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Original research

Geospatial patterns of excess mortality in Belgium: Insights from the first year of the COVID-19 pandemic

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ARTICLE INFO

Keywords: Belgium COVID-19 Excess mortality Spatio-temporal analysis

ABSTRACT

Objectives: Belgium experienced multiple COVID-19 waves that hit various groups in the population, which changed the mortality pattern compared to periods before the pandemic. In this study, we investigated the geographical excess mortality trend in Belgium during the first year of the COVID-19 pandemic.

Methods: We retrieved the number of deaths and population data in 2020 based on gender, age, and municipality of residence, and we made a comparison with the mortality data in 2017–2019 using a spatially discrete model.

Results: Excess mortality was significantly associated with age, gender, and COVID-19 incidence, with larger effects in the second half of 2020. Most municipalities had higher risks of mortality with a number of exceptions in the northeastern part of Belgium. Some discrepancies in excess mortality were observed between the north and south regions.

Conclusions: This study offers useful insight into excess mortality and will aid local and regional authorities in monitoring mortality trends.

1. Introduction

Four years have passed since the World Health Organization declared COVID-19 a pandemic (World Health Organization, 2020). Globally, there were more than 6.7 million new cases and 64,000 deaths reported between 16 January–12 February 2023, which correspond to a decrease of 92% and 47%, respectively, compared to the previous 28 days (World Health Organization, 2023). Despite this seemingly positive report, we need to be vigilant and revisit previous reports to anticipate changes in the future, which is relevant not only for the still ongoing pandemic but also as a component of pandemic preparedness.

Belgium experienced multiple COVID-19 waves that hit differently across groups in the population. The first wave in March–April 2020 hit hard within the elderly and nursing home population, while the next wave in the second half of 2020 hit the younger population harder (Sciensano, 2022). Consequently, these waves also changed the mortality pattern in 2020. Belgium had a COVID-19-reported mortality rate of 1675.37 per million inhabitants in 2020, which was one of the most severe worldwide (Our World in Data, 2020). This should however be seen against the background of very extensive reporting in the country, with different reporting practices in some countries (Aron et al., 2020; Verbeeck et al., 2021). Considering different preventive

Many studies have reported the estimation of excess mortality during the COVID-19 crisis in different settings (Wong et al., 2023; Ceccarelli et al., 2022; Nucci et al., 2021; Woolf et al., 2021), including Belgium (Molenberghs et al., 2022; Meurisse et al., 2022). The Bayesian spatio-temporal analysis is one of the many methods used to assess excess mortality patterns within a certain area (Blangiardo et al., 2020; Konstantinoudis et al., 2022; Saavedra et al., 2021). To date, no such studies have been conducted that account for the spatial association among different areas in Belgium. This study aimed to examine excess mortality trends in Belgium during the first year of the COVID-19 pandemic. The excess mortality trend was evaluated in association with gender, age group, and COVID-19 incidence. We used spatial conditional auto-regressive models to account for spatial association among municipalities.

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measures and testing strategies during the pandemic, this number was not suitable to compare different countries in this period (Molenberghs et al., 2022). Therefore, we need to consider the excess mortality, i.e., the mortality above and beyond deaths that would have occurred in normal, pre-pandemic conditions (Checchi and Roberts, 2005), and hence likely attributable to the crisis.

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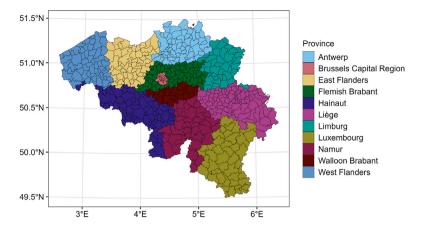


Fig. 1. Border of municipalities and provinces in Belgium.

2. Materials and methods

2.1. Data

We retrieved the number of deaths and population data in 2020 based on gender, age, and municipality of residence from StatBel, the Belgian national statistics authority (https://statbel.fgov.be/en/). For comparison's sake, we used the mortality data from 2017–2019 as a base of reference to provide adequate comparison while avoiding considerable changes in the population characteristics. We also retrieved data on COVID-19 cases per gender, age, and municipality of residence from Sciensano, the Belgian Institute for Public Health (https://www.sciensano.be/en), between 1 January-31 December 2020. The map used to present our results was modified from the statistical sector map made available online by Statbel (2020).

2.2. Statistical analysis

For the exploratory data analysis, we aggregated the data based on five age groups: <25 years, 25–44 years, 45–64 years, 65–84 years, and ≥85 years, respectively, as well as male or female gender. Considering two distinct COVID-19 waves that hit Belgium in 2020, the data were divided in two separate time intervals: 1 January–30 June 2020 and 1 July–31 December 2020. We explored the mortality trend among different age groups and gender within these two intervals.

