Public Health 234 (2024) 98–104

Contents lists available at ScienceDirect

Public Health

journal homepage: www.elsevier.com/locate/puhe

Original Research

Surveillance bias in the assessment of the size of COVID-19 epidemic waves: a case study

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ARTICLE INFO

Article history:
Received 29 January 2024
Received in revised form
13 May 2024
Accepted 7 June 2024

Keywords:
COVID-19 pandemic
Surveillance bias
SARS-CoV-2
Seroprevalence
Epidemiology
Public health

ABSTRACT

Objectives: To estimate the size of COVID-19 waves using four indicators across three pandemic periods and assess potential surveillance bias.
Study design: Case study using data from one region of Switzerland.
Methods: We compared cases, hospitalizations, deaths, and seroprevalence during three periods including the first three pandemic waves (period 1: Feb–Oct 2020; period 2: Oct 2020-Feb 2021; period 3: Feb–Aug 2021). Data were retrieved from the Federal Office of Public Health or estimated from population-based studies. To assess potential surveillance bias, indicators were compared to a reference indicator, i.e. seroprevalence during periods 1 and 2 and hospitalizations during the period 3. Timeliness of indicators (the duration from data generation to the availability of the information to decision-makers) was also evaluated.
Results: Using seroprevalence (our reference indicator for period 1 and 2), the 2nd wave size was slightly larger (by a ratio of 1.4) than the 1st wave. Compared to seroprevalence, cases largely overestimated the 2nd wave size (2nd vs 1st wave ratio: 6.5), while hospitalizations (ratio: 2.2) and deaths (ratio: 2.9) were more suitable to compare the size of these waves. Using hospitalizations as a reference, the 3rd wave size was slightly smaller (by a ratio of 0.7) than the 2nd wave. Cases or deaths slightly underestimated the 3rd wave size (3rd vs 2nd wave ratio for cases: 0.5; for deaths: 0.4). The seroprevalence was not useful to compare the size of these waves due to high vaccination rates. Across all waves, timeliness for cases and hospitalizations was better than for deaths or seroprevalence.
Conclusions: The usefulness of indicators for assessing the size of pandemic waves depends on the type of indicator and the period of the pandemic.

Introduction

During the COVID-19 pandemic, surveillance systems and indicators were crucial to monitor the size and severity of the pandemic, evaluate control measures, assess population-level immunity and vaccination, and adapt preventive strategies accordingly.[1,2] However, interpreting and translating information from indicators into practical actions was challenging. One major problem was that indicators could be prone to surveillance bias, a bias that occurs when differences in an indicator result from differences in the frequency or modality of detection of an health event over time or across healthcare settings and regions, rather than an actual difference in the frequency of this event.[1] This problem was particularly relevant when indicators built on data from healthcare providers were used to assess the size of the COVID-19 epidemic waves, leading to misinterpretations of trends, and potentially wrong public health actions.

A prime example of an indicator prone to surveillance bias is the number of COVID-19 reported cases. This indicator was frequently used to monitor the virus spread but is influenced by differences over time or across regions in screening and diagnostic strategies, test availability, or care-seeking behaviors.[3] Hence, especially in the early stages of the pandemic, the number of reported cases largely underestimated the actual spread of the virus.[4] In Switzerland, a

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https://doi.org/10.1016/j.puhe.2024.06.006

seroprevalence study showed that for every confirmed case reported in April/May 2020, there were roughly 12 infections in the community.[5] A study conducted in France found that 9 out of 10 cases were missed by the COVID-19 surveillance system in May/June 2020.[6] These high shares of missed cases were mainly due to a large proportion of non-tested, asymptomatic, or mildly symptomatic individuals, and greatly biased the assessment of the actual size of pandemic waves at the beginning of the pandemic. Later, the vaccine rollout also influenced case reporting rates because vaccinated individuals experienced milder COVID-19 symptoms[7,8] and vaccine availability altered the risk perception, changing health-seeking behaviors and reducing the willingness to get tested.[9] Other indicators, such as deaths or hospital admissions, were probably prone to surveillance bias as well. For instance, the accuracy of the number of COVID-19 deaths depended on definition or testing practices at or close to death.[10] Hospitalization rates could be biased by the threshold for hospitalization changing over time, based on changing risk perception, medical attitudes about who should be hospitalized, and beliefs about the availability of effective in-hospital treatments, and hospital bed capacity.[11]

