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Unveiling the Underlying Severity of Multiple Pandemic Indicators

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SUMMARY

Background: Multiple interconnected key metrics are frequently available to track the pandemic progression. One of the difficulties health planners face is determining which provides the best description of the status of the health challenge.
Methods: The aim of this study is to capture the information provided by multiple pandemic magnitudes in a single metric. Drawing on official Spanish data, we apply techniques of dimension reduction of time series to construct a synthetic pandemic indicator that, based on the multivariate information, captures the evolution of disease severity over time. Three metrics of the evolution of the COVID-19 pandemic are used to construct the composite severity indicator: the daily hospitalizations, ICU admissions and deaths attributable to the coronavirus. The time-varying relationship between the severity indicator and the number of positive cases is investigated.
Results: A single indicator adequately explained the variability of the three time series during the analyzed period (May 2020–March 2022). The severity indicator was stable until mid-March 2021, then fell sharply until October 2021, before stabilizing again. The period of decline coincided with mass vaccination. By age group, the association between underlying severity and positive cases in those aged 80+ was almost 20 times higher than in those aged 20-49.
Conclusion: Our methodology can be applied to other infectious diseases to monitor their severity evolution with a single metric. The synthetic indicator may be useful in assessing the impact of public health interventions on reducing disease severity.

Keywords: Factor analysis; Principal component analysis; Pandemics; Vaccination.

INTRODUCTION

One of the difficulties for health planners in monitoring an ongoing disease over time is deciding which metric best describes its status when several interrelated measures are available [1]. In this context, methods for dimension reduction of multiple time series can be very important to find lower-dimensional representations of multiple (correlated) measures. One of the most popular techniques for dimension reduction of time series was proposed by Brillinger, who defined dynamic principal components (DPC) based on the criterion of optimal reconstruction of the original time series [2]. Peña et al generalised the concept of dynamic principal components by relaxing the assumption that the components are linear combinations of the data [3]. They called this method one-sided dynamic principal components (ODPC).

In this study, we illustrate the application of the ODPC methodology to construct a synthetic pandemic indicator that, based on multivariate information, captures the evolution of disease severity over time in a single magnitude. We focus on the coronavirus (COVID-19) pandemic declared by the World Health Organization in 2020. Most people infected with the SARS-CoV-2 virus experienced mild to moderate respiratory illness and recovered without needing hospitalization; however, a significant number fell seriously ill and required regular hospitalization or admission to an intensive care unit (ICU). Some failed to survive the disease.

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Previous research has mainly attempted to assess the evolution of disease severity based on single COVID-19 indicators, addressing, for example, the number of hospital admissions [4-6], hospital bed occupancy [7,8], the number of ICU admissions [9-11], ICU bed occupancy [12-14], or the number of deaths [15-17]. Other studies have used multivariate principal component techniques, but again focusing on a single COVID-19 indicator, albeit for multiple countries, to cluster countries according to their similarities in the evolution of the pandemic [18-20].

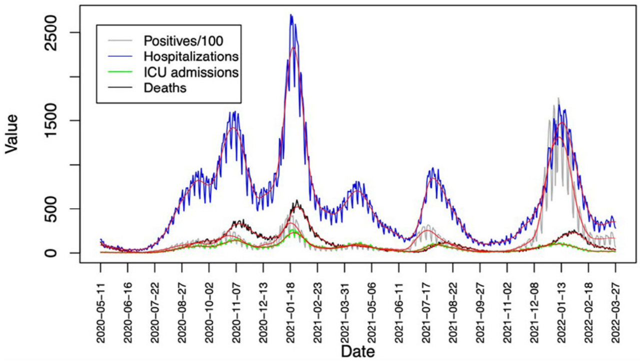
Here, we undertake a joint analysis of three COVID-19 severity indicators: namely, the number of hospitalizations, the number of ICU admissions and the number of deaths. We aim to explore whether applying the ODPC methodology to official Spanish data from May 2020 to March 2022 results in a single component capable of explaining the joint evolution of the three disease-severity time series. This would, first, provide us with a component that reveals the underlying severity of COVID-19 and, second, enable us to analyze in a straightforward fashion the relationship between the synthetic indicator proposed and the number of COVID-19 positive cases detected at each point in time, considering the Spanish population as a whole and by age groups. To analyze how the underlying severity indicator and the number of positive cases are related, a time-varying coefficient linear model (TVLM) is applied [21].

