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RESEARCH ARTICLE

Estimating COVID-19-Related Excess Mortality Excluding Seasonal Phenomena in Belgium

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ABSTRACT

Excess mortality, rather than reported COVID-19 deaths has been suggested to evaluate the impact of the SARS-CoV-2 induced Corona Virus Disease (COVID-19) pandemic on mortality. However, the relationship between excess mortality and COVID-19 mortality is perturbed by seasonal phenomena, such as extreme temperatures and seasonal influenza. Models used to estimate excess mortality often ignore these underlying patterns. We propose a dynamic linear state-space model to estimate all-cause mortality, which accounts for extreme temperatures above 25°C and seasonal influenza via the Goldstein index. The state-space model prediction of the excess mortality that is not explained by heat waves and seasonal influenza coincides with the reported COVID-19 mortality in the year 2020 in Belgium.

Keywords: all-cause mortality; COVID-19; excess mortality; heat wave; seasonal influenza; *state-space* model

1. Introduction

The global spread of the SARS-CoV-2 virus has caused waves of Coronavirus Disease (COVID-19) to surge in most countries, closely followed by waves of increased all-cause mortality ¹. The increase in all-cause mortality in the year 2020 compared to previous years is apparent in many countries². For instance, the all-cause mortality in April and November 2020 in Belgium was the highest since World War II^{3,4}. The all-cause mortality is impacted by the pandemic, both in a direct and an indirect way. Besides the direct effect of deceased SARS-CoV-2 infected patients, mortality can increase indirectly due to an overloaded health care system, patients delaying their seeking medical attention for other health risks or lack of funding. Additionally, mortality can decrease indirectly by mitigation measures against the spread of SARS-CoV-2, for example by a reduction in lethal traffic accidents.

To estimate the impact of the pandemic on all-cause mortality, one can study either the reported COVID-19-related deaths or excess mortality. The latter is commonly obtained by subtracting expected allcause mortality from observed all-cause mortality, although variations in computation exist. While countries worldwide have reported regularly the number of COVID-19-related deaths as part of the monitoring strategy, reporting differences of COVID-19-related deaths exist between countries and regions. These differences arise, for example, from varying testing strategy, availability of testing material, and in- or exclusion of nursing home deaths. Since all-cause mortality data is more reliable, excess mortality has been preferred to measure the impact of COVID-19 on mortality 5,6,7. However, seasonal phenomena, such as extreme temperatures and seasonal respiratory infections, particularly influenza, also lead to excess mortality. For example, the heat wave of August 2020 in the Northern hemisphere increased the excess mortality in the year 2020, perturbing the association between excess mortality and COVID-19 mortality⁸. These underlying seasonal causes for excess mortality should be accommodated when estimating the impact of COVID-19 on mortality. Since all-cause mortality encompasses mortality of the yearly varying extreme temperatures and seasonal influenza, the estimation of expected allcause mortality should allow for these highly variable causes to be modelled separately. The subsequently obtained excess mortality can then be attributed to the common seasonal phenomena as well as to other causes, such as COVID-19.

Commonly used methodology to estimate expected all-cause mortality, such as the weekly average of

historical mortality data^{1,7,9,10,11}, linear models^{8,12,13} and (S)ARIMA models¹⁴ ignore these underlying seasonal patterns or assume that they always occur in the same weeks. Other models either account solely for weather conditions^{15,16} or circumvent the effect of extreme temperatures and seasonal influenza by excluding historical periods with excess mortality^{17,18}. However, excluding seasons, as in the EURO-MOMO models, will not eliminate the effects of extreme temperature or seasonal influenza on mortality and may not be sufficient to eliminate the influence of these events on mortality⁵. Indeed, mortality in the Spring may be lower than expected after a Winter with severe seasonal influenza. Some extensions of the EURO-MOMO models do not exclude historical seasons by introducing a cyclic pattern, and address underlying patterns such as extreme temperatures, ozone concentration and seasonal influenza^{19,20,21}. However, the EURO-MOMO model and its extensions are all based on Poisson models with additionally allowance for overdispersion, of which nevertheless the constant mean and independence over time assumptions are criticized⁵.

The aim of this paper is to propose a statistical model for estimating excess mortality in the year 2020 in Belgium, taking account of mortality due to extreme temperatures and seasonal influenza. Besides these highly variable phenomena, the model should allow as well for stabler, known effects on mortality. The evolution of population size and its composition is often slow and rather stable, which results in a discernible long-term trend on mortality. On the other hand, mortality is correlated over time, both in the short-term time domain as well as across seasons.