No matter the epidemic indicator, the degree to which each indicator was biased could change across different stages of the pandemic, depending on testing capacity, diagnostic strategies, hospital capacity, vaccine availability, and other factors. It is therefore challenging to determine the reliability of each indicator to assess the size of epidemic waves during different pandemic periods, since the information provided by each indicator changed over time. Therefore, to ease the critical evaluation of surveillance data, using data from one region in Switzerland, we aimed to estimate the size of epidemic waves using various indicators across different periods of the pandemic. This allowed us to compare their variation between waves and to assess to what extent each indicator is prone to surveillance bias.

Methods

This is an observational, retrospective study conducted using data from one region in Switzerland, the canton of Fribourg. We estimated the size of COVID-19 epidemic waves, comparing four indicators: 1) seroprevalence, expressed as the proportion of the population who developed SARS-CoV-2 antibodies due to infections or vaccination, 2) number of COVID-19 reported cases, 3) number of COVID-19 hospitalizations, and 4) number of COVID-19 deaths. These indicators were compared across three different periods, i.e. period 1: from 24 February 2020 to 14 October 2020; period 2: from 15 October 2020 to 5 February 2021; and period 3: from 6 February to 16 August 2021. The three periods included the first three pandemic waves in the canton of Fribourg (Fig. 1). These periods were chosen based on the dates of the end of each seroprevalence study, i.e. following each of the first three pandemic waves in Switzerland, in line with the World Health Organization (WHO) recommendations for cross-sectional seroprevalence studies.[12] To better interpret our results, it is key to specify that the vaccination campaign in Switzerland started in January 2021 for people aged above 65 years and in May 2021 for younger adults. During period 1, vaccination was not available in Switzerland. Period 2 included a very short time window in which vaccination was available, but the proportion of vaccinated people was overall negligible (roughly 4%). Period 3 covered a time window in which vaccination was broadly available in Switzerland.[13]

Seroprevalence estimates

Seroprevalence was estimated by carrying out three population-based studies at the end of each study period on random samples of the adult population in the canton of Fribourg. These studies were conducted within the framework of Corona Immunitas, a nationally coordinated Swiss research project that consisted of repeated population-based seroprevalence studies conducted in several Swiss cantons with shared coordination and methodology.[14] Random samples of the general population were drawn from the population register of the Federal Statistical Office. The first serosurvey was conducted between July 8th and October 14th, 2020, at the end of the first pandemic wave. The second serosurvey was conducted after the second pandemic wave, between November 30th, 2020, and February 5th, 2021, and the third serosurvey was conducted between May 20th and August 13th, 2021, after the third pandemic wave (Fig. 1).

Participants provided venous blood samples that were analyzed using the SenASTrIS assay to measure the amount of human immunoglobulin G (IgG) that binds the trimeric SARS-CoV-2 spike protein, induced either by infection or vaccination. The test was validated on a sample of the general population, specificity and sensitivity were 99.7% and 96.6% for the detection of IgG antibodies, respectively.[15] Seroprevalence was estimated using a Bayesian logistic regression model, adjusted for the test sensitivity and specificity performances. Estimates were weighted by age and sex distribution of the general population of the canton of Fribourg. Seroprevalence estimates were reported as percentages. The Ethics Committees of the canton of Vaud, Switzerland, approved the seroprevalence studies used in this study (BASEC 2020-01247).

COVID-19 cases, hospitalizations, and deaths

Data on the number of COVID-19 reported cases, hospitalizations, and deaths were retrieved from the Swiss Federal Office of Public Health (FOPH).[16] The number of COVID-19 reported cases included data on individuals in the canton of Fribourg diagnosed with a laboratory-confirmed SARS-CoV-2 infection (polymerase chain reaction or antigen tests). This data was provided by laboratories, physicians, and hospitals to the FOPH. The number of COVID-19 hospitalizations included data on individuals admitted to hospitals in Switzerland who had been diagnosed with a laboratory-confirmed SARS-CoV-2 infection, regardless of the reason for hospitalization. The number of COVID-19 deaths included data on individuals in Switzerland who had died with a laboratory-confirmed SARS-CoV-2 infection. The information was based on data submitted by physicians using the form for reporting clinical findings related to a death to the FOPH. All these indicators were unadjusted. The number of COVID-19 cases, hospitalizations, and deaths were reported as counts.