METHODS

Data

In conducting this study, free-access datasets have been used. The daily number of COVID-19 detected cases, hospital admissions, ICU admissions and deaths were obtained from the Spain's National Centre of Epidemiology [22]. Data for each time series is disaggregated by province, age, and gender from May 11, 2020 to March 27, 2022. Multiplicative weekly seasonality was observed, with lower values during weekends. Seasonal effects were adjusted using the LOESS method for seasonal-trend decomposition (STL) [23]. Additionally, the Nadaraya–Watson kernel smoother was applied to remove the noise of the resulting time series [24,25]. Figure 1 displays the original and smoothed COVID-19 time series for the observation period. Stationarity of the time series was investigated to avoid spurious results when analysing the association between time series [26]. After removing weekly seasonality and noise from the original COVID-19 indicators, the stationarity of the resulting time series was confirmed using the augmented Dickey-Fuller (ADF) test.

Figure 1. Original COVID-19 time series with smoothed values (red lines) for Spain. Period from May 11, 2020 to March 27, 2022



One-sided dynamic principal components

Dimension reduction is critical in multivariate vector time series for finding simplifying structures or factors. The application of ODPC is useful when the variability of different time series can be explained with a small number of components. This occurs when time series are highly correlated. Consider the vectors of stationary time series $\boldsymbol{z}_1,\ldots,\boldsymbol{z}_T$, with $\boldsymbol{z}_T=(z_{t,1},\ldots,z_{t,m})'$, $t=1,\ldots,T$. The ODPC can be defined as linear combinations of present and previous values of the series that minimize the mean squared error of the reconstruction. We define the first one-sided dynamic principal component as:

$$f_t(\boldsymbol{a}) = \sum_{h=0}^{k_1} \boldsymbol{z}'_{t-h}\boldsymbol{a}_h, \quad t = k_1+1,\ldots,T \qquad (1)$$

where $\boldsymbol{a}'=(\boldsymbol{a}'_0, \ldots, \boldsymbol{a}'_{k1})$ being $\boldsymbol{a}'_h=(\boldsymbol{a}'_{h,1}, \ldots, \boldsymbol{a}'_{h,m})$, $h = 0,\ldots, k_1$, the coefficients associated with the lagged values of the time series, and $k_1 \geq 0$ an integer denoting the number of lags used to compute the dynamic principal component. Only the first component is shown, given that it is the only one computed in this study [3].

Then, defining a matrix $\boldsymbol{B}'=[\boldsymbol{b}_0, \ldots, \boldsymbol{b}_{k2}]$, $\boldsymbol{b}_h \in \mathrm{R}^m$, $h = 0,\ldots, k_2$, the lagged values of the dynamic principal component can be used to reconstruct the original time series $\boldsymbol{z}_T$ as

$$\boldsymbol{z}_t^R(\boldsymbol{a},\boldsymbol{B}) = \sum_{h=0}^{k_2} \boldsymbol{b}_h f_{t-h}(\boldsymbol{a}), \quad t = k_1+k_2+1,\ldots,T \qquad (2)$$

where $k_2 \geq 0$ is an integer indicating the number of lags of the principal component to be used in the reconstruction. Note that if $k_1 = k_2 = 0$, the first ODPC is simply the first ordinary principal component of the data.

The mean squared error (MSE) in the reconstruction of the data is defined as

$$MSE(\boldsymbol{a},\boldsymbol{B}) = \frac{1}{T'm}\sum_{t=(k_1+k_2)+1}^{T} ||\boldsymbol{z}_t - \boldsymbol{z}_t^R(\boldsymbol{a},\boldsymbol{B})||^2$$

where $T' = T - (k_1 + k_2)$ and $\|\cdot\|$ is the Euclidean norm. The optimal values $(\hat{a}, \hat{B})$ of $\boldsymbol{a}$ and $\mathbf{B}$ satisfy

$$(\hat{\boldsymbol{a}}, \hat{\boldsymbol{B}}) = \min_{\|\boldsymbol{a}\|=1, \boldsymbol{B}} MSE(\boldsymbol{a}, \boldsymbol{B})$$

