Commentary

# Generalisation of COVID-19 incidences provides a biased view of the actual epidemiological situation

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Differences in reported COVID-19 incidence levels exist between neighbouring countries and regions in Europe. The levels are widely used as indicators to define high-risk areas. However, these are greatly influenced by differences in testing strategies (e.g. access to testing limited to symptomatic persons or mass screening with or without systematic testing of all contacts). Since the beginning of the pandemic, Luxembourg has pursued a broad testing strategy including mass screening of its population and systematic testing of contacts [1]. Based on publicly available (data considered until 21 March 2021) [2,3], Luxembourg has reported 58,955 cases based on 2,280,826 PCR tests. Given its population size of around 626,000 residents, on average every resident has therefore been tested at least 3.6 times. Since the beginning of the pandemic, Luxembourg has exhibited an overall positivity rate of 2.6% whereas the surrounding countries Belgium, France and Germany have exhibited positivity rates of 8.1%, 7.4% and 5.6%, respectively [2,3]. The fact that Luxembourg's positivity rates have remained comparatively low has to also be seen in the context of extensive cross-border traffic including around 47,500, 105,000 and 48,000 daily commuters from Belgium, France and Germany, respectively. Although this traffic has been somewhat reduced since the beginning of the pandemic, other countries in Europe with less cross-border exchanges, but which have also pursued equally aggressive test strategies to that of Luxembourg, also show low overall positivity rates (2.0% in the case of Norway) [2,3]. In contrast, countries with relatively low coverage exhibit high positivity rates (17.0% as in the case of The Netherlands) [2,3].

To account for these differences, a more nuanced approach not solely based on incidences but also accounting for positivity rates is considered for travel restrictions within the European Union [4,5]. In this context, the availability of coherent data about different countries is fundamental to setting targets aimed at achieving low case numbers and keeping them low in a well-coordinated, pan-European manner [6]. The differing positivity rates and resulting incidences are likely also linked to differences in decision-making between countries, especially in relation to non-pharmaceutical interventions, which can differ markedly between neighbouring countries both in terms of quality and impact [7]. Different testing strategies are likely to also impact case fatality rates which are more than twofold higher in Germany and Belgium (2.8%) compared to Luxembourg (1.2%) [2,3] despite these countries having similar age structures, healthcare systems and pre-pandemic life expectancies.

Given the inherent biases linked to differing test coverages, thresholds based on hospital occupancies, in particular data on intensive care unit (ICU) occupancy [8], might therefore be more reliable. On 21 March, 3.2 ICU beds were occupied by COVID-19 patients per 100,000 inhabitants in Luxembourg. In comparison, the numbers for Belgium, France and Germany were 4.9, 6.7 and 3.6, respectively. Hereby, the ICU bed occupancy between Germany and Luxembourg was comparable. However, given the lack of data on daily hospital bed occupancy for Germany, only Belgium and Luxembourg were comparable on this metric (19.3 per 100,000 inhabitants versus 19.5), which, in turn, again highlights the general need for coherent data to allow meaningful comparisons between neighbouring countries.

In addition to mass screening and systematic contact tracing for SARS-CoV-2, Luxembourg has also performed a representative serological sampling on a weekly basis among its residents since November 2020. The data up until the beginning of the vaccination campaign (15 January 2021; Fig. 1) indicated a seroprevalence of 7.7% [9]. Extrapolation to the entire population yields 48,264 expected cases compared to the actual 48,630 cases recorded cumulatively until this date. Consequently, a very low proportion of cases (0.8%) appears to have gone undetected suggesting very high case ascertainment of COVID-19 in Luxembourg. Albeit with shallower population-wide coverage, analogous data for Belgium [10] (sampling period considered: 18-20 January 2021) indicated a seroprevalence of 15.6% which would suggest that on the order of 62.3% of cases might have gone undetected. While comparable data on seroprevalence is presently lacking for most countries, differences in country-specific COVID-19 incidence levels should be adjusted for testing

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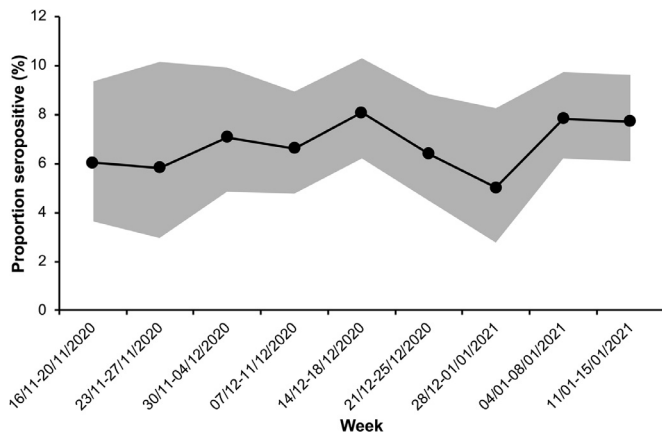
**Fig. 1.** Representative seroprevalence data for Luxembourg residents [9] showing the proportion of seropositive individuals per week with corresponding 95% binomial confidence intervals. A randomly selected sample comprised of a maximum target of 1,000 residents was tested per week on workdays in the period shown from 16 November 2020 until 15 January 2021.

coverage and certainly not be used on their own for defining high risk countries, as they might be more a reflection of different case ascertainment levels than reflect actual epidemiological risks for infection.

In future, it would therefore be desirable for countries to also publish the results of population-wide seroprevalences in addition to COVID-19 incidences to be able to relate detected case numbers by testing with caseloads inferred from serological data. Apart from also considering case fatality rates and hospitalisation rates, the impacts of varying country-wide vaccination programmes and coverages for variants of concerns will also need to be factored into more inclusive risk assessments in the coming weeks and months.

### Authors' contributions

The authors are solely responsible for all aspects of this article including the research, the interpretation and the writing thereof. PW performed data analysis and interpretation, and wrote the manuscript. JM performed data analysis and interpretation, and contributed to manuscript writing. TGD contributed to data analysis and interpretation, and contributed to manuscript writing.

### Declaration of Competing Interest

The authors have nothing to disclose.

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