Analyses

We compared the size of the 1st epidemic wave (period 1) with the 2nd wave (period 2), and the size of the 2nd wave (period 2) with the 3rd wave (period 3), respectively. Our analysis consisted of two steps. First, we calculated three simple metrics for each indicator (absolute difference, percentage difference, and ratio) to describe how the indicators changed between waves. The formulas for the metrics were as follows: (p_1 and p_2 represent the values of each indicator at period 1 and period 2, respectively):

Metric 1, absolute difference:

$$p_2 - p_1$$

Metric 2, percentage difference:

$$\frac{p_2 - p_1}{p_1} \times 100$$

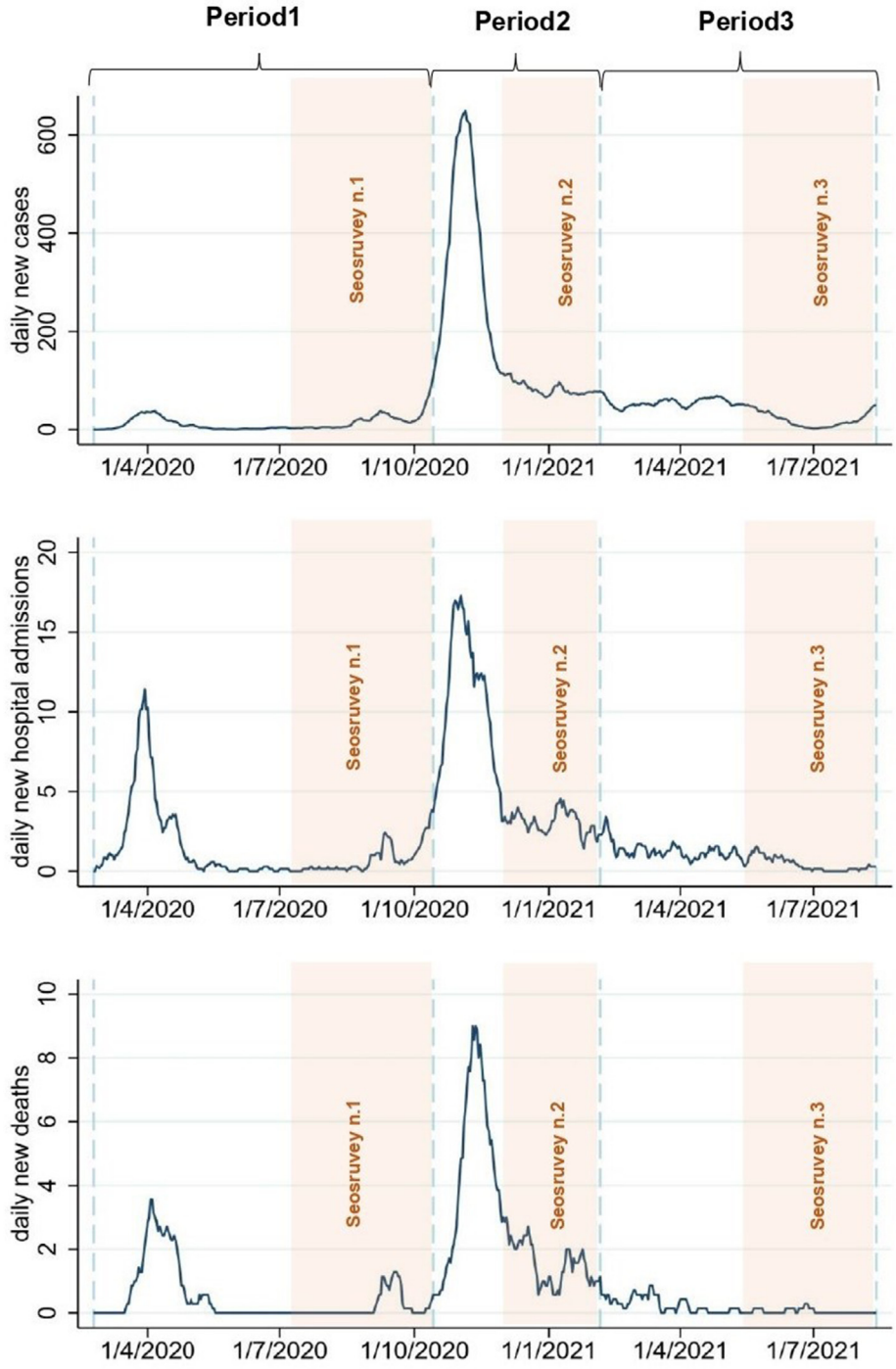

Fig. 1. 7-days rolling average of daily cases, hospital admissions and deaths in the Canton of Fribourg across the 3 periods. In orange, the time windows during which blood samples for the seroprevalence studies were taken.

Metric 3, ratio:

$$\frac{p_2}{p_1}$$

The same formulas were used to compute these metrics between period 2 and period 3, using the respective indicators' values from those periods.

The second step of our analyses consisted of selecting a reference indicator to benchmark surveillance bias in other indicators. We chose as reference indicators—the indicators that we judged to be the least bias in each comparison. This choice was made based on the authors' expertise, with the aim of clearly highlighting the phenomenon of surveillance bias through the comparison of different indicators. Specifically, we selected seroprevalence as the reference indicator when comparing indicators between period 1 and period 2, and the number of hospitalizations when comparing indicators between period 2 and period 3. Seroprevalence was chosen because during the initial two periods of the pandemic, testing strategies and

availability frequently changed, and population-based seroprevalence was the only indicator not influenced by testing differences. During period 3, seroprevalence was not directly informative due to the vaccination, and the number of cases was potentially exposed to the same type of bias seen during periods 1 and 2. Hospitalizations were therefore considered a better marker of the size of the epidemic.

