ASPHER Report

COVID-19 Pandemic Waves Surveillance in another Severe Winter of 2021: A basic guide to understand epidemic contexts, interpret pandemic waves and trends, ahead of the curve

How can we understand and interpret alert signals from pandemic waves considering pitfalls and stay ahead of the virus?

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Abstract

Interpretation of COVID-19 epidemic situations, trends and pandemic waves poses a challenge to epidemiologists and public health specialists around the world. The multiple mechanisms that shape pandemic waves characteristics are complex and it is often difficult and time consuming to create reliable predictive models, accurate forecasts and scenarios. However, a series of insights from field and intervention

epidemiology can help interpret trends and signals by considering common pitfalls associated with context-free models. Interpretation of pandemic situations and trends must consider a minimum set of indicators over time by age group and region and from specific sentinel populations. These include incidences of infection, hospitalizations, ICU admissions and death rates plus excess mortality measures, testing per capita, test positivity and sales of self-tests, and a range of severity indicators and clinical profile of those tested. Force of transmission indicators are required, including measures in place to prevent transmission (stringency index), mobility and contact indicators as well as adherence to preventive measures. Hospital bed occupancy (proportion occupied with COVID-19 patients overall and percentage of beds that changed purpose from their normal functions, genomic surveillance of variants, long/persistent COVID-19 rates, vaccination coverage and real-time effectiveness for infection, hospitalization and death. This minimum set of indicators should be publicly available, enabling early detection and interpretation of trends, examination of likely levels of under ascertainment in different populations and periods and visualization of impact of different scenarios and measures. Longer-term scenarios with specific assumptions are important before potential peak periods to allow for timely action to avoid worse case scenarios.

Trends must be interpreted cautiously when incidence is low and under-ascertainment is likely to be high as early identification of exponential growth is difficult to detect. When incidence is moderate or higher, changes in population behavior have the potential to create large, abrupt rises in cases following the emergence of numerous clusters in the same time period, or super-spreader events. A new or imported variant accounting for a rising proportion of cases must be an early warning signal of potentially greater transmissibility or lower levels of immunity to the variant with impact later on in severe disease frequency.

Better interpretation of wider emerging data may help decision makers to be ahead of the curve and reduce the negative impact of further epidemic waves in public health and mitigate the broader social impact of the disease. We are deeply concerned that the Christmas and New Year holiday periods in some countries will lead to even further deteriorating pandemic status, in the face of the rise of Omicron variant, unless suitable measures are adopted. We remain concerned that other respiratory viruses are spreading easily in some countries before the influenza season accelerates. We advocate wider dual testing for influenza and COVID-19 this winter. This article provides deeper insights into the interpretation of pandemic waves and epidemic situations in context and may be used as a guide for training and surveillance reporting, while generating further research hypotheses.

1. Background:

Pandemic waves are more than incidence curves. Field/intervention epidemiology insights are of utmost importance so that the dynamics of transmission between people, settings and communities is clear below the surface.

Many indicators are relevant to interpret trends and to create better predictive models[1,2]. However, it is often difficult or impractical to create reliable models in a timely manner with correct assumptions to inform model parameters that can be correctly interpreted in their limitations. Models should consider a range of indicators and estimates or scenarios based on emerging and existing evidence. Indicators should include exposure: number, nature and settings of contacts through time, mixing patterns within populations, use of physical protective equipment; susceptibility including: level of population immunity, probability of severe disease by age group, deprivation; multimorbidity and estimates of under-ascertainment. Such models warrant more detailed approaches outside the scope of this article.

However, in practical terms, to aid surveillance and policy making, insights from field/intervention epidemiology are essential to interpret trends and signals and consider common pitfalls. Even if predictive models are being produced, these insights are fundamental to understand limitations facing often assumed or biased input parameters. Where predictive models are not being produced regularly, these insights are fundamental to tailor surveillance, communication of trends and possible scenarios even when assuming stable preventive measures and behaviours.