We further calculated the standardized mortality ratio (SMR) and its 95% confidence interval using the Delta method to approximate probability distribution for a function of an asymptotically normal estimator (Liu, 2012). We assume that the logarithm of SMR ($\log \theta_i$) could be approximated by a normal distribution with $\mathrm{Var}(\log \theta_i) = \frac{1}{\theta_i^2} \mathrm{Var}(\theta_i) = \frac{1}{Y_i}$. Here, Y_i denotes the observed mortality in a certain period for each age group and gender. With a back-transformation, the 95% confidence interval for θ_i is further given by $\left[\theta_i \exp(-Z_{1-\frac{\alpha}{2}} \frac{1}{\sqrt{Y_i}}); \theta_i \exp(Z_{1-\frac{\alpha}{2}} \frac{1}{\sqrt{Y_i}})\right]$. Belgium consists of 581 municipalities within 10 different provinces

Belgium consists of 581 municipalities within 10 different provinces and one capital region as shown in Fig. 1. A spatially discrete geostatistical model was fitted to the mortality data originating from the two time intervals. It should be noted that based on the exploratory data analysis, we found a different mortality pattern in the age groups younger than 45 years. To prevent any misinterpretation of the results, we excluded the younger age groups from the following spatial analysis.

For each municipality i in each time interval, O_{ijk} denotes the number of deaths in municipality i, for age group j=1,2,3 corresponding to age groups 45–64 years, 65–84 years, and ≥ 85 years, respectively, with gender k= male, female. E_{ijk} represents the average expected mortality based on the mortality rate over the years 2017–2019 per

municipality, age group, and gender. We assumed a Poisson regression model for O_{ijk} given by:

$$O_{ijk}|\theta_{ijk} \sim \text{Poisson}(E_{ijk}\theta_{ijk}),$$
 (1)

with θ_{ijk} the relative risks of mortality in 2020 in municipality i, for age group j, and gender k, as compared to the pre-pandemic reference period 2017–2019, which is modeled on the logarithmic scale by way of the linear predictor:

$$\eta_{ijk} = \log(\theta_{ijk}) = \alpha + \beta_{1j} + \beta_{2k} + \beta_3 \log(\text{covir})_{ijk} + \nu_i + \nu_i, \tag{2}$$

with parameters β_{1j} and β_{2k} representing the effect of age and gender groups. Considering the large heterogeneity in COVID-19 incidence per age group and gender, we used the logarithmic scale of COVID-19 incidence rate, denoted as $log(covir)_{ijk}$, as a covariate in the model.

We used the Besag, York, and Mollié (BYM) model (Besag et al., 1991) to account for spatial heterogeneity. This model consists of two random effects: a spatially-unstructured effect v_i that follows an independent Gaussian distribution with mean 0 and variance σ_v^2 , and a spatially-structured effect v_i conditional on all shared boundaries v_j for $j \neq i$, given by:

$$v_i | v_{-i} \sim N\left(\bar{v}_i, \sigma_i^2\right)$$

$$\bar{v}_i = \frac{1}{|\mathcal{N}_i|} \sum_{j=1}^n c_{ij} v_j,$$

$$\sigma_i^2 = \frac{\sigma_v^2}{|\mathcal{N}_i|},$$
(3)

where the weights c_{ij} are defined as 1 if areas i and j are adjacent and 0 otherwise (queen's adjacency); and $|\mathcal{N}_i|$ denotes the number of neighbors of area i. Of note, the inclusion of random effects automatically ensures that the model can handle overdispersion. To compare the variability explained by the spatially structured random effect, we scaled the precision matrix as suggested by Sørbye and Rue (2014).

To assess unusual elevations of mortality risks, we calculated the exceedance probability defined as the proportion of the relative risk's posterior probability that exceeds a given threshold value. The probability can be calculated using the marginal posterior distribution of θ_{ijk} . In this study, we used a threshold relative risks of 1.2.