A family of models, the so-called State-Space Models (SSM), naturally handles this auto- or serial correlation, by estimating future states of a system based on historical observations, and allows for adjustment of seasonal and other phenomena in a systematic part. State-space models are a very flexible class of models that encompasses wellknown time series models such as exponential smoothing and (S)ARIMA models with good forecasting characteristics^{22,23}. They consists of a measurement equation, that describes the relation between observations and the unobserved (state) variables, and one or several state equations, that describe the dynamics of the unobserved state variables. The state variables are a set of variables that describe the system at any given time point, for example long-term trends, seasonal trends, regression elements and disturbances. The state values evolve over time in a way that depends on values in their past and possibly additional variables. Model parameter estimation and forecasting depends on filtering and smoothing techniques.

After introducing the data and study design in Section 2.1, we present in Section 2.2 a SSM to forecast the weekly mortality in the year 2020 in while accounting for seasonality, Belgium, autocorrelation, extreme temperature, and seasonal influenza. The forecast mortality for the year 2020 by the SSM will lead to an excess mortality that is not explained by such phenomena as extreme temperatures and seasonal influenza and reflects the effects of COVID-19 on mortality. Finally, the SSM model is applied to the year 2020 for Belgium in Section 3.

2. Methods

2.1 Data and study design

This research can be conducted without additional data collection. Indeed, daily all-cause mortality data of Belgium from the year 2009 onward are publicly available from the national statistical institute, Statistics Belgium²⁴. The same is true for many other countries and regions, allowing the methodology to be used elsewhere. The Belgian data were downloaded on January 25th 2021 and temporally aggregated in weekly periods. The weeks are defined according to the International Standard ISO 8601 definition, i.e., Monday is the first day of the week and the first week of the year is the week that contains the first Thursday of January. The first week of the year 2009 was excluded from the data, since it is incomplete.

In Belgium, daily COVID-19 mortality data are registered and reported by the Belgian national public health institute Sciensano²⁵. These open source data were extracted on January 26th 2021 and aggregated in weeks using the aforementioned week definition. Registered COVID-19 related deaths in Belgium include confirmed and possible COVID-19 deaths^{4,26}.

Sciensano is also responsible for registering seasonal influenza. Weekly percentage of Influenza Like Illness (ILI) reported by sentinel general practitioners and the weekly percentage of samples tested positive for influenza were made available from January 2009 onward, for the entire population and by age category (<1 year, 1–4 years, 5–14 years, 15–19 years, 20–64 years, 65–84 years and >85 years). The weekly Goldstein index (GI)^{27,28} is an influenza activity indicator, which is obtained by multiplying the percentage ILI with the percentage of positive samples for influenza per week.

Finally, the daily maximum temperature from the official meteorological station in Uccle, Belgium,

was obtained from the Royal Meteorological Institute²⁹. The data were subsequently aggregated to weekly data by taking the weekly average of the daily temperatures, using the above week definition.

2.2 State-space Model

State-space models are a large and flexible class of models that describe the evolution of observed measurements over time that depend on an underlying system of unobserved variables^{22,23}. Hence, a state-space model consists of a measurement equation, which describes the relation between observed variables and the unobserved state variables, and state equations, which describe the dynamics of the unobserved state variables. Both deterministic and stochastic systems can be defined for the state and measurement equations. A special class of SSM are the dynamic linear models, where the errors in the state and measurement equations are assumed normally distributed. Although the number of deaths is frequently modelled with a Poisson distribution, the mean of weekly deaths is sufficiently high for the central limit theorem to be invoked.

For the dynamic linear models, the optimal inference algorithm is based upon recursive Kalman filtering, which estimates the unknown parameters in the system and produces successive one-step ahead predictions \hat{y}_t , conditional on the past and concurrent observations. With these predictions the variance of the prediction error F_t is calculated and 95% confidence intervals of the predictions constructed by $y_t = \hat{y}_t \pm 1.96\sqrt{F_t}$.

We propose a dynamic linear model for the observed weekly mortality, y_t , for t = 1, ..., T, from week 2 in year 2009 to week 52 in 2019, and perform a sensitivity analysis by evaluating different strategies to model the effects of extreme temperatures and seasonal influenza on mortality.

The exact relation between extremely high temperatures and mortality is subject to ongoing debate. Some evidence suggests that the intensity of the heat is the main driver of the effect of temperature on mortality, while duration only adds a relatively small effect. The effect on mortality of increasing temperature was found to be almost immediate³⁰. We evaluate two strategies to model the effect of extreme temperatures on mortality, by defining a binary indicator, I_{tr} , if the weekly average maximum temperature $\overline{T}_{max,tr}$, is above 25° C, i.e. $I_t = 1_{\overline{T}_{max,tr} > 25^{\circ}C}$ and by defining a continuous variable:

$$H_t = \begin{cases} 0, & \text{if } \bar{T}_{max,t} \leq 25^{\circ}C, \\ \bar{T}_{max,t} - 25^{\circ}C, & \text{otherwise.} \end{cases}$$

Nielsen et al.²⁰ investigated several strategies to model the effect of influenza on mortality, namely influenza like illness, percentage of positive samples for influenza in hospital-admitted subjects and the Goldstein index. While ILI may overestimate influenza activity, as other respiratory infections may cause ILI, and the percentage of positive samples for influenza may not fully reflect the

intensity of influenza activity in the population, the Goldstein index was found to better capture influenza activity. Following the results of a recent systematic review³¹, we postulate that it is mostly the elderly (
$$\geq 65$$
 year) that die after an influenza infection with a lag of about 0–2 weeks.