It is vital to acknowledge that in COVID-19 surveillance there is always a level of under-ascertainment[3] of infections in the community levels of under-ascertainment that may be high (20-90%)[4,5,6,7] and must be considered at all times when interpreting other indicators.

Cases of infection go undetected because:

1. Many asymptomatic or mildly symptomatic infections are unrecognized and/or not tested[8]
2. Symptomatic infections that present with symptoms that are not included in the case definition so people do not seek or cannot access testing[9]
3. Symptomatic infection with clinical criteria from case definitions that are not prioritised as reasons for testing for other reasons (lack of available tests, difficult access to tests, lack of social protection for isolation (income, pay, accommodation, education), individuals not wanting to report symptoms and/or contacts, among many others)
4. Symptomatic infections that are tested but are not notified (including self-tests) (failure to comply with reporting recommendations by the public, employers and health professionals (including laboratories); failure of public health authorities/institutions to communicate and explain how to report suspected and confirmed cases, out of date public health legislation that does not require reporting of novel infections/syndromes as health risk states
5. Identified infections, hospitalizations and deaths by COVID-19 not reported for political reasons; not wanting to expose the lack of response by the government/party in power, lack of systems for data consolidation.

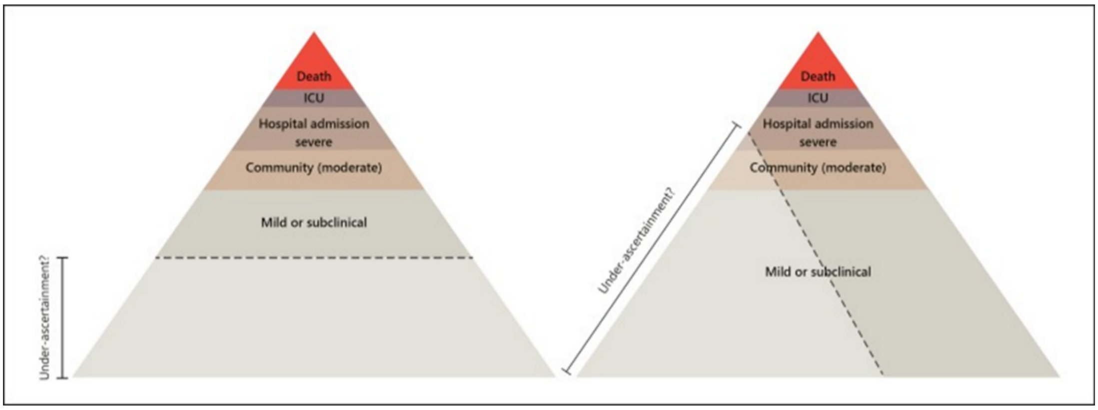

Figure 1 Hypothetical examples of surveillance pyramids for COVID-19 with two of many possible under-ascertainment lines

The most common causes of under-ascertainment /unrecognized infections highlight the importance of strong public communication campaigns and local engagement to ensure all symptomatic individuals, contacts and others with high-risk exposures are tested promptly. Surveillance methods for early detection in high-risk environments, ongoing wastewater[10], serological surveillance and PCR testing should be considered among other surveillance strategies, where high under-ascertainment of cases is likely[11].

Each of the indicators adds a layer of understanding of what is happening beneath the surface of the surveillance headlines. These data warrants careful interpretation by surveillance specialists, considering the impact of all the other indicators. This will be specially relevant for the 2021/2022 winter[12].

Under-ascertainment must be considered at all times when considering trends and healthcare services demand. Under-ascertainment rates may change significantly over time (e.g. with changes in incidence, media attention/risk perception, testing policy and practice).