The analysis was performed in R 4.3.1 (R Core Team, 2023), through the package R-INLA (Lindgren and Rue, 2015). In a Bayesian framework, the prior plays a crucial role. Therefore, we compared the default prior in our proposed model with a penalized complexity (PC) prior as proposed by Simpson et al. (2017), which is defined as:

$$\pi(\tau) = \frac{\lambda}{2} \tau^{-3/2} \exp(-\lambda \tau^{-1/2}), \tau > 0, \lambda > 0 \tag{4}$$

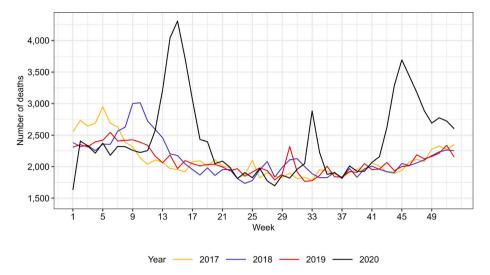


Fig. 2. All-cause mortality in 2017-2020.

with $\lambda = -\log(a)/U$. A value of one was considered a reasonable upper bound for the marginal standard deviation U with weight a = 1. The prior for τ_v and τ_v is then expressed as $P(\frac{1}{\sqrt{\tau}} > 1) = 0.1$.

3. Results

3.1. Mortality trend in Belgium

A total of 455,858 deaths was reported between 2017–2020, with 109,273 deaths in 2017, 110,339 deaths in 2018, 108,431 deaths in 2019, and 127,815 deaths in 2020. The weekly number of deaths showed a relatively stable trend between 2017–2019 with higher numbers of deaths reported between weeks 1–8 in 2017 and weeks 8–14 in 2018 (Fig. 2). This trend changed completely in 2020 when a considerable increase in mortality was reported in weeks 11–20. Smaller peaks could be observed in weeks 32–34 and then again a considerable peak (less high but broader) in weeks 41–52.

We further calculated the standardized mortality ratio, defined as the number of deaths in 2020 divided by the average number of deaths in 2017–2019, stratified by age group and gender within a period of six months as shown in Table 1. The standardized mortality ratios in age groups younger than 45 years were fairly close to or even lower than one, which means that the mortality in these age groups was lower compared to the pre-pandemic period. For this reason, we excluded the younger age group from our subsequent spatio-temporal analysis.

3.2. Effect of age group, gender, and COVID-19 incidences

The prior sensitivity analysis showed no considerable changes in the effect of the linear covariates as well as the posterior density of each random effect (see Table S1 in the Supplementary Materials). However, we observed an improvement in the variability explained by the spatially structured random effect using PC prior. For this reason, we presented the following results based on this model.

The multiplicative effects of gender, age group, and COVID-19 incidences on the relative risks of mortality in 2020 as compared to the pre-pandemic period were estimated by $\exp(\beta_{1j})$, $\exp(\beta_{2k})$, and $\exp(\beta_3)$, respectively (Fig. 3). We observed that older age groups (age groups 65–84 years and \geq 85 years) and COVID-19 incidence were significantly associated with increased relative risks of mortality in 2020 while being female was associated with lower risks. These associations were more pronounced in the second half of 2020.

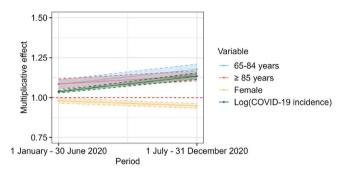


Fig. 3. Effects of the linear covariates.

3.3. Spatial effects

The map of posterior relative risks per age group, gender, and municipality is shown in Fig. 4. The relative risks of mortality were higher compared to the identical time interval in 2017–2019 for all age groups, particularly in the second half of 2020. Some exceptions could be observed in the northeastern part of Belgium where we found lower relative risks in age groups 65–84 years and \geq 85 years between 1 July–31 December 2020 compared to 1 January–30 June 2020.

Fig. 5 shows the exceedance probability with a threshold relative risk of 1.2. The exceedance probabilities were clearly higher in the oldest age groups for most municipalities. However, we also found a distinct change in the municipalities with exceedance probabilities higher than 80% in both time intervals. For age groups 65–84 years and \geq 85 years, higher exceedance probabilities were observed in the northeastern and eastern municipalities and, to some extent, in municipalities in the capital region and some larger cities in the western part of Belgium in the first half of 2020. The pattern changed in the second half of 2020, where higher exceedance probabilities could be observed more in the northern, western, and southern parts of Belgium.

4. Discussion

In this study, we found considerable excess mortality in Belgium during the first year of the pandemic. Before the pandemic, we could observe higher mortality in the first months of 2017 and 2018, which might be attributed to the influenza virus and/or cold weather (Vestergaard et al., 2017). However, it is clear that the mortality in the first half of 2020 exceeded this. We could see smaller peaks in the second half of 2017 until 2019 (between weeks 24–32), which might

Table 1Standardized mortality ratio per age group and gender.