The proposed SSM contains 6 components:

$$\begin{aligned} y_t &= \mu_t + \psi_t + y_t^{AR} + \beta_{1,t} X_{1,t} + \beta_{2,t} X_{2,t} + \varepsilon_t, & \varepsilon_t \sim N(0, \sigma^2) \\ \mu_t &= \mu_{t-1} + \eta_t, & \eta_t \sim N(0, \sigma_\eta^2) \\ \beta_{1,t} &= \beta_{1,t-1} + \zeta_t, & \zeta_t \sim N(0, \sigma_\zeta^2) \\ \beta_{2,t} &= \beta_{2,t-1} + \upsilon_t, & \upsilon_t \sim N(0, \delta\sigma_{\upsilon_t}^2) \\ y_t^{AR} &= \phi y_{t-1} + \xi_t, & \xi_t \sim N(0, \sigma_{\xi_t}^2) \\ \psi_t &= \sum_{j=1}^n \left[\alpha_j \sin \frac{2\pi j t}{52.18} + \gamma_j \cos \frac{2\pi j t}{52.18} \right] + \nu_t, & \nu_t \sim N(0, 0) \end{aligned}$$

with $X_{1,t}$, the weekly seasonal influenza variable and $X_{2,t}$, the weekly extreme temperature variable. All stochastic components are assumed to be independent.

A first component is a stochastic trend, μ_{t} , which captures long-term trends in mortality, such as increasing population, improving health care systems or changing age-distribution in the population. A second component, ψ_t , is a deterministic seasonal component of mortality, capturing the increased mortality in winter compared to summer. We assume that the underlying seasonal trend does not change over the years and that it can be modelled by n Fourier series. A third component, y_t^{AR} , is a stochastic heteroskedastic autoregressive component, which allows for a time-varying autocorrelation between mortality of consecutive weeks. A fourth component, $\beta_{1,t}$, is a stochastic heteroskedastic component of seasonal influenza that allows for a time-varying effect on mortality. As the influenza strains per year vary, including in intensity and the fatality rate, the time-varying aspect is important to capture this varying strain effect on mortality. The fifth component, $\beta_{2,t}$, is the effect of extreme temperature on mortality. Because the effect of extreme temperature is debated, we will evaluate both deterministic ($\delta = 0$) as well as stochastic ($\delta =$ 1) effects. A stochastic effect allows variation between weeks with the same temperature, to include additional effects such as duration of the heat wave or humidity. Finally, the sixth component, ε_t , is white noise, capturing mortality that cannot be explained by the other components.

Model parametrizations will be compared by evaluating diffuse likelihood based Akaike Information Criteria (AIC), which is equivalent to restricted maximum likelihood, and diagnostics for normality, heteroscedasticity and white noise. For each of the models, the excess mortality is obtained via the state-space model prediction for the full year and the first 6 months of 2020 and compared to the reported COVID-19 mortality in Belgium. The data analyses were performed and figures produced using SAS 9.4 Software. The SAS code can be requested from the first author.

3. Results

A correlogram of the all-cause mortality time series in Belgium indicates that a yearly cycle is strongly present with a less pronounced half-yearly as well as a year and a half cycle. Therefore, models with two Fourier series (year and half-year cycle) and three Fourier series (adding a year and a half's cycle) are evaluated. Additionally, we evaluate the postulate that it is mostly elderly (≥ 65 year) who die from seasonal influenza and if a lag of 0, 1, and 2 weeks is required between the Goldstein Index (GI) and mortality. Finally, the effect of temperature on mortality is evaluated through I_t , which assumes that the absolute value of the temperature above 25°C is not important, and a continuous variable $H_{t,t}$ which assumes that the absolute temperature is important.

Based on the diffuse likelihood AIC, the models with three Fourier series are fitting the data better than the models with two Fourier series (Table 1-2 and supplementary material Figure 1-12). The mortality due to seasonal influenza does seem to be well represented by the elderly (≥ 65 year) only, since there is virtually no difference between models with all ages and the subgroup with only 65 years and above (Table 1). Moreover, no lag between the GI and mortality seems necessary, as models with 1week or 2-week lags between these two variables fit the data considerably worse (Table 3). Finally, the effect of heat waves on mortality are better described by the absolute temperature above 25° C, since the models with a binary indicator provide a worse fit. The absolute temperature itself is sufficient to capture the effect of heat waves on mortality given that the AIC for the deterministic effect is very similar to the stochastic effect and the stochastic variance is not important to correct for (Table 1). The similarity between estimation of excess mortality (Table 1) shown in the sensitivity analysis of model parametrization (Table 2), shows the robustness of the state-space model in estimating mortality.