<u>Desirable set of public surveillance indicators to interpret epidemic situations and trends in context</u>

ASPHER recommends that the epidemic situation and evolution of pandemic waves should consider a broader set of aspects and indicators, preferably presented as epicurves over time by age group and region (short term forecasts with simple methods can be presented with the epicurves). These indicators representations should be publicly available and include:

a. **Incidence** of cases, seeking healthcare, hospitalizations (general and ICU and deaths)
    i. Regional and local incidence curves (geographic representation and changes in time)
    ii. Incidence curves in specific sentinel populations (Long term care facilities, school settings, high risk exposures)

b. **Testing**
    i. Testing per capita (PCR and rapid antigen tests) and self-test including commercial sales (as indicator of symptoms, exposure and SARS-CoV-2 infection, and potential under-ascertainment by

age group and by region, (by reporting of self-test sales and performed tests by labs should use automated systems and mandatory for reliability of reports)

ii. Test positivity rate by age group region and type of test (as indicators of under-ascertainment) estimations of under-ascertainment considering test positivity and severe cases by age groups, considering estimates of probability of hospitalization by age group and vaccination coverage)

iii. Percentage of new asymptomatic cases and % of new tests performed on asymptomatic people or on those with symptoms that do not fit in the current COVID-19 clinical criteria for testing -to reduce under-ascertainment a broader clinical definition should be considered including upper respiratory symptoms: coryza, runny/stuffy nose, odynophagia, fatigue and gastrointestinal upset -in combination with known exposure/other symptoms)

c. Severe disease and health care impact (by age group)

i. Rates of hospitalization in general ward and intensive care units per 100,000 inhabitants in the last 7/14 days by age group and region

ii. COVID-19 mortality rates per 100,000 inhabitants in the last 7/14 days by age group and region

iii. Case fatality rate in the last 7/14 days by age group and region (although nts. this may reflect under-ascertainment if higher)

iv. Proportion of lab confirmed cases with outcome: hospitalization ICU admission and death

v. Occupancy of beds by COVID patients in general wards and ICU overall and by region (as a proportion of total beds and as a proportion of COVID-19 dedicated beds)

vi. Excess mortality by all causes and by disease group including COVID-19 (to infer health system coping capacity)

vii. Population covered by health services and access to health services: This may impact ascertainment and reporting of severe COVID-19 cases (this may be relevant in countries where people may have severe disease and die without reaching healthcare and where large parts of the population may live far from hospitals, in rural areas and also in periods where healthcare overload is present)

d. Force of transmission indicators (when adequate by age group and region):

i. Measures in place to prevent transmission in different countries in relevant context (e.g. Mask: Legal requirement in specific places or totally voluntary) (Oxford Stringency Index can be used as a general proxy for the combinations of all governmental preventive measures) (ECDC Country overview present measures in place in each moment in time along the course of the pandemic)

ii. Mobility data (Google Mobility trends (by type of location) and Apple mobility (by walking, driving and public transportation use)

iii. Average number of unprotected contacts in previous 7 days (and type of contact by setting)

iv. Proportion of people who wear masks when in contact with others by context (sources may include regular population surveys that already exist in some countries)

v. Potential number and size of superspreader events per 100.000 population e.g. indoor events without mask requirements or physical distance; other mass events above a different thresholds (>100 people; >500; >1000; >5000> 10.000 >50.000; >100.000, (considering indoor and outdoor events)

vi. Proportion of people with detectable antibody levels above certain threshold

vii. Vaccination coverage, including boosters and distribution in place and person (work, geographical area, specific communities)

viii. Real time vaccine effectiveness (for infection, symptomatic infection, hospitalization, ICU admission and death) including comparisons of outcomes proportion among vaccinated and unvaccinated cases in recent periods as a proxy of vaccine effectiveness in real time.

ix. Winter/Summer status: as proxy of poorer ventilation of indoor spaces and potentially increase in severe disease due to cold and lower physiological reserve in frail population (% contacts outside/versus inside)

x. Weather status: periods of bad weather may force people indoors and dramatically reduce ventilation, contributing to higher transmission. However they may reduce the average number of contacts in some countries.