Period	Age group	Gender	Average mortality pre-pandemic	Mortality in 2020	SMR (95% CI)
1 January–30 June	<25 years	Male	302.33	239	0.79 (0.70,0.90)
		Female	188	158	0.84 (0.72,0.98)
	25-44 years	Male	720.67	737	1.02 (0.95,1.10)
		Female	379.67	373	0.98 (0.89,1.09)
	45–64 years	Male	4258.33	4,425	1.04 (1.01,1.07)
		Female	2602.33	2,605	1.00 (0.96,1.04)
	65–84 years	Male	13,628.33	15,352	1.13 (1.11,1.14)
		Female	10,552	11,746	1.11 (1.09,1.13)
	≥85 years	Male	68,968.33	10,526	1.17 (1.15,1.20)
		Female	15,631	18,229	1.17 (1.15,1.18)
1 July–31 December	<25 years	Male	317.67	219	0.69 (0.60,0.79)
		Female	194.33	142	0.73 (0.62,0.86)
	25-44 years	Male	721.33	738	1.02 (0.95,1.10)
		Female	367.33	372	1.01 (0.91,1.12)
	45–64 years	Male	4036.33	4,486	1.11 (1.08,1.14)
		Female	2548.67	2,601	1.02 (0.98,1.06)
	65-84 years	Male	12,613.33	15,314	1.21 (1.20,1.23)
	·	Female	9633	11,473	1.19 (1.17,1.21)
	≥85 years	Male	7649.67	10,343	1.30 (1.28,1.33)
		Female	13,735	17,124	1.25 (1.23,1.27)

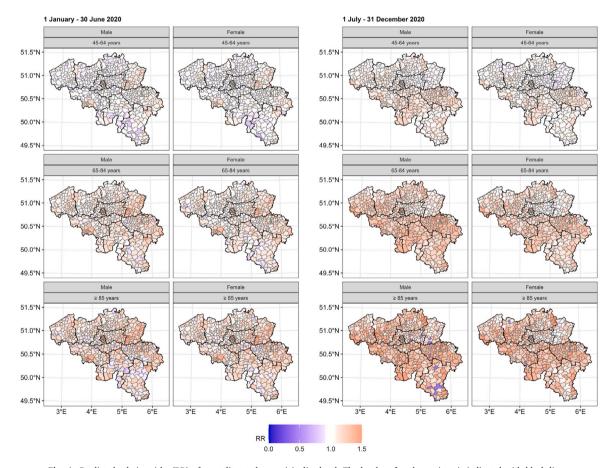


Fig. 4. Predicted relative risks (RR) of mortality at the municipality level. The border of each province is indicated with black lines.

be attributed to heatwaves and surface ozone pollution (Bustos Sierra and Asikainen, 2018; Bustos Sierra et al., 2019, 2022). Again, the mortality in the second half of 2020 exceeded that of the previous years, especially from week 40 onward. These patterns corroborate the report of the European monitoring of excess mortality for public health action (EuroMOMO) network that there was excess mortality in the period March–April 2020 which mainly affected the older age group (Vestergaard et al., 2020). Similar patterns of excess mortality during the first COVID-19 wave were reported in Israel (Peretz et al.,

2022), the United States (Rossen et al., 2020), China (Li et al., 2021), and many other countries (Islam et al., 2021).

We found an association between gender, age group, and COVID-19 incidence and excess mortality in Belgium. We found lower risks of excess mortality among females. A study in Malaysia reported higher excess mortality among males in the years 2020–2021 (Jayaraj et al., 2023). Similar results were also reported in Minnesota, although men already had higher mortality rates than women before the pandemic (McCoy et al., 2022). Higher excess mortality among males

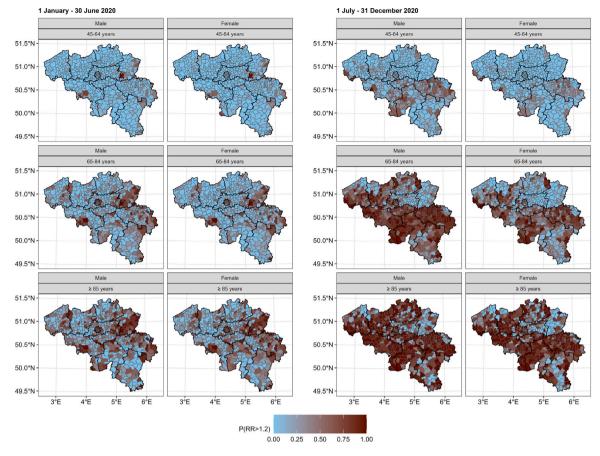


Fig. 5. Exceedance probability at the municipality level. RR = relative risks. The border of each province is indicated with black lines.

has been observed in many European countries before and during the pandemic, which arguably is a general sex-specific phenomenon rather than specific to COVID-19 (Nielsen et al., 2021). The exact underlying mechanism is still under investigation, although results are starting to emerge (Haitao et al., 2020). However, we need to consider differences in biological properties between males and females (Klein and Flanagan, 2016), the presence of underlying conditions that are more prevalent in men, e.g. cardiovascular or metabolic diseases (Di Angelantonio et al., 2015), or other health-related behaviors (D'Angelo et al., 2022; Thompson et al., 2016) that could have an impact on health conditions and eventually, death.