To better interpret our results and the usefulness of surveillance indicators, we also descriptively assessed the timeliness of each indicator. We defined timeliness as the duration in days between the generation of the information, such as a positive test for cases, hospitalizations, and deaths, and the availability of this information to decision-makers for making informed decisions. Specifically, the timeliness of the number of cases, hospitalizations, and deaths was defined as the time between the conduction of the test and the availability of results for the public health officials of the canton of Fribourg. This information was retrieved from the 'Service du médecin cantonal' which is the medical health authority of the canton of Fribourg. For seroprevalence studies, timeliness was assessed by calculating the difference in days between the average date of the recruitment process and the average date of result availability, as results were progressively available for different batches of samples as participants were enrolled (e.g. for serosurvey 1, results were available in two batches in September and November 2020; for serosurvey 2, in three batches in January, February, and April 2021; and for serosurvey 3, in four batches in July, the end of July, September, and November 2021).

Results

The characteristics of participants of the three serosurveys are reported in Table 1. Seroprevalence was 8% (confidence interval (CI) = 4%–12%) at the end of period 1, 19% (CI = 15%–23%) at the end of period 2, and 74% (CI = 69%–79%) at the end of period 3, meaning that 8%, 11%, and 55% of the population became seropositive in the periods 1, 2, and 3, respectively. The number of cases, hospitalizations, and deaths were, respectively, 3′488, 330, and 108 for period 1, 22′771, 721, and 318 for period 2, and 10′675, 487, and 135 for period 3 (Tables 2 and 3). The absolute difference, the percentage difference, and the ratio computed for each indicator comparing period 1 vs period 2 and period 2 vs period 3 are also shown in Tables 2 and 3.

Comparison of the size of epidemic waves in period 1 and period 2

Based on seroprevalence (our reference indicator when comparing indicators between period 1 and period 2), 8% of the population got infected in period 1, and 11% got infected during period 2, representing a 38% increase between the two periods. In other words, the size of the epidemic wave of COVID-19 during period 2 was slightly larger (by a ratio of 1.4) than the size of the wave in period 1 (Table 2).