xi. Other aspects (e.g. Cultural behaviour: the way people relate, for example the distance at which they speak, mass gatherings, the circulation of people in high density housing and high risk occupations, eating habits and socialization habits, religious, political and ethnic attitudes towards preventive measures).

e. Variant surveillance:

i. Real time proportion of variants and sub-variants among sequenced cases; proportion of sequenced samples among all reported cases (when genomic surveillance is representative and samples have enough statistical power, early, steady rises in prevalence of specific variants must be considered an early warning signal of a more transmissible variant.

ii. Case fatality rate, hospitalization rate and vaccine effectiveness monitoring in relevant variants

f. **Surveillance system performance monitoring**

i. Percent of lab confirmed cases with clinical data (clinical notification) by week

ii. Percent of lab confirmed cases with epidemic context data (epidemic investigation registry) / contact tracing data by week

iii. Percent of lab confirmed case with outcome data by week

g. **Long term sequelae**

i. Proportion of lab confirmed cases with a registered long COVID-19 symptoms /sequela

h. **Sentiment analysis and misinformation on media and social media**:

i. Although unfortunately difficult to assess, social media sentiment analysis indicators and circulation and reach of misinformation can be included in surveillance reports as an indirect measures of sentiment and adherence to measures of specific groups and to address misinformation circulation through communication initiatives and fact-checking.

In the absence of reliable predictive models or scenarios that should nonetheless be pursued, these indicators can help in generating broader insight of likely levels of under-ascertainment and detect early signals before larger increases in healthcare pressure, including pressure on public health teams, particularly in relation to contact tracing/outbreak control.

In general, simple forecast models can reliably make short term (1-2 weeks) forecasts if conditions are stable[13] [14]. Predictive models allow for longer predictive scenarios considering assumptions in how model parameters change (eg changes in number of contacts, increase in mask use, changes in number of super spreader events). However, they need to consider uncertainty in scenarios and assumptions related to surveillance data collection, completeness levels, bias and under-ascertainment that are often hard to capture quantitatively)

These insights must also allow for anticipation of measures to prevent early spread and higher wave peak incidence for variants that can put additional pressure on health services and society.

The ECDC Country overviews[15] include some of the surveillance indicators referred to above; together these form a helpful surveillance tool for use across Europe that often include more information on specific countries epidemic situations than those made available by individual member states.

<u>Insights into surveillance considering pitfalls</u>

1. **Surveillance indicators almost always point towards a direction**, **they are not neutral**. It is often necessary to make judgement calls based on all the available data considering uncertainty (with or without quantitative predictive model scenarios). Often, quantitative data cannot support these judgements fully

(insights into field epidemiology and data collection are essential) and information from surveillance systems may be biased. In that case, it is the responsibility of surveillance personnel to identify and characterize the bias and interpret the data accordingly, always communicating these aspects to decision makers and broader society.

2. **Communication with policy makers and the public must be clear on the limitations of surveillance** and experts must go through all the surveillance indicators and insights and point towards the most likely scenarios. Epidemic findings and reasonably justified assumptions must be communicated to decision makers and society even if technical personnel are uncertain, referring to levels of confidence (low, medium, high). Findings should be communicated irrespective of expected effectiveness of intervention measures.
3. **Failure to act early on incomplete but sound data and reasoning, hinders our capacity to act in a timely manner** to impact positively the course of the pandemic [16] [17] [18] (in detecting early signs of alert from a new variant that will imply further health burden and possible reduction in vaccine effectiveness. These variants could be avoided, controlled and/or importation delayed to minimize impact in winter; early recognition of exponential growth; recognizing that undetected cases may be driving transmission in younger population with higher number of unprotected contacts and presence in potentially super-spreader events, risking a fast growth in hospitalization at a later period in other age groups. Surveillance should consider different speed of spread though age groups in different settings and networks and be aware that mixing patterns are heterogeneous).
4. **Changes in testing behaviour, guidelines for case management and contact tracing, preventive behavior, border control (testing or quarantines) and number of average contacts and immunity in the population will all contribute to how easily the virus circulates** and causes more severe disease. Some of these changes are difficult to quantify but must be in the mind when analyzing trends and indicators.
5. **Exponential growth starting from low incidence levels and with high under-ascertainment may not be understood as such for a long period** and may be neglected leading to very fast and difficult to curb rises in cases, hospitalizations and deaths[19]. When baseline incidence is medium or high, social events and broad behavioral changes that reduce barriers to viral transmission and increase contacts can have a large and fast impact on transmission[20] (e.g. festive events over Christmas and new years eve/ periods; mass gatherings seasons, mass religious performances)
6. **Testing and positivity should be analysed by age group and socio-economic/ethnic group so that different levels of under-ascertainment** and trends by groups can be imputed, taking into account societal preventive measures in place, adherence to individual preventive measures, mobility and average contacts in previous 7-days or proxies where available.
7. **New hospital admission by age group as well as bed occupancy (% of free**