In the younger age groups, we found lower or similar mortality in 2020 compared to the pre-pandemic period as shown in Table 1. In contrast to these results, some studies found higher excess mortality in younger age groups due to different population structures (Fantin et al., 2023) and other contributing factors such as acute substance poisoning (Beesoon et al., 2022). In our study, the effect of age on excess mortality became notably pronounced starting from the age group of 45 years old. This is logical since the Belgian population is dominated by older age groups. On top of this, excess mortality was also reported to be higher in people who reside in nursing homes in the pandemic period (Molenberghs et al., 2022; Torres et al., 2023; Basso et al., 2023). In the nursing home setting, additional factors such as medical conditions or treatments administered to the residents (Vila-Corcoles et al., 2021), as well as the quality of care delivered by the facility (Cronin and Evans, 2022), may also influence the mortality.

COVID-19 incidence was significantly associated with an increased risk of excess mortality in 2020. The association was more pronounced between 1 July–31 December 2020 following the relaxation in travel (Hodcroft et al., 2021) and a substantial increase in COVID-19 transmission among the younger population (Boehmer et al., 2020). This was also reflected in the spatial analysis of relative risks (Fig. 4) and

exceedance probabilities (Fig. 5), which showed higher values in the second half of 2020.

The spatial analysis also showed higher relative risks and exceedance probabilities in age groups 65 years or older. It should be noted that a distinct pattern could be observed in the northeastern part of Belgium (i.e., Limburg province) where the relative risks and exceedance probability were higher in the first half of 2020. This area was greatly affected by the first wave of COVID-19, yet it experienced comparatively milder incidences during the subsequent Fall wave of 2020 (Sciensano, 2022). Next to the high COVID-19 incidences in the first wave, Limburg province also had the highest COVID-19-related mortality among nursing home residents in this period (Sciensano, 2023). On the other hand, some provinces such as Liège, Luxembourg, and Hainaut had relatively lower incidences in the first half of 2020, followed by a surge during the second wave, leading to escalated relative risks and exceedance probabilities for mortality in these areas. The Brussels Capital Region showed consistently high relative risk and exceedance probability throughout both waves, which was an indication of persistent high COVID-19 incidences over the year 2020.

The introduction of spatial random effects in regression models has the potential to induce changes in the fixed effects, a phenomenon commonly referred to as spatial confounding (Reich et al., 2006). To assess this potential bias, we compared the results of models with and without the spatial effects. As shown in Table S1, we found only minimal changes in the fixed effect estimates after including the spatial random effects. Therefore, there is no substantial indication of spatial confounding within the scope of our analysis.

The strength of our study lies in the extensive dataset at our disposal, encompassing mortality records by age, gender, and residential location over multiple years. However, it should be noted that analyzing data at the municipality level could minimize differences that might be observed at a smaller area level. On top of this, the completeness of

mortality reporting warrants consideration, especially during the peak periods in 2020, when data collection capabilities may have reached their threshold. Third, COVID-19 was not yet recorded as a cause of death at the time of analysis, despite the implementation of an efficient ad-hoc reporting system. It will be interesting to investigate trends within this specific group when the data are available. Last but not least, the study period was prior to the vaccination campaign which started in late December 2020. Given the strong influence of vaccination status on COVID-19 transmission and its potential to mitigate disease severity, eventually, it is important that future analyses incorporate vaccination data to enhance the accuracy of excess mortality modeling.

5. Conclusion

To conclude, we observed substantial excess mortality in Belgium during the first year of the COVID-19 pandemic. The excess mortality is influenced by age, gender, and COVID-19 incidences within this period. Our spatial analysis provides extra insight into the distribution of excess mortality at the municipality and provincial levels. This is useful for local and regional authorities when they need to monitor mortality trends in a relatively simple manner.

CRediT authorship contribution statement

Yessika Adelwin Natalia: Formal analysis, Methodology, Software, Visualization, Writing – original draft. Geert Molenberghs: Conceptualization, Supervision, Writing – review & editing. Christel Faes: Conceptualization, Methodology, Supervision, Writing – review & editing. Thomas Neyens: Data curation, Investigation, Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

Acknowledgments

The authors thank Patrick Lusyne and his colleagues at StatBel for providing daily mortality data.