	2 cycles				3 cycles			
	AIC	1 year (95% CI)	6 months (95% CI)	AIC	1 year (95% Cl)	6 months (95% Cl)		
Reported COVID-19								
deaths		19288	9621		19288	9621		
65y GI + determ H _t	6763	19067	9260	6743	19005	9599		
		(11501-26636)	(6399-12123)		(11503-26515)	(6760-12440)		
GI + determ H _t	6766	19023	9251	6745	19049	9638		
		(11425-26624)	(6397-12107)		(11512-26591)	(6807-12473)		
65y GI + stoch H _t	6775	19002	9270	6755	18969	9607		
		(11019-26987)	(6423-12118)		(11039-26895)	(6774-12439)		
$GI + stoch H_t$	6777	18958	9264	6757	19008	9647		
		(10936-26975)	(6421-12104)		(11045-26972)	(6822-12475)		
65y Gl + determ I _t	6784	19169	9173	6764	19149	9537		
		(11388-26955)	(6230-12117)		(11431-26867)	(6618-12459)		
GI + determ I _t	6787	19127	9166	6766	19195	9576		
		(11324-26928)	(6230-12097)		(11453-26938)	(6661-12488)		

Table 1. Reported COVID-19 mortality versus excess mortality predicted by various fitted state-spacemodels in the first 6 months and the full year of 2020. AIC=Diffuse likelihood Akaike Information Criteria,CI=Confidence Interval, GI=Goldstein Index, determ=deterministic, stoch=stochastic, H_t =continuousvariable for temperature, I_t = binary indicator for temperature.

	AIC	φ	$\sigma^2_{\xi_t}$	$\beta_{2,t}$	$\sigma_{\upsilon_t}^2$	$\sigma_{\zeta_t}^2$	σ_{η}^2	σ^2
		2 cycles						
65y GI + determ H _t	6763	0.76 (0.06)	2079 (548)	66.2 (5.5)		27.94 (11.04)	2.77 (4.21)	2853 (462)
GI + determ H _t	6766	0.76 (0.06)	2224 (568)	66.0 (5.4)		4.21 (1.48)	3.1 0 (4.46)	2698 (461)
65y GI + stoch H _t	6775	0.77 (0.06)	2056 (538)		19.23	28.87	2.43 (3.97)	2749 (451)
		. ,	· · ·			· · ·		
$GI + stoch H_t$	6777	0.76 (0.06)	2197 (558)		19.35 (14.68)	4.32 (1.49)	2.74 (4.21)	2598 (450)
65y GI + determ I _t	6784	0.75 (0.06)	2396 (597)	158.0 (14.6)		25.29 (10.62)	2.90 (4.36)	2824 (491)
		0.75	2551	157.0		2.02	214	2459
GI + determ I _t	6787	(0.06)	(620)	(14.5)		(1.43)	(4.52)	2058 (491)

Medical Research Archives

Estimating COVID-19-Related Excess Mortality Excluding Seasonal Phenomena in Belgium

		3 cycles							
65y GI + determ H _t	6745	0.74	2133	66.1		27.04	3.23	2804	
		(0.07)	(570)	(5.5)		(10.85)	(4.40)	(477)	
GI + determ H _t	1755	0.74	2274	65.9		4.13	3.56	2646	
	0/33	(0.07)	(589)	(5.4)		(1.46)	(4.66)	(475)	
65y GI + stoch H_t	6757	0.75	2109		18.38	27.85	2.86	2703	
		(0.07)	(560)		(14.04)	(10.97)	(4.20)	(465)	
	6764	0.74	2248		18.53	4.21	3.17	2549	
		(0.07)	(579)		(14.20)	(1.47)	(4.45)	(464)	
65y GI + determ I _t	6766	0.73	2458	157.0		24.27	3.37	2767	
		(0.07)	(621)	(14.6)		(10.37)	(4.57)	(507)	
GI + determ I _t	6766	0.72	2611	157.0		3.81	3.61	2598	
		(0.07)	(643)	(14.5)		(1.41)	(4.73)	(507)	

Table 2. Model parameter estimates (standard error) of the influenza and various temperature parametrization in the state-space model. GI=Goldstein Index, determ=deterministic, stoch=stochastic, H_t =continuous variable for temperature, I_t = binary indicator for temperature.

