predicts that transmission will quickly rebound if interventions are relaxed and suggests that intermittent social distancing – triggered by trends in disease surveillance – may allow interventions to be relaxed temporarily [15]. This strategy needs robust surveillance systems that allow for acceptable sensitivity to timely decide on interventions. We believe these triggers must consider evidence and debate around surveillance system sensitivity and under-ascertainment. As suggested by another Imperial College Report [16], this would be relevant to produce early evidence when exiting the COVID-19 social distancing policy after achieving containment.

Due to different surveillance systems, different measures at different timings, different levels of stringency [14], and different demographic and social dynamics, the outcomes within Europe may be heterogeneous. Undetected introduction of imported cases and many mild undetected cases making up those transmission chains may warrant early measures. By looking at the death epidemic curves (likely less sensitive to variations in surveillance system sensitivity) of different countries we see differences that can be related to earlier detection and implementation of measures (Fig. 4). Notably, South Korea has managed to keep new deaths by COVID-19 low despite being in a relatively advanced stage of the epidemic and

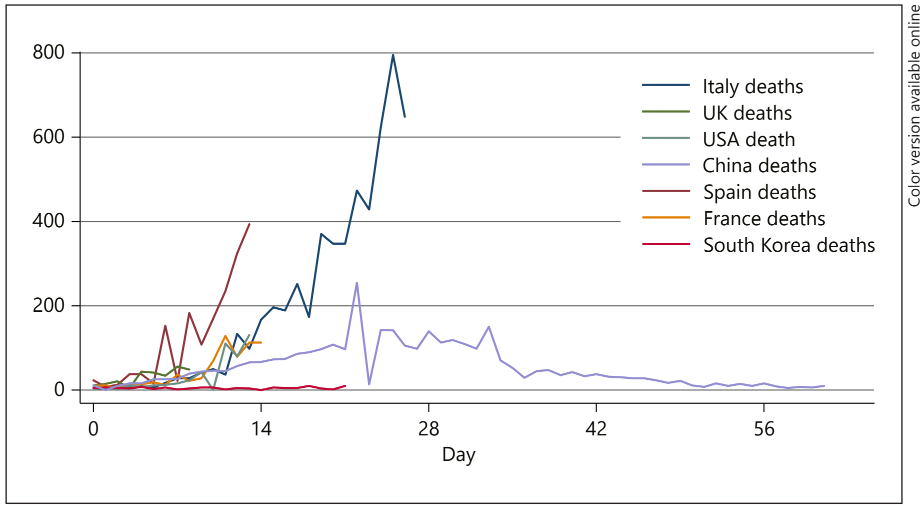

Fig. 4. Number of deaths each day by selected countries starting from the first day with ≥5 deaths (data source: ECDC as of March 23, 2020).

is one of the countries with a higher testing rate [8]. An early study [17] estimated the transmission potential of COVID-19 in the country and suggested early sustained disease transmission in the region which contributed to the rapid early implementation of social distancing measures to contain the outbreak [14].

Considering uncertainty and under-ascertainment is critical for decision when 500 cases could possibly mean 5,000. Delay from exposure and infection to reporting must also be considered.

There is at this stage high uncertainty about the behaviour of the disease in Europe, the effectiveness of measures in different contexts, and the timing for their implementation. Often, measures should be implemented early with imperfect scientific knowledge. On the other hand, estimated total infection numbers can be important to justify measures for public opinion, engage them in preventive action, and reinforce recommendations for those who are tested positive as well as to inform decisions on exiting social distancing policies.

More robust models will be produced soon, but models make assumptions based on surveillance data and other sources with different levels of uncertainty. Under-ascertainment should be considered, and the best available information and data should be included and pursued by improving surveillance strategies to reduce or better estimate under-ascertainment. With more epidemiological evidence, namely greater certainty in relation to the proportion of asymptomatic infections and their risk of transmission, different surveillance system sensitivity, effective R in different contexts and effectiveness of containment measures and with the results of the First Few X Cases FFX investigation proposed by WHO [18] for COVID-19 models will better take into account under-ascertainment in different countries. Understanding the extent of transmission in different regions can help policy makers tailor their response. Acknowledging that "we can't fight a pandemic blindfolded," on March 16, 2020, the WHO urged countries to test.

Conclusion

Under-ascertainment may be of relevance for COVID-19 policy. There is uncertainty on this subject and in the studies mentioned in this article and presented reflections. However, it is the role of the scientific community in public health and epidemiology not only to communicate what is certain and based in robust established science, but also of what is uncertain, when it may be of relevance for decision making and can be further researched, discussed, and shared. As in most infectious disease surveillance, under-ascertainment can be a relevant piece of the puzzle for COVID-19 science, policy making, and public opinion and should be systematically addressed and communicated.

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Author Contributions

All authors contributed in a relevant way to the literature review and writing of the article.

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