Funding

T.N. gratefully acknowledges funding by the Internal Funds KU Leuven, Belgium (project number 3M190682) and the Fund for Scientific Research – Flanders, Belgium (grant number G0A4121N). C.F. acknowledges support from the European Union's Horizon 2020 – project EpiPose (Grant agreement number 101003688) and European Union's Horizon Europe – project ESCAPE (Grant agreement number 101095619). Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

Ethical approval statement

The authors do not have permission to share data.

Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.sste.2024.100660.

References

- Aron, J., Muellbauer, J., Giattino, C., et al., 2020. A pandemic primer on excess mortality statistics and their comparability across countries. https://ourworldindata.org/covid-excess-mortality. (Accessed 22 March 2023).
- Basso, C., Barbiellini Amidei, C., Casotto, V., et al., 2023. Veneto region dementiarelated mortality during the COVID-19 pandemic: multiple causes of death and time series analysis. Eur. J. Public Health http://dx.doi.org/10.1093/eurpub/ckad005.
- Beesoon, S., Bakal, J.A., Youngson, E., et al., 2022. Excess deaths during the COVID-19 pandemic in Alberta, Canada. IJID Reg. 5, 62–67. http://dx.doi.org/10.1016/j.iiregi.2022.08.011.
- Besag, J., York, J., Mollié, A., 1991. Bayesian image restoration, with two applications in spatial statistics. Ann. Inst. Statist. Math. 43, 1–20. http://dx.doi.org/10.1007/ BF00116466
- Blangiardo, M., Cameletti, M., Pirani, M., et al., 2020. Estimating weekly excess mortality at sub-national level in Italy during the COVID-19 pandemic. PLoS One 15, e0240286. http://dx.doi.org/10.1371/journal.pone.0240286.
- Boehmer, T.K., DeVies, J., Caruso, E., et al., 2020. Changing age distribution of the COVID-19 pandemic United States, May-August 2020. MMWR. Morb. Mortal. Wkly Rep. 69, 1404–1409. http://dx.doi.org/10.15585/mmwr.mm6939e1.
- Bustos Sierra, N., Asikainen, T., 2018. Rapport over de surveillance van de mortaliteit door alle oorzaken in België in de zomer van 2017. https://epistat.sciensano.be/docs/momo/2017_Rapport_surveillance_van_de_mortaliteit_zomer_Belgie.pdf. (Accessed 1 March 2023).
- Bustos Sierra, N., Asikainen, T., Bossuyt, N., et al., 2019. Surveillance van de mortaliteit door alle oorzaken in België, Vlaanderen, Wallonië en Brussel tijdens de zomer van 2018. https://epistat.sciensano.be/docs/momo/Be-MOMO%20summer% 202018%20report_NL.pdf. (Accessed 1 March 2023).
- Bustos Sierra, N., Fierens, S., Bossuyt, N., et al., 2022. Surveillance van de mortaliteit door alle oorzaken in België, Vlaanderen, Wallonië en Brussel tijdens de zomer van 2019. https://epistat.sciensano.be/docs/momo/Be-MOMO-zomer%20rapport% 202019-NL.pdf. (Accessed 1 March 2023).
- Ceccarelli, E., Dorrucci, M., Minelli, G., et al., 2022. Assessing COVID-19-related excess mortality using multiple approaches-Italy 2020–2021. Int. J. Environ. Res. Public Health 19. http://dx.doi.org/10.3390/ijerph192416998.
- Checchi, F., Roberts, L., 2005. Interpreting and using mortality data in humanitarian emergencies. https://odihpn.org/wp-content/uploads/2005/09/networkpaper052.pdf. (Accessed 22 March 2023).
- Cronin, C.J., Evans, W.N., 2022. Nursing home quality, COVID-19 deaths, and excess mortality. J. Health Econ. 82, 102592. http://dx.doi.org/10.1016/j.jhealeco.2022. 102592.
- D'Angelo, S., Bevilacqua, G., Bloom, I., et al., 2022. Predictors and consequences of not seeking healthcare during the COVID-19 pandemic: Findings from the HEAF cohort. Int. J. Environ. Res. Public Health 19. http://dx.doi.org/10.3390/ijerph192013271.
- Di Angelantonio, E., Kaptoge, S., Wormser, D., et al., 2015. Association of cardiometabolic multimorbidity with mortality. JAMA 314, 52–60. http://dx.doi.org/ 10.1001/jama.2015.7008.
- Fantin, R., Barboza-Solís, C., Hildesheim, A., et al., 2023. Excess mortality from COVID-19 in Costa Rica: A registry based study using Poisson regression. Lancet Reg. Health Am. 20, 100451. http://dx.doi.org/10.1016/j.lana.2023.100451.2023.
- Haitao, T., Vermunt, J.V., Abeykoon, J., et al., 2020. COVID-19 and sex differences: mechanisms and biomarkers. Mayo Clin. Proc. 95, 2189–2203. http://dx.doi.org/ 10.1016/j.mayocp.2020.07.024.
- Hodcroft, E.B., Zuber, M., Nadeau, S., et al., 2021. Spread of a SARS-CoV-2 variant through Europe in the summer of 2020. Nature 595, 707–712. http://dx.doi.org/10.1038/s41586-021-03677-y.
- Islam, N., Shkolnikov, V.M., Acosta, R.J., et al., 2021. Excess deaths associated with COVID-19 pandemic in 2020: age and sex disaggregated time series analysis in 29 high income countries. Bmj 373, n1137. http://dx.doi.org/10.1136/bmj.n1137.
- Jayaraj, V.J., Chong, D.W., Wan, K.S., et al., 2023. Estimating excess mortalities due to the COVID-19 pandemic in Malaysia between January 2020 and September 2021. Sci. Rep. 13, 86. http://dx.doi.org/10.1038/s41598-022-26927-z.
- Klein, S.L., Flanagan, K.L., 2016. Sex differences in immune responses. Nat. Rev. Immunol. 16, 626–638. http://dx.doi.org/10.1038/nri.2016.90.
- Konstantinoudis, G., Cameletti, M., Gómez-Rubio, V., et al., 2022. Regional excess mortality during 2020 the COVID-19 pandemic in five European countries. Nature Commun. 13, 482. http://dx.doi.org/10.1038/s41467-022-28157-3.
- Li, L., Hang, D., Dong, H., et al., 2021. Temporal dynamic in the impact of COVID-19 outbreak on cause-specific mortality in Guangzhou, China. BMC Public Health 21, 883. http://dx.doi.org/10.1186/s12889-021-10771-3.
- Lindgren, F., Rue, H., 2015. Bayesian spatial modelling with R-INLA. J. Stat. Softw. 63, 1–25, URL: http://www.jstatsoft.org/v63/i19/.