beds and % of COVID-19 occupied beds) are relevant to assess burden on healthcare services in real time and to inform the public. A reduction in incidence of hospital admission, especially in ICU among people over 75 years while admissions in young people keep rising may be an early sign of increased overall healthcare pressure and some level of patient selection.[21]

8. **Increases in case fatality rates or proportion of admitted cases (by age group) may have different reasons** e.g. increased healthcare pressure, winter and other external factors or, possibly due to higher levels of under ascertainment of the real number of infections.

   Reductions in case fatality rate may be possible in summer due to biological and behavioural factors and eventually lower infectious dose exposure [22]due to less time indoors and better ventilation. Reduction in severity and clinical presentation profile may be related to lower infectious doses because of protection measures.This should also occur with higher vaccination rates.

9. **Any increase in hospital admissions and death will depend on population coverage of vaccination and real world vaccine effectiveness across time.** Vaccination coverage is relevant as it reduces infection, transmission, hospitalization and death. This should be taken into account alongside under-ascertainment in predictive models, forecasts and estimates of the proportion of infections that will result in hospitalization by age group.

10. **Vaccine effectiveness information should always be presented as a comparison of outcomes between vaccinated and unvaccinated**. Presenting the proportion of total cases, total hospitalizations or deaths that are vaccinated does not quantify risk or effectiveness and misleads the public interpretation (e.g. if everyone is vaccinated in a country, all cases, hospitalizations and death will happen in vaccinated people; that says nothing about vaccine protection)

11. **Long term care (institutions and community settings), schools and nurseries are special settings because they may have enhanced surveillance** (regular testing, test mild symptoms more often and better contact tracing registries) For this reason, data from these settings may warn about a changing trend that is not yet visible in the general population, particularly if case ascertainment is low (e.g. due to low testing rates and mild symptoms in vaccinated people going unrecognized as COVID).

12. **All indicators and trends must be seen in light of the social, mobility and preventive measures context.** If few and less effective preventive measures are in place, lower rates of testing and higher levels of under ascertainment are to be expected. Initial rapid growth can go undetected in younger more active populations and later give rise to a rapid rise in severe cases. The Oxford Stringency Index[23] can summarize measures taken by countries' measures in a single value and may help visualize the picture across jurisdictions.

13. **Cultural and behavioural background matters.** Surveillance must consider the broader social contexts and indicators to interpret others. This can include, but not limited to: Human Development Index , life expectancy, poverty and

social exclusion, population density, urbanization density, healthcare expenditure/per capita, and social protection).