Compared to seroprevalence, other indicators provided a different description of the epidemiological situation: based on the number of reported cases, hospitalizations, and deaths, the size of the epidemic wave during period 2 compared to period 1 was overestimated (a ratio of 6.5, 2.2, and 2.9, respectively). From period 1 to period 2, reported cases, hospitalizations, and deaths increased by 553%, 118%, and 154%, respectively. Compared to the 38% increase of the chosen reference indicator (seroprevalence), the number of cases was a very biased indicator (553% increase between waves vs 38% increase), followed by the number of deaths (154% increase vs 38%) and the number of hospitalizations (118% vs 38%).

Comparison of the size of epidemic waves in period 2 and period 3

Based on the number of hospitalizations (our reference indicator when comparing indicators between period 2 and period 3), the size of the epidemic wave of COVID-19 during period 3 was slightly smaller (by a ratio of 0.7) than the wave in period 2, representing a 32% decrease in hospitalizations (Table 3).

Other indicators provided a different description of the epidemiological situation: based on seroprevalence, the size of the epidemic waves during period 3 was much higher (by a ratio of 5) than period 2. Cases or deaths slightly underestimated the size of the 3rd wave (3rd vs 2nd wave ratio for cases: 0.5; for deaths: 0.4). Seroprevalence increased by 400%, and cases and deaths decreased by 53% and 58%, respectively. Compared to our reference (hospitalizations), seroprevalence resulted to be a very biased indicator in

Table 1
Characteristics of the participants of the three serosurveys conducted in the canton of Fribourg, Switzerland.

Characteristics	Serosurvey 1	Serosurvey 2	Serosurvey 3
	July–October 2020	November 2020–February 2021	May 2021–August 2021
Number of participants (%)	418 (100%)	449 (100%)	504 (100%)
Female/male, *n* (%)	226 (54%)/192 (46%)	245(55%)/104 (45%)	277 (55%)/227 (45%)
Age, mean (SD)	58 (17)	54 (16)	58 (16)
Age groups, *n* (%)			
20–64	227 (54%)	302 (67%)	261 (52%)
≥ 65	191 (46%)	147 (33%)	243 (48%)
Educational level, *n* (%)			
Primary	38 (9%)	29 (6%)	39 (8%)
Secondary	207 (50%)	222 (49%)	254 (50%)
Tertiary	169 (40%)	198 (44%)	211 (42%)
Employment status, *n* (%)			
Retired	190 (45%)	160 (36%)	251 (50%)
Student	12 (3%)	16 (4%)	12 (2%)
Self employed	32 (8%)	30 (7%)	34 (7%)
Employed	176 (42%)	240 (53%)	209 (41%)
Not employed	17 (4%)	17 (4%)	21 (4%)
Comorbidities, *n* (%)			
Cancer	15 (4%)	10 (2%)	12 (2%)
Diabetes	26 (6%)	22 (5%)	20 (4%)
Immunological diseases	20 (5%)	10 (2%)	19 (4%))
Hypertension	94 (22%)	74 (16%)	115 (23%)
Cardiovascular diseases	39 (9%)	45 (10%)	47 (9%)
Respiratory diseases	22 (5%)	32 (7%)	31 (6%)

Table 2
Surveillance indicators in period 1 and 2, and metrics computed to compare period 1 and 2, canton of Fribourg, Switzerland.

Indicators	Period 1 (24 Feb 2020–14 Oct 2020)	Period 2 (15 Oct 2020–5 Feb 2021)	Metrics comparing period 1 and period 2			Surveillance bias magnitude
			Absolute difference	Percentage difference	Ratio	
Proportion of individuals who became seropositive	8%	11%	3%	38%	1.4	Ref
Reported cases	3488	22,771	19,283	553%	6.5	++
Hospitalizations	330	721	391	118%	2.2	+
Deaths	108	318	210	194%	2.9	+

Table 3
Surveillance indicators in period 2 and 3, and metrics computed to compare period 2 and 3, Canton of Fribourg, Switzerland.