	2 cycles			3 cycles			
	no lag	1 week lag	2week lag	no lag	1 week lag	2week lag	
65y GI + determ H _t	6763	6797	6806	6743	6777	6787	
GI + determ H _t	6766	6798	6829	6745	6779	6811	
65y GI + stoch H_t	6775	6809	6818	6755	6789	6799	
GI + stoch H_t	6777	6810	6817	6757	6791	6799	
65y GI + determ It	6784	6817	6825	6764	6797	6805	
GI + determ It	6787	6818	6835	6766	6799	6816	

Table 3. Model fit (AIC) of the various temperature and influenza parametrization in the state-space model, with several choices of lag between the Goldstein Index and mortality. GI=Goldstein Index, determ=deterministic, stoch=stochastic, H_t =continuous variable for temperature, I_t = binary indicator for temperature.

When comparing the reported COVID-19 deaths with the predicted all-cause mortality from the best fitting state-space model (a deterministic continuous temperature effect, 3 Fourier cycles and the 65y GI), it is clear that between 2/03/2020-11/05/2020 (weeks 10 and 20) and between 18/09/2020-21/12/2020 (weeks 40 and 52), there is excess mortality (Figure 1) that can be explained by COVID-19 (Figure 2). Moreover, the

summer mortality peak in 2020 is not completely covered by the temperature effect alone (Figure 1). Indeed, there seems to be a small increase in reported COVID-19 deaths during the summer peak (Figure 2). Overall, the reported COVID-19 deaths in the year 2020 and the first half of the year 2020 coincide well with the excess mortality predicted from the state-space model (Table 1).



Figure 1. Reported all-cause mortality versus predicted all-cause mortality by the state-space model.



Figure 2. Reported COVID-19 mortality versus predicted excess mortality by the state-space model.

4. Discussion

The year 2020 was hall-marked with one of the most lethal pandemics in the recent history. The allcause mortality in many countries worldwide underscores the severity of the pandemic. While allcause mortality is often reliably reported, the impact of COVID-19 on mortality needs to be estimated, as the reporting of COVID-19 related deaths varies between countries. A worldwide estimation of COVID-19 mortality or international comparisons based on COVID-19-related deaths is therefore subject to bias. Rather, excess mortality, that is based on all-cause mortality, is recommendable^{5,6,7}. However, excess mortality requires the estimation of mortality under nonpandemic conditions, which results in a wide array of models in the literature^{1.7-21,33,34}. While the weekly average of historical mortality data1,7,9,10,11 and simple linear model^{12,13,33,34} ignore the auto- or serial correlation in the mortality time series, other models ignore seasonal phenomena, such as heat waves and influenza, or assume that they occur in the same week every year. Consequently, the excess mortality based on these predictions will include deaths attributable to heat waves and seasonal influenza, perturbing the connection between excess and COVID-19 mortality⁸. For example, the excess mortality for the year 2020 in Belgium, estimated by the BE-MOMO model³², The Economist¹² and COVID-19 Excess Mortality Collaborators³³, all include the heat wave excess mortality in August 2020. While one strategy could be to exclude the weeks of the excess mortality of extreme temperatures and seasonal influenza³⁴ in assessing COVID-19 mortality, we propose to account for extreme temperatures and seasonal influenza in the model. More specifically, we have proposed a state-space model to forecast all-cause accounting for flexible mortality seasonal phenomena, such as extreme temperature and seasonal influenza. Subtracting the forecast mortality of this model from the observed all-cause mortality results in an estimate of excess mortality that cannot be explained by heat waves and seasonal influenza. For the year 2020 in particular, excess mortality not explained by heat waves and seasonal influenza arguably coincides with the effects of COVID-19 on mortality.

We have shown that the forecast excess mortality by the state-space model in Belgium that is not explained by extreme temperature and seasonal influenza coincides well with the reported COVID-19 mortality. As it has been established that Belgium reports fairly accurately its COVID-19 mortality^{4,8}, this shows that the state-space model can be used to predict the effects of COVID-19 on mortality for any region with historical information on mortality, maximum temperature and the Goldstein index. The appropriateness of the normally distributed error assumption of the proposed state-space in the state and measurement equations, is confirmed by the one-step ahead residual plots (Supplementary Figures 1-12).

Models that do not exclude excess mortality due to seasonal phenomena in estimating the COVID-19 mortality, result in lower^{12,32,34} or higher³³ values of the excess mortality caused by COVID-19 in Belgium. The model proposed in the COVID-19 Excess Mortality Collaborators³³ joins, by means of year 2019 prediction accuracy weights, three models. Two Poisson regression models corrected for population size with either splines or yearly and weekly random intercepts to model seasonality and a model taking the corresponding weekly mortality in the year 2019 into account. This ensemble model, however, does not correct for excess mortality due to heat waves or seasonal influenza. Moreover, for Belgium specifically, the year 2019 contained excess mortality due to a heat-wave, calling the appropriateness of the weights into question.