An alternating least-squares algorithm defined in Peña et al. [27] can be used to estimate the parameters. In practice, the number of lags (k_1,k_2) need to be chosen. One possible approach to selecting them is to minimize the cross-validated forecast error in a stepwise manner. Consider the *h*-steps ahead forecasts and specify a maximum number of lags and the size of the rolling window used to estimate the forecast error *w*. Then, the first component is computed for each combination of lags up to the maximum number considered, using periods $1,\ldots,T-h-t+1$ for $t = 1,\ldots,w$. The mean squared prediction error of the *h*-steps ahead forecasts is then calculated for each combination of lags. The number of lags chosen is the one that minimizes the mean squared prediction error. If more than one component is considered, the procedure would be repeated, including the additional component(s) progressively, in order to select the optimal lags and the optimal number of components. The previous stepwise approach could be used to minimize an information criterion instead of the cross-validated prediction error [3].

RESULTS

The analysis was conducted using the R software [28].

Synthetic indicator of underlying severity

High pairwise correlation coefficients were obtained between the number of hospital admissions, ICU admissions and number of deaths, with values between 0.87 and 0.95. Thus, we performed an ODPC analysis to construct a single severity indicator capable of capturing the information from these three COVID-19 series. After rescaling the three time series, the number of lags has to be selected and the parameters estimated. A maximum of 10 lags was considered for the selection of the optimal number of lags. The *h*-steps ahead forecast and the window size chosen were one and ten, respectively.

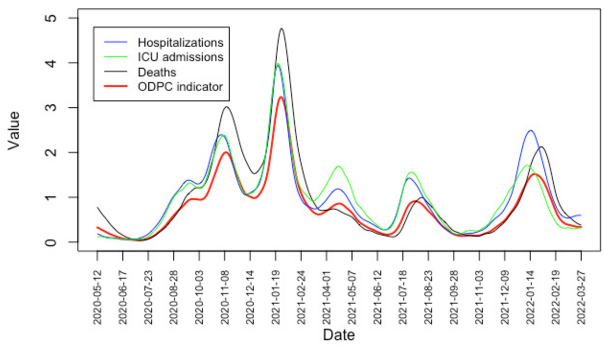
The number of lags that minimized the mean squared error of prediction was one. The estimated coefficients of vector $\boldsymbol{a}$ were:

$$\hat{\boldsymbol{a}}' = (0.03 \quad -0.4 \quad -0.21 \quad 0.22 \quad 0.65 \quad 0.52)$$

This vector $\hat{\boldsymbol{a}}$ contains the estimated weights in the linear combination to construct the dynamic principal component in (1), which captures the underlying severity of COVID-19. Its first three values are the coefficients associated, respectively, with the number of hospitalizations, ICU admissions and deaths in period *t*, while the following three coefficients are those associated with the one-lagged values of the same series.

The MSE of the optimal ODPC was 0.031. This value is considerably lower than the MSE associated with one component in non-dynamic principal components analysis (0.051). The optimal model explained 95.83% of the variability in the three corrected severity time series. Figure 2 shows the three standardized series used to capture the severity of COVID-19, along with the component obtained from the ODPC analysis, which captures this evolution in a synthetic indicator.

Figure 2. Standardized smoothed COVID-19 time series and ODCP indicator for underlying severity. Period from May 11, 2020 to March 27, 2022



The number of positive cases diagnosed showed a moderate correlation with hospital admissions (0.56), ICU admissions (0.36), and deaths (0.30), suggesting that disease severity varies over time. This moderate correlation between positive cases and other indicators is also evident in Figure 1.

Reconstruction and prediction of severity indicators

The underlying severity indicator can be used with matrix $\hat{\boldsymbol{B}}$ to reconstruct the standardized corrected COVID-19 time series, as shown in (2). The resulting estimation of matrix $\boldsymbol{B}$ was the following:

$$\hat{\boldsymbol{B}} = \begin{pmatrix} 7.94 & -6.77 \\ 6.80 & -5.66 \\ -1.81 & 3.31 \end{pmatrix}$$