- Liu, X., 2012. Appendix A: The delta method. In: Liu, X. (Ed.), Survival Analysis. Wiley Online Books.
- McCoy, R.G., Campbell, R.L., Mullan, A.F., et al., 2022. Changes in all-cause and cause-specific mortality during the first year of the COVID-19 pandemic in Minnesota: Population-based study. BMC Public Health 22, 2291. http://dx.doi.org/10.1186/s12889-022-14743-z.
- Meurisse, M., Lajot, A., Devleesschauwer, B., et al., 2022. The association between area deprivation and COVID-19 incidence: A municipality-level spatio-temporal study in Belgium 2020–2021. Arch Public Health 80, 109. http://dx.doi.org/10.1186/ s13690-022-00856-9.
- Molenberghs, G., Faes, C., Verbeeck, J., et al., 2022. COVID-19 mortality, excess mortality, deaths per million and infection fatality ratio Belgium, 9 March 2020 to 28 June 2020. Eur. Surveill. 27, http://dx.doi.org/10.2807/1560-7917.Es.2022. 27.7.2002060.
- Nielsen, J., Nørgaard, S.K., Lanzieri, G., et al., 2021. Sex-differences in COVID-19 associated excess mortality is not exceptional for the COVID-19 pandemic. Sci. Rep. 11, 20815. http://dx.doi.org/10.1038/s41598-021-00213-w.
- Nucci, L.B., Enes, C.C., Ferraz, F.R., et al., 2021. Excess mortality associated with COVID-19 in Brazil: 2020–2021. J. Public Health (Oxf) http://dx.doi.org/10.1093/ pubmed/fdab398.
- Our World in Data, 2020. COVID-19 data explorer. https://ourworldindata.org/covid-deaths. (Accessed 16 February 2023).
- Peretz, C., Rotem, N., Keinan-Boker, L., et al., 2022. Excess mortality in Israel associated with COVID-19 in 2020–2021 by age group and with estimates based on daily mortality patterns in 2000–2019. Int. J. Epidemiol. 51, 727–736. http://dx.doi. org/10.1093/jie/dyac047.
- R Core Team, 2023. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, URL: https://www.R-project.org/.
- Reich, B.J., Hodges, J.S., Zadnik, V., 2006. Effects of residual smoothing on the posterior of the fixed effects in disease-mapping models. Biometrics 62, 1197–1206. http://dx.doi.org/10.1111/j.1541-0420.2006.00617.x.
- Rossen, L.M., Branum, A.M., Ahmad, F.B., et al., 2020. Excess deaths associated with COVID-19, by age and race and ethnicity United States, January 26-October 3 2020. MMWR Morb. Mortal. Wkly. Rep. 69, 1522–1527. http://dx.doi.org/10. 15585/mmwr.mm6942e2.
- Saavedra, P., Santana, A., Bello, L., et al., 2021. A Bayesian spatio-temporal analysis of mortality rates in Spain: Application to the COVID-19 2020 outbreak. Popul. Health Metr. 19, 27. http://dx.doi.org/10.1186/s12963-021-00259-y.
- Sciensano, 2022. Belgium COVID-19 epidemiological situation. https://epistat.wiv-isp. be/covid/covid-19.html. (Accessed 16 February 2023).
- Sciensano, 2023. Epidemiology of COVID-19 mortality in Belgium from wave 1 to wave 7 (March 2020 11 September 2022). https://www.sciensano.be/en/biblio/epidemiology-covid-19-mortality-belgium-wave-1-wave-7-march-2020-11-september-2022. (Accessed 13 October 2023).