Indicators	Period 2 (15 Oct 2020–5 Feb 2021)	Period 3 (6 Feb 2021–13 Aug 2021)	Metrics comparing period 2 and period 3			Surveillance bias magnitude
			Absolute difference	Percentage difference	Ratio	
Proportion of individuals who became seropositive	11%	55%	44%	400%	5.0	++
Reported cases	22,771	10,675	−12,096	−53%	0.5	−
Hospitalizations	721	487	−234	−32%	0.7	Ref
Deaths	318	135	−183	−58%	0.4	−

this pandemic phase due to the large share of vaccinated individuals (400% increase between waves vs 32% decrease), while deaths and cases were much less biased (58% decrease vs 32% and 53% decrease vs 32%).

Timeliness of surveillance indicators

Across all periods, the number of cases and hospitalizations were the timeliest indicators, followed by deaths and seroprevalence. Decision-makers in the canton of Fribourg were able to obtain information on days and hospitalizations within 1–2 days for cases and hospitalizations, regardless of the period under consideration. Information on deaths was less timely: although sometimes unofficial information was available for decision-makers in a few days, it took up to several weeks to receive official certificates filled out by physicians. For seroprevalence, the average time between recruitment and availability of results was 53 days (37, 64, and 57 days for serosurveys 1, 2, and 3, respectively).

Discussion

This case study shows that different surveillance indicators used during the COVID-19 pandemic provided information on the impact of pandemic waves that vastly varied depending on the indicator used and the period of the pandemic taken into consideration.

Many studies have investigated biases in COVID-19 surveillance.[17–21] Here, we focused on four commonly used indicators of epidemic size at once, to gain insights on challenges in surveillance and decision-making during the pandemic. We found that the number of confirmed cases of COVID-19, routinely used as a primary indicator of the size of epidemic waves due to the daily availability and ease of collection of this data, was greatly biased at the beginning of the pandemic. This was likely due to the unavailability of tests during period 1 and was observed in many other countries and regions.[17,22] Comparing our estimates with other studies is challenging, as most studies estimated under ascertainment by comparing the number of cases with seroprevalence within the same period, which differs from our approach that consisted of comparing waves. However, if we compare seroprevalence estimates to the number of cases found in period 1, the level of under-ascertainment we found was similar to estimates found during a comparable period in other regions of Switzerland (for every case found during period 1, there were roughly 8 infections in the population of the canton of Fribourg and 12 in the population of the Canton of Geneva).[5] As test availability improved and testing strategies became more consistent, the bias in this indicator diminished in periods 2 and 3.

Seroprevalence was considered the least biased indicator to assess the size of epidemic waves in periods 1 and 2. Nevertheless, it became the most biased indicator in period 3, due to the large share of vaccinated individuals in the population. Although we selected seroprevalence as a reference indicator in periods 1 and 2, it is important to underline that it has some limitations. For instance, it's not always feasible to select a representative sample of the general population, and seroprevalence can be underestimated because of waning immunity,[23] people failing to produce antibodies[24] or low participation rates.[25] Hospitalization and deaths, although biased to a certain degree, appeared to be indicators that could estimate the size of COVID-19 epidemic waves more consistently over time. Although these indicators were also prone to surveillance bias, they were more reliable than case counts or seroprevalence when assessing the size of waves over time during the periods examined in this case study.

The timeliness of surveillance indicators plays a major role in the decision-making process and was also estimated in this study. Across all waves, cases, and hospitalizations were timelier than deaths or seroprevalence. It must be noted that timeliness is difficult to assess due to under-reporting, and that timeliness can be defined differently than the way we defined it in this case study. For instance, if we defined timeliness as the time lag between the spread of the virus in a setting and the availability of information to be able to control the spread, deaths would be much less timely, as the time lag between infection and information on death is influenced by the fact that individuals need time to become ill, die, and then have their deaths reported.[26–29] Seroprevalence was the least timely indicator and to be more useful in the decision-making process, seroprevalence studies should be conducted more promptly. In general, surveillance tools that collect data at a population level, such as seroprevalence studies are less timely than indicators based on data from healthcare providers, such as cases,

hospitalizations, and deaths, because it takes time to design and execute the studies and retrieve data at a population level. However, since in some pandemic phases population-based methods are less prone to surveillance bias, these methods should be made more timely. This could be achieved, for instance, by establishing rapidly scalable surveillance teams with ad hoc infrastructures and preplanned protocols.[10]