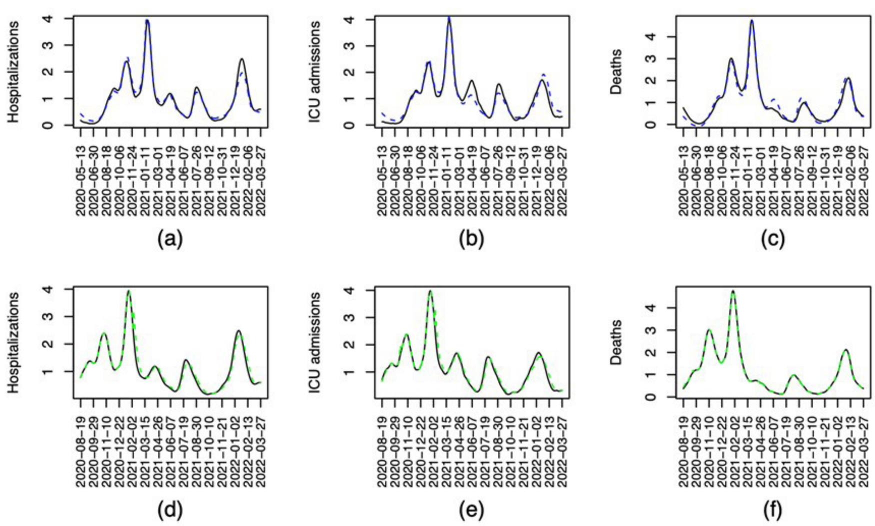
Thus, to reconstruct the hospitalization and ICU admissions time series, the underlying severity indicator has to be multiplied by a positive scalar (7.94 and 6.80, respectively) and the one-lagged indicator by a negative scalar (-6.77 and -5.66, respectively). The series of deaths, on the other hand, is reconstructed by multiplying the underlying severity indicator by a negative scalar (-1.81) and the one-lagged indicator by a positive scalar (3.31). The differing signs of the coefficients for reconstructing these original time series indicate that deaths follow hospital and ICU admissions. Unlike non-dynamic principal components, the flexibility of ODPC captures this sequentiality between the time series.

The reconstructed standardized time series of the number of hospitalizations, ICU admissions and deaths are shown in Figure 3 (upper panel). Note that an accurate reconstruction of these three COVID-19 time series is achieved, particularly for hospitalizations and deaths. The MSE was 0.022 for the number of hospital admissions, 0.038 for the number of ICU admissions and 0.033 for the number of deaths. The underlying severity indicator can then be used to predict the number of hospitalizations, ICU admissions, and deaths. Alternative prediction models for pandemic values have been used in the literature [4,29]. Here, time series forecasting of the future behaviour of the severity indicator is conducted using a SARIMA model, as recommended by Peña et al [27].The predicted severity indicator is multiplied by $\hat{\mathrm{B}}$ to reconstruct the forecasted COVID-19 time series. SARIMA-based forecast residuals are included in the predictions of the COVID-19 time series. Based on the first one hundred observations made in the period of study, one-step-ahead predictions of the number of hospitalizations, ICU admissions and deaths were performed from August 19, 2020 to March 27, 2022. These results are shown in Figure 3 (lower panel). A good forecasting performance is observed. When comparing actual observations with the predicted values, the mean squared prediction error was 0.028 for the number of hospital admissions, 0.019 for the number of ICU admissions and 0.001 for the number of deaths.

Association between positive cases and underlying severity

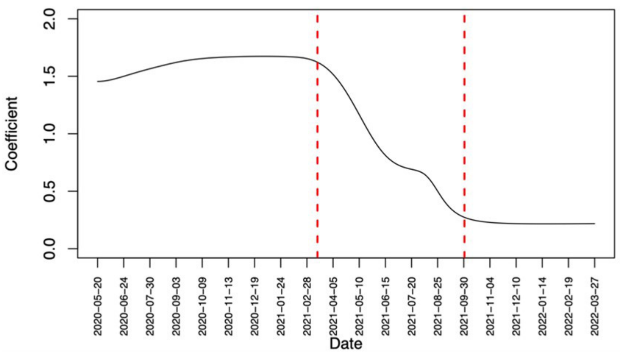
A TVLM is used to analyze the relationship between the underlying severity indicator and the daily number of coronavirus cases detected. Compared to the classical linear model, the TVLM is characterised by allowing the coefficient associated with the independent variable to vary over time [21,30]. As symptoms of severity usually appear later than the onset of the disease [4], we examine the correlation between the underlying severity indicator and the lagged series of positive cases. The highest correlation with the underlying severity indicator was observed for the number of positive cases with eight lags. Therefore, the explanatory variable included in the TVLM is the eight-lagged number of positive cases, as follows, $\mathbf{y}_t=\mathbf{x}_{t-8}\beta_t+\varepsilon_t, t=9,\dots,T$, where $\mathbf{y}_t$ corresponds to the estimated underlying severity indicator at time t, the regressor $\mathbf{x}_{t-8}$ is the rescaled (to be centred in one) number of diagnosed cases at time t-8 and ε_t is the error term. This model is best estimated using a combination of ordinary least squares and the local polynomial kernel estimator [31]. A bandwidth must be selected to indicate the size of the window in which weighted local regressions are estimated [32]. The chosen bandwidth (0.25) prevented the particular phase of the pandemic wave from affecting the estimation of the time-varying coefficient.