During the heat wave in the European summer of 2020, the temperature alone could however not explain completely the observed all-cause mortality in Belgium. Interestingly, during this period a slight increase in COVID-19 deaths is noted, likely due to the flare-up of COVID-19 incidences that was observed in the preceding weeks, predominantly in the Province of Antwerp²⁵.

The models applied show that deaths from seasonal influenza can be properly modelled taking only the elderly (≥ 65 years) into account and when using the Goldstein index, no lag is necessary. Finally, the effect of heat waves on mortality is direct and the absolute weekly maximum temperature above 25° C is important. The cut-off of the maximum temperature is based on the definition of Cox et al.¹⁹, who consider heat-related events as 5 consecutive days above 25° C. As the impact of extreme temperatures on mortality is debated^{30,35}, potentially other definitions of a heat wave may lead to an even more refined analysis of excess mortality.

An additional limitation of the proposed model is that the state-space model specification of seasonal cycles and phenomena may be country specific. For example, the Northern European countries excess mortality may also be caused by periods of extremely low temperatures²¹. Although the exact model parametrization may not be generally applicable to other countries and regions, such as less complex linear models and the 5-year average method^{1,7-13,33,34}, the underlying principles can be applied to adapt the model to any geographical seasonal phenomena. Finally, our proposed model assumes that besides extreme temperature and seasonal influenza no other major seasonal factors influence mortality.

The state-space model can perhaps be improved further by allowing stochastic seasonality to allow for example for varying seasons over time due to climate change, or by including additional potential cause of excess mortality, such as humidity, and/or ozone concentration. For any additional cause of excess mortality that is included in the model, appropriate data or a proxy should be available, potentially limiting the addition of these causes and/or its generalizability.

5. Conclusion

Rather than reported COVID-19-related deaths, excess mortality is recommended as a more reliable alternative to assess the overall impact on mortality of the SARS-CoV-2 virus. This, however, requires a reliable estimate of the mortality that is expected under non-pandemic conditions. Since the relationship between excess mortality and COVID-19 mortality may be perturbed by excess mortality due to seasonal phenomena, such as extreme temperatures and seasonal influenza, models forecasting expected all-cause mortality should correct for these effects. We proposed a dynamic linear state-space model to estimate the weekly allcause mortality, which accounts for extreme

temperature and seasonal influenza. The model uses the Goldstein index to capture influenza and the weekly average of the maximum temperature in addition to the historic mortality data to forecast mortality. The state-space model prediction of the excess mortality that is not explained by heat waves and seasonal influenza coincides with the reported COVID-19 mortality in the year 2020 in Belgium.

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Conflict of interest

No potential conflict of interest was reported by the author(s).

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References

- Giattino C, Ritchie H, Roser M, Ortiz-Ospina E, Hasell J. Excess mortality during the Coronavirus pandemic (COVID-19); 2021. https://ourworldindata.org/excess-mortalitycovid.
- 2. Nørgaard SK, Vestergaard LS, Nielsen J, Richter L, Schmid D, Bustos N, Braye T, Athanasiadou M, Lytras T, Denissov G, Veideman T, Luomala O, Möttönen T, Fouillet A, Caserio-Schönemann C, An der Heiden M, Uphoff H, Gkolfinopoulou K, Bobvos J, Paldy A, Rotem N, Kornilenko I, Domegan L, O'Donnell J, Donato F, Scortichini M, Hoffmann P, Velez T, England K, Calleja N, van Asten L, Stoeldraijer L, White RA, Paulsen TH, da Silva SP, Rodrigues AP, Klepac P, Zaletel M, Fafangel M, Larrauri A, León I, Farah A, Galanis I, Junker C, Perisa D, Sinnathamby M, Andrews N, O'Doherty MG, Irwin D, Kennedy S, McMenamin J, Adlhoch C, Bundle N, Penttinen P, Pukkila J, Pebody R, Krause TG, Mølbak K. Real-time monitoring shows substantial excess all-cause mortality during second wave of COVID-19 in Europe, October to December 2020. Euro Surveill. 2021 Jan;26(2):2002023. doi: 10.2807/1560-

7917.ES.2021.26.1.2002023.

 Molenberghs G, Faes C, Verbeeck J, Deboosere P, Abrams S, Willem L, Aerts J, Theeten H, Devleesschauwer B, Bustos Sierra N, Renard F, Herzog S, Lusyne P, Van der Heyden J, Van Oyen H, Van Damme P, Hens N. COVID-19 mortality, excess mortality, deaths per million and infection fatality ratio, Belgium, 9 March 2020 to 28 June 2020. Euro Surveill. 2022 Feb;27(7):2002060. doi: 10.2807/1560-

7917.ES.2022.27.7.2002060.