- Simpson, D., Rue, H., Riebler, A., et al., 2017. Penalising model component complexity: A principled, practical approach to constructing priors. Statist. Sci. 32, 1–28. http://dx.doi.org/10.1214/16-STS576.
- Sørbye, S.H., Rue, H., 2014. Scaling intrinsic Gaussian Markov random field priors in spatial modelling. Spatial Stat. 8, 39–51. http://dx.doi.org/10.1016/j.spasta.2013. 06.004.
- Statbel, 2020. Statistical sectors 2020. https://statbel.fgov.be/en/open-data/statistical-sectors-2020. (Accessed 18 January 2023).
- Thompson, A.E., Anisimowicz, Y., Miedema, B., et al., 2016. The influence of gender and other patient characteristics on health care-seeking behaviour: A qualicopc study. BMC Fam. Pract. 17, 38. http://dx.doi.org/10.1186/s12875-016-0440-0.
- Torres, M.J., Coste, J., Canouï-Poitrine, F., et al., 2023. Impact of the first COVID-19 pandemic wave on hospitalizations and deaths caused by geriatric syndromes in France: A nationwide study. J. Gerontol. A Biol. Sci. Med. Sci. http://dx.doi.org/10.1093/gerona/glad032.
- Verbeeck, J., Faes, C., Neyens, T., et al., 2021. A linear mixed model to estimate COVID-19-induced excess mortality. Biometrics 00, 1–9. http://dx.doi.org/10.1111/biom.
- Vestergaard, L.S., Nielsen, J., Krause, T.G., et al., 2017. Excess all-cause and influenza-attributable mortality in Europe, December 2016 to February 2017. Eurosurveillance 22, 30506. http://dx.doi.org/10.2807/1560-7917.ES.2017.22.14. 30506.
- Vestergaard, L.S., Nielsen, J., Richter, L., et al., 2020. Excess all-cause mortality during the COVID-19 pandemic in Europe - preliminary pooled estimates from the EuroMOMO network, March to April 2020. Eur. Surveill. 25. http://dx.doi.org/10. 2807/1560-7917.Es.2020.25.26.2001214.
- Vila-Corcoles, A., Satue-Gracia, E., Vila-Rovira, A., et al., 2021. COVID19-related and all-cause mortality risk among middle-aged and older adults across the first epidemic wave of SARS-COV-2 infection: A population-based cohort study in Southern Catalonia, Spain, march. BMC Public Health 21, 1795. http://dx.doi.org/ 10.1186/s12889-021-11879-2.
- Wong, M.K., Brooks, D.J., Ikejezie, J., et al., 2023. COVID-19 mortality and progress toward vaccinating older adults - World Health Organization, worldwide, 2020– 2022. MMWR Morb. Mortal. Wkly. Rep. 72, 113–118. http://dx.doi.org/10.15585/ mmwr.mm7205a1.
- Woolf, S.H., Chapman, D.A., Sabo, R.T., et al., 2021. Excess deaths from COVID-19 and other causes in the US, March 1 2020, to January 2 2021. Jama 325, 1786–1789. http://dx.doi.org/10.1001/jama.2021.5199.
- World Health Organization, 2020. Coronavirus disease (COVID-19) pandemic. https://www.who.int/emergencies/diseases/novel-coronavirus-2019. (Accessed 16 February 2023).
- World Health Organization, 2023. Coronavirus disease (COVID-19) weekly epidemiological update and weekly operational update. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports. (Accessed 16 February 2023).