Figure 3. Reconstructed and predicted COVID-19 smoothed time series for Spain. Figures (a), (b) and (c) show the rescaled smooth original time series (black) and reconstructed time series (dashed blue) of COVID-19 for the period May 13, 2020 to March 27, 2022. Figures (d), (e) and (f) show the rescaled smooth original time series (black) and the predicted time series (dashed green) of COVID-19 for the period from August 19, 2020 to March 27, 2022



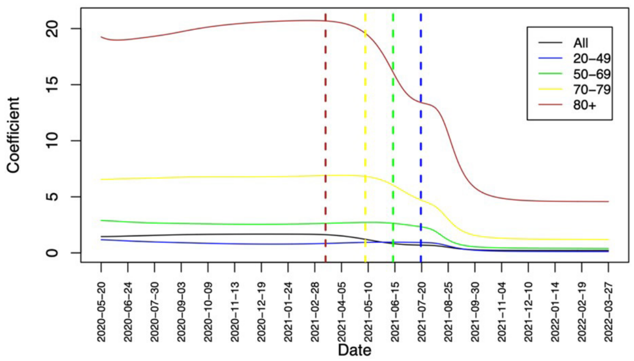
The estimated model has a good explanatory capacity (pseudo-R^2=0.93). The estimated vector of coefficients β_t contains values from 0.22 (minimum) to 1.67 (maximum), with a mean value of 1.04 and a median of 1.37. Figure 4 shows this evolution over the study period. It can be observed that the relationship between the underlying severity and the number of positive cases is quite stable until around mid-March 2021. Up to that point, the estimated coefficient is almost constant around 1.5, before it falls sharply. The drop in value of the coefficient and, therefore, in the expected underlying severity of COVID-19, continues until the beginning of October 2021. After this date, the coefficient value stabilizes at around 0.22 until the end of the period.

Figure 4. Estimated time-varying coefficient of the regression model in which the underlying COVID-19 severity is regressed on the rescaled series of positive cases. Red dashed lines are set at March 15, 2021 and October 1, 2021



To conclude, the underlying severity indicator and its relationship with the number of positives is estimated for the following age groups: 20–49, 50–69, 70–79 and 80 years or more (80+). To obtain comparable results, COVID-19 time series by age group were rescaled by the expected value of the time series for the whole population. Figure 5 shows the estimated coefficients of the TVLM between underlying severity and the number of positive cases in each age group. First, time varying coefficients seem clearly associated with age. Note that the estimated coefficients are higher for the older age groups at any point in time, particularly for the 80+ age group. In addition, all age group coefficients present the same 'constant-drop-constant' pattern, albeit at different moments in time: the younger the age group, the later the drop in the coefficient value begins. In Figure 5, the approximate date when the time-varying coefficient associated with each age group starts to decrease is indicated with a dashed vertical line – March 15, 2021 for the 80+ population (vaccination rate of 23.8%, brown dashed line); May 7, 2021 for 70-79 age interval (37.22%, yellow); June 13, 2021 for the 50–69 age interval (32.8%, green); and July 17, 2021 for the 20–49 age group (37.79%; blue).

Figure 5. Estimated time-varying coefficients for age-group based regression models in which the underlying COVID-19 severity is regressed on the rescaled series of positive cases. Brown, yellow, green and blue dashed lines are set at March 15, 2021; May 7, 2021; June 13, 2021 and July 20, 2021, respectively



DISCUSSION

Policy decisions by public health authorities during a pandemic are based, at least in part, on the evolution of disease severity indicators. Traditionally, these indicators are analyzed individually [10,13,33]. However, here, dynamic principal component techniques were used to synthesize the information from a set of highly correlated indicators, aiming to monitor their evolution with a single metric that can capture the underlying severity of the pandemic.