- Bustos Sierra N, Bossuyt N, Braeye T, Leroy M, Moyersoen I, Peeters I, Scohy A, Van der Heyden J, Van Oyen H, Renard F. All-cause mortality supports the COVID-19 mortality in Belgium and comparison with major fatal events of the last century. Arch Public Health. 2020 Nov 13;78(1):117. doi: 10.1186/s13690-020-00496-x.
- Aron J, Giattino C, Muellbauer J, and Ritchie H. A pandemic primer on excess mortality statistics and their comparability across countries; 2020. https://ourworldindata.org/covid-excessmortality
- Morgan D, Ino J, Di Paolantonio G, and Murtin F. Excess mortality: Measuring the direct and indirect impact of COVID-19. OECD. 2020; https://dx.doi.org/10.1787/c5dc0c50-en

- Beaney T, Clarke JM, Jain V, Golestaneh AK, Lyons G, Salman D, Majeed A. Excess mortality: the gold standard in measuring the impact of COVID-19 worldwide? J R Soc Med. 2020 Sep;113(9):329-334. doi: 10.1177/0141076820956802.
- Verbeeck J, Faes C, Neyens T, Hens N, Verbeke G, Deboosere P, Molenberghs G. A linear mixed model to estimate COVID-19-induced excess mortality. *Biometrics*. 2021 Oct 25:10.1111/biom.13578. doi: 10.1111/biom.13578.
- Michelozzi P, de'Donato F, Scortichini M, Pezzotti P, Stafoggia M, De Sario M, Costa G, Noccioli F, Riccardo F, Bella A, Demaria M, Rossi P, Brusaferro S, Rezza G, Davoli M. Temporal dynamics in total excess mortality and COVID-19 deaths in Italian cities. BMC Public Health. 2020 Aug 14;20(1):1238. doi: 10.1186/s12889-020-09335-8.
- Modig K, Ahlbom A, Ebeling M. Excess mortality from COVID-19: weekly excess death rates by age and sex for Sweden and its most affected region. *Eur J Public Health*. 2021 Feb 1;31(1):17-22. doi: 10.1093/eurpub/ckaa218.

 Stang A, Standl F, Kowall B, Brune B, Böttcher J, Brinkmann M, Dittmer U, Jöckel KH. Excess mortality due to COVID-19 in Germany. J Infect. 2020 Nov;81(5):797-801. doi: 10.1016/j.jinf.2020.09.012.

- 12. The Economist. Tracking COVID-19 excess deaths across countries.2020; https://www.economist.com/graphicdetail/2020/07/15/ tracking-covid-19excess-deaths-across-countries
- The New York Times. The pandemic's hidden toll: half a million deaths. 2020; https://www.nytimes.com/interactive/2020/0 4/21/world/coronavirus-missing-deaths.html
- 14. Faust JS, Krumholz HM, Du C, Mayes KD, Lin Z, Gilman C, Walensky RP. All-Cause Excess Mortality and COVID-19-Related Mortality Among US Adults Aged 25-44 Years, March-July 2020. JAMA. 2021 Feb 23;325(8):785-787. doi: 10.1001/jama.2020.24243.
- 15. Scortichini M, Schneider Dos Santos R, De' Donato F, De Sario M, Michelozzi P, Davoli M, Masselot P, Sera F, Gasparrini A. Excess mortality during the COVID-19 outbreak in Italy: a two-stage interrupted time-series analysis. Int J Epidemiol. 2021 Jan 23;49(6):1909-1917. doi: 10.1093/ije/dyaa169.

- 16. Blangiardo M, Cameletti M, Pirani M, Corsetti G, Battaglini M, Baio G. Estimating weekly excess mortality at sub-national level in Italy during the COVID-19 pandemic. *PLoS One.* 2020 Oct 9;15(10):e0240286. doi: 10.1371/journal.pone.0240286.
- 17. Vestergaard LS, Nielsen J, Richter L, Schmid D, Bustos N, Braeye T, Denissov G, Veideman T, Luomala O, Möttönen T, Fouillet A, Caserio-Schönemann C, An der Heiden M, Uphoff H, Lytras T, Gkolfinopoulou K, Paldy A, Domegan L, O'Donnell J, De' Donato F, Noccioli F, Hoffmann P, Velez T, England K, van Asten L, White RA, Tønnessen R, da Silva SP, Rodrigues AP, Larrauri A, Delgado-Sanz C, Farah A, Galanis I, Junker C, Perisa D, Sinnathamby M, Andrews N, O'Doherty M, Marquess DF, Kennedy S, Olsen SJ, Pebody R; ECDC Public Health Emergency Team for COVID-19, Krause TG, Mølbak K. Excess all-cause mortality during the COVID-19 pandemic in Europe pooled preliminary estimates from the EuroMOMO network, March to April 2020. Euro Surveill. 2020 Jul;25(26):2001214. doi: 10.2807/1560-

7917.ES.2020.25.26.2001214.