This case study has several limitations. First, other surveillance strategies, such as population-based random surveys of infections[30] or wastewater surveillance[31] were not assessed. These population-based surveillance tools could be used in phases where testing strategies were not consistent or standardized, and are not influenced by vaccination. Unfortunately, we could not include these indicators in our analyses because wastewater surveillance in Switzerland only started in January 2022, and, to our knowledge, no study to randomly test a sample of the population was conducted in the canton of Fribourg. Data from these methods would have probably offered less biased information compared to data reported by healthcare providers (e.g. cases, hospitalizations, and deaths) since they are population-based. Second, by focusing on one single Swiss region, we only assessed surveillance bias over time, and we could not assess the impact of this bias on surveillance indicators due to regional differences in data collection. Third, we have not taken into account factors like the impact of changing SARS-CoV-2 variants. The spread of more or less aggressive variants over time may have influenced the number of cases, hospitalizations, and deaths. During periods 1 and 2, the distribution of variants was roughly similar in Switzerland.[32] During period 3, the most common variants were Alpha and Delta,[32] which could have negatively impacted the number of hospitalizations and deaths (although these indicators decreased compared to period 2, likely due to the COVID-19 vaccination). Moreover, the implementation of new treatments, such as corticosteroids, could have also had an influence on the number of deaths.[33] Fourth, in this case-study, we only evaluated surveillance indicators as markers of epidemic size, despite their usefulness for other purposes. For instance, seroprevalence studies are used to assess the level of protection against infection and severe outcomes, identifying COVID-19 cases plays a key role in contact tracing and interrupting the transmission chain, and hospitalizations and deaths are needed to evaluate the pressure of the pandemic on the healthcare system. Fifth, we did not evaluate the costs of producing each indicator, which is an important factor in designing a surveillance system.[34] Finally, our definition of waves may be imprecise, as providing an exact definition of epidemic waves proves challenging.[35,36]

The main strength of this case study is that, despite its simple methodology, it highlights that each indicator should have a different weight in the decision-making process depending on the pandemic phase. Possible questions to consider when making decisions include: How many tests were available during the examined period? What was the share of vaccinated individuals in the population? What were the admission criteria in the hospitals in my region? Have the definitions of COVID-19 cases or deaths changed over time? Are there new treatments available that are currently used that can reduce the hospitalization rate? This information is needed to correctly interpret indicators in each pandemic phase and to make sound public health decisions.

Conclusions and implication

The usefulness of indicators for assessing the size of pandemic waves depends on the type of indicator and the period of the pandemic under consideration. No indicator proved to be without bias at any stage, and each of them could be influenced by several external factors, such as vaccination, testing capacity and compliance, or access and effectiveness of treatment. The weight of the surveillance bias of each indicator should be taken into consideration in different pandemic phases before making any critical decisions. Population-based surveillance strategies, such as seroprevalence, were less biased in the early phase of the pandemic but lacked timeliness. Diagnosed-based tools, such as the number of cases and hospitalizations were more timely but also more biased in some pandemic periods. Integrating population-based tools, preferably with improved timeliness, and diagnosis-based surveillance strategies could ensure both timeliness and a lower risk of bias during different pandemic phases.

Author statements

Ethical approval

The Ethics Committees of the canton of Vaud (BASEC 2020-01247) approved the seroprevalence studies used in this study.

Funding

No specific funding was used for this study.

Competing interests

None declared.

Author contributions

AC and ST conceived the study. ST, AC, and SC drafted the manuscript. All authors made substantial contributions and approved the final version of the manuscript before submission.

Informed consent

The subjects of the seroprevalence studies provided written informed consent prior to their participation in the study.

Data availability

Data on the number of cases, hospitalizations and deaths are publicly available and retrievable from the website of the Swiss Federal Office of Public Health. Deidentified individual participant data from seroprevalence studies will be available for researchers submitting a methodologically sound proposal to achieve the aims of the proposal after the publication of this article. Access to data requires contacting Corona Immunitas.

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