In this research, we demonstrate that one-sided dynamic principal components, when used to reduce the dimensionality of COVID-19 metrics, accurately capture serial dependence of time series. Moreover, this methodology performs well in forecasting, helping to anticipate future epidemic outcomes [34,35]. Previous studies reporting the dimensional reduction of a set of COVID-19 indicators are scarce. One exception is Swallow et al [1], who conducted their static principal component analysis to a set of COVID-19 indicators in the United Kingdom. We believe our approach may facilitate the interpretation of results when there is sequentiality in the time series data, as observed here with deaths following hospitalizations and ICU admissions.

We found that the relationship between the number of positives and the underlying severity indicator was almost constant until March 2021, showing a high linear correlation between these indicators during that period. However, as of March 2021, the relationship steadily decreased until October 2021, reflecting a decline in the consequences for the population with a positive diagnosis. From October 2021 onwards, the relationship between these metrics was once again constant over time, albeit at a much lower intensity. The period marked by a fall in the estimated association broadly coincided with the mass vaccination of the Spanish population [36]. Many studies have highlighted the effectiveness of vaccination against the serious health consequences associated with COVID-19 [37,38].

Age is a well-known risk factor for serious illness or death after SARS-CoV-2 infection [39]. In our study, we detected three relevant features associated with age. First, older age groups presented higher values of the underlying severity indicator for the same number of people diagnosed with COVID-19, with this ratio being especially high for those over eighty. Second, the same pattern – a decrease in the severity of COVID-19 depending on the number of positive cases after a period of stable association – was observed in all age groups; however, the older the group, the earlier the onset of the fall in the coefficients of the relationship between positives and underlying severity. This could be at least partially attributable to the fact that Spain's vaccination program was initiated among the oldest age groups, with vaccines being made progressively available to younger groups once a high percentage of older people had been vaccinated. Third, the reduction in underlying severity associated with positive diagnoses was more intense (in absolute numbers) with increasing age. However, if we analyze the reduction in relative terms, we find that this association fell by 84% among those aged 20 to 49, by almost 83% among those aged 50 to 69, by almost 80% among those aged 70 to 79, and by 75% in those aged over eighty, indicating that the relative reduction was lower among the older age groups [40,41].

This study is not free of limitations. In constructing the composite index of underlying severity, it would be useful for health decision-making in pandemic settings if the single metric could include more information. We use publicly available Spanish data from the National Centre of Epidemiology [22] from 2020 to 2022. The selection of only three time series in the construction of the single metric was due to the availability of reliable information from the Spanish surveillance system. However, we do not include potentially important variables in the analysis such as excess of mortality, vaccination rate [5], or socio-economic factors [42] of the population under study. In addition, all three time series are considered equally important, but hospitalizations, ICU admissions, and deaths reflect different levels of coronavirus severity. This limitation could be overcome by using time series dimensional reduction techniques that weight the different severities according to health decision-maker criteria. Finally, the underlying severity index is certainly useful for analysing the evolution of the indicators during the observation period, although its value is not easily and directly interpretable, as the reconstruction of the coronavirus time series involves the underlying severity indicator and its one period lagged value.

The methodology used in this research to create a synthetic metric of pandemic severity can be applied to other areas of public health. Multiple interconnected metrics are frequently available in relation to public health issues, and one difficulty health planners face is determining which best describes the health challenge status. This study shows how these alternative metrics can be unified while retaining most of their information, thus providing policymakers with a single metric that describes the health issue's severity and enables them to monitor disease evolution. Analysis of this synthetic indicator can be useful, for example, in assessing the impact of health interventions such as vaccination in reducing disease severity. Health policymakers will be interested in monitoring the evolution of the severity indicator and its relationship with the vaccination coverage of the population in order to evaluate the effectiveness of vaccination policies. Another relevant application for health policymakers is to examine the relationship between the synthetic severity indicator of a disease and alternative socio-economic factors when analyzing the evolution of the disease in different regions and/or population groups.

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COMPETING INTERESTS

The authors declare no competing interests.

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