- Fouillet A, Pontais I, Caserio-Schönemann C. Excess all-cause mortality during the first wave of the COVID-19 epidemic in France, March to May 2020. Euro Surveill. 2020 Aug;25(34):2001485. doi: 10.2807/1560-7917.ES.2020.25.34.2001485.
- Cox B, Wuillaume F, Van Oyen H, Maes S. Monitoring of all-cause mortality in Belgium (Be-MOMO): a new and automated system for the early detection and quantification of the mortality impact of public health events. Int J Public Health. 2010 Aug;55(4):251-9. doi: 10.1007/s00038-010-0135-6.
- Nielsen J, Krause TG, Mølbak K. Influenzaassociated mortality determined from all-cause mortality, Denmark 2010/11-2016/17: The FluMOMO model. Influenza Other Respir Viruses. 2018 Sep;12(5):591-604. doi: 10.1111/irv.12564.
- Nielsen J, Rod NH, Vestergaard LS, Lange T. Estimates of mortality attributable to COVID-19: a statistical model for monitoring COVID-19 and seasonal influenza, Denmark, spring 2020. Euro Surveill. 2021 Feb;26(8):2001646. doi: 10.2807/1560-7917.ES.2021.26.8.2001646.
- 22. Harvey SJ. Forecasting, structural time series models and the Kalman filter. 1st edition Cambridge University Press, New York; 1989.

- 23. Durbin J and Koopman SJ. Time series analysis by state space methods. 2nd edition Oxford University Press, Oxford; 2012.
- 24. STATBEL. Number of deaths per day, sex, age, region, province, district. 2020. https://statbel.fgov.be/en/opendata/number-deaths-day-sex-district-age.
- 25. EPISTAT: COVID-19. Sciensano. 2020. https://epistat.wiv-isp.be/covid/
- 26. Renard F, Scohy A, Van der Heyden J, Peeters I, Dequeker S, Vandael E, Van Goethem N, Dubourg D, De Viron L, Kongs A, Hammami N, Devleesschauwer B, Sasse A, Rebolledo Gonzalez J, Bustos Sierra N. Establishing an ad hoc COVID-19 mortality surveillance during the first epidemic wave in Belgium, 1 March to 21 June 2020. Euro Surveill. 2021 Dec;26(48):2001402. doi: 10.2807/1560-7917.ES.2021.26.48.2001402.
- Goldstein E, Cobey S, Takahashi S, Miller JC, Lipsitch M. Predicting the epidemic sizes of influenza A/H1N1, A/H3N2, and B: a statistical method. *PLoS Med.* 2011 Jul;8(7):e1001051. doi: 10.1371/journal.pmed.1001051.
- Goldstein E, Viboud C, Charu V, Lipsitch M. Improving the estimation of influenza-related mortality over a seasonal baseline. *Epidemiology*. 2012 Nov;23(6):829-38. doi: 10.1097/EDE.0b013e31826c2dda.
- 29. Royal Meteorological Institute. 2021. https://www.meteo.be/en/belgium.
- 30. Gasparrini A, Armstrong B. The impact of heat waves on mortality. *Epidemiology*. 2011 Jan;22(1):68-73. doi: 10.1097/EDE.0b013e3181fdcd99.
- Li L, Wong JY, Wu P, Bond HS, Lau EHY, Sullivan SG, Cowling BJ. Heterogeneity in Estimates of the Impact of Influenza on Population Mortality: A Systematic Review. Am J Epidemiol. 2018 Feb 1;187(2):378-388. doi: 10.1093/aje/kwx270.
- Leroy M, Dupont Y, Braeye T, Bossuyt N, Bustos Sierra N. EPISTAT, Belgian mortality monitoring (BE-MOMO), Sciensano. 2021. https://epistat.wiv-isp.be/momo/.
- COVID-19 Excess Mortality Collaborators. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020-21. Lancet. 2022 Apr 16;399(10334):1513-1536. doi: 10.1016/S0140-6736(21)02796-3.
- 34. Karlinsky A, Kobak D. Tracking excess mortality across countries during the COVID-19 pandemic with the World Mortality Dataset. *Elife*. 2021 Jun 30;10:e69336. doi: 10.7554/eLife.69336.

Estimating COVID-19-Related Excess Mortality Excluding Seasonal Phenomena in Belgium

35. Xu Z, FitzGerald G, Guo Y, Jalaludin B, Tong S. Impact of heatwave on mortality under different heatwave definitions: A systematic review and meta-analysis. *Environ Int.* 2016;89-90:193-203.