14. **Data on average individual average number of contacts per week, and mask wearing are harder to monitor but very useful.** Some countries attempt to monitor this in periodic online surveys[24]. Barometers of key behaviours are relevant.
15. **Google and apple mobility data[25] [26] can be used to understand changes in mobility including use of public transport, retail and leisure**, grocery and pharmacy, parks and alike, work and residential places. Other mobility and payment data may be available from banking and mobile phone operators[27].
16. **Monitoring of incidence and test positivity by age group can help understand early increases in virus circulation** among age groups where under-ascertainment may be higher due to mild symptoms[28] and asymptomatic/pauci-symptomatic disease that may precede a latter increase in other age groups if preventive measures, rapid communication of positive results and support for self-isolation and quarantine are not in place.
17. **Monitoring surveillance system performance[29], data quality and formal evaluation of attributes is essential**, including usefulness, completeness of specific information/registries (clinical or epidemiological/contact tracing) and timeliness (time from test to notification, time from notification to contact tracing registry/isolation of contacts/testing of contacts), because it may give information on needs to update/change system functioning and may identify pressure in public health contact tracing systems and signify that more personnel should be mobilized for contact tracing activities[30]. Countries that deploy resources in line with the ECDC guidance at minimum should be better able to cope with the needs of detailed local investigation and contact tracing. Local level public health units are of great importance in these contexts.
18. **Variants should be monitored to early detect lineages that increase in proportion related to dominant ones. This must always be considered an early warning sign and communicated.** In most surveillance circumstances this will almost certainly imply that this variant will signify an increased public health impact and healthcare burden. In places with high vaccination coverage, a variant´s increase in proportion will likely signify some level of immune escape (vaccine or previous infection) that may not be visible in early vaccine effectiveness analysis often due to under ascertainment and low numbers of sequenced samples and of severe outcomes (e.g. hospitalization, death). These slightly higher transmission or immune escape may become very relevant in winter and holiday seasons with further pressure on healthcare services easily reaching tipping points. Interventions to delay importation intensity and spread should be considered with early warning signs in a watch and wait perspective. During the winter of 2021 the Delta sublineage AY.4.2 (ECDC Variant under investigation as of 11th November and Variant of Interest by 18th November)[31] may become an example of this. Soon after, strong early warning signals come from South Africa and Omicron was considered a new variant of concern. As

with early rising trends, exponential growth of a more transmissible variant and in the proportion of total sequenced genomes may be mistaken for linear, non-worrying growth especially if a low proportion of cases is sequenced and if high levels of under-ascertainment are expected.

19. **Short-term forecasts of two weeks for key indicators may be visually represented** to help understand the growth rate in recent weeks. This may help visualize trends and understand growth for decision makers and the population considering "red lines".
20. **Longer term scenarios are essential before potential peak periods**, to allow for discussion and anticipation of measures to avoid worse case scenarios with different assumptions considering uncertainty, specially with new variants arising.

Conclusions

Investment is necessary by many European countries in comprehensive, rapid and reliable surveillance systems and in public health teams[32], using insights from field and intervention epidemiology that can organize and interpret the proposed indicators[33], that understand the epidemic situation in context and point towards what will most likely happen next, even in face of some uncertainty. This is a very cost-effective investment given the alternative. Surveillance information systems must be improved and sustainable to allow for rapid visualization of all relevant indicators and critical factors to adequately inform public health policy and decisions considering most likely scenarios.

A set of indicators should be publicly available and should be read considering insights from common pitfalls in interpreting surveillance data, considering strengths and limitations. While ECDC-led surveillance systems may go part way within the wider European region there is still scope for enhancement while those outside the EU/EEA have even further to advance.

Irrespective of predictive model´s, forecasts and assumed scenarios considering different possibilities and probabilities, understanding of the interrelation of different indicators and a deep understanding of epidemic surveillance systems (from bottom to top) and societies in its many determinants is necessary to interpret epidemic situations and trends and act ahead of the curve.

Longer-term scenarios may be extremely relevant before potential peak periods to allow for action to avoid worst-case scenarios facing uncertainty, especially when facing emergent variants.

This interpretation of epidemic situations should be discussed with partners and experts in each country and across Europe in considering a broader range of indicators to inform public opinion and decision makers regarding courses of action if we are to maximize health and well-being and act timely to minimize COVID-19 negative impact during this winter[34].

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