

# BMJ Open Trend of pneumonia diagnosis in emergency departments as a COVID-19 surveillance system: a time series study

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## ABSTRACT

**Objective** In Italy, the first diagnosis of COVID-19 was confirmed on 20 February 2020 in the Lombardy region. Given the rapid spread of the infection in the population, it was suggested that in Europe, and specifically in Italy, the virus had already been present in the last months of 2019. In this paper, we aim to evaluate the hypothesis on the early presence of the virus in Italy by analysing data on trends of access to emergency departments (EDs) of subjects with a diagnosis of pneumonia during the 2015–2020 period.

**Design** Time series cohort study.

**Setting** We collected data on visits due to pneumonia between 1 October 2015 and 31 May 2020 in all EDs of the Agency for Health Protection of Milan (ATS of Milan). Trend in the winter of 2019–2020 was compared with those in the previous 4 years in order to identify unexpected signals potentially associated with the occurrence of the pandemic. Aggregated data were analysed using a Poisson regression model adjusted for seasonality and influenza outbreaks.

**Primary outcome measures** Daily pneumonia-related visits in EDs.

**Results** In the studied period, we observed 105 651 pneumonia-related ED visits. Compared with the expected, a lower occurrence was observed in January 2020, while an excess of pneumonia visits started in the province of Lodi on 21 February 2020, and almost 10 days later was observed in the remaining territory of the ATS of Milan. Overall, the peak in excess was found on 17 March 2020 (369 excess visits compared with previous years, 95% CI 353 to 383) and ended in May 2020, the administrative end of the Italian lockdown.

**Conclusions** An early warning system based on routinely collected administrative data could be a feasible and low-cost strategy to monitor the actual situation of the virus spread both at local and national levels.

## INTRODUCTION

China confirmed the first cases of COVID-19 in late December 2019. In Italy, the first diagnosis was confirmed on 20 February 2020 in Lombardy. Four days later, the rapid spread of the infection led to defining a ‘red zone’ (highest risk zone), the area most affected by the pandemic, with related rules limiting displacements and activities that involve gathering of people and travelling, as well

## Strengths and limitations of this study

- This is a large retrospective study conducted in the territory of the Agency for the Health Protection of Milan, which covers a total population of 3.48 million inhabitants.
- Evaluation of the early presence of COVID-19 was performed using long-term time series and Poisson regression models adjusted for seasonality and influenza epidemics.
- Available data do not allow differentiation of diagnoses of viral pneumonia versus other types of pneumonia, in particular due to potential misclassification of the International Classification of Diseases, Ninth Revision codes.
- We cannot exclude the possible presence of unmeasured variables that may affect the number of emergency department visits.

as introducing incentives to smart working wherever possible in Lombardy. The national lockdown was implemented on 8 March, with closure of all non-essential recreational and commercial activities, schools and universities and prohibition of travel across the country. On 21 March, all non-essential activities were closed nationally. A gradual easing of the restrictive measures began on 4 May, even if until 4 June rules on social distancing, obligation to use masks, travel limitations on the national territory, and closure of schools and other services for childhood remained in place.

To date, COVID-19 surveillance systems have relied only on testing and contact tracing, but these methods imply that the specific virus infection is already diagnosed in the population. In order to promptly implement preventive policies, we need methods that can detect the presence of the virus as early as possible. Recently, researchers have proposed several approaches to early recognition of a COVID-19 outbreak. These include wastewater-based epidemiology studies<sup>1–7</sup> and studies on digital data from Google, Twitter or social media apps in order to recognise

early traces of the virus in the population.<sup>8 9</sup> In March 2020, in order to justify the rapid spread of COVID-19 in Lombardy, it was suggested that in Europe, and specifically in Italy, the virus had already been present in the last months of 2019. The Italian Institute of Health (ISS) tested samples of wastewater from Milan and Turin and showed that genetic virus traces were already present in December.<sup>3 10</sup> In Spain, scientists found virus traces in wastewater collected in mid-January<sup>11</sup> and late February,<sup>5</sup> when evidence of a Spanish outbreak was only starting to circulate.

The major concern in timely detecting patients with COVID-19 is the similarity between influenza-like illness (ILI) and symptoms of COVID-19.<sup>12</sup> Common symptoms are fever, fatigue, cough, dyspnoea, sore throat and myalgia. On the other hand, ILI usually causes mild to severe illness, while COVID-19 may cause more serious conditions especially in the fragile population.<sup>12 13</sup> One of the most common complications is pneumonia, which in the case of influenza may appear as a primary complication or as secondary bacterial pneumonia.<sup>14</sup>

In this study we tested the hypothesis on the early presence of the virus in Italy, before the first diagnosed case, by using long-term time series extracted from the administrative health data of the Agency for Health Protection of Milan (ATS of Milan). The time series of visits to emergency departments (EDs) due to pneumonia in the winter of 2019–2020 were compared with those in the previous 4 years in order to assess unexpected signals potentially related to the occurrence of the pandemic. Most importantly, our aim is also to evaluate the role of this approach as a surveillance system capable of promptly detecting the initial signals of the epidemic outbreak so that important preventive public health measures can be defined early in the pandemic.

## METHODS

This is a retrospective study conducted in the territory of the ATS of Milan, which covers 193 municipalities in the Northern Italian region of Lombardy, with a total population of 3.48 million inhabitants. The study area includes the municipality of Codogno, where the first Italian COVID-19 case occurred. We collected visits due to pneumonia between 1 October 2015 and 31 May 2020 in all EDs of the ATS of Milan (all visits, from residents and from non-residents of the ATS of Milan). In order to evaluate the overall incidence in the population of the ATS of Milan, we also included visits that residents carried out to hospitals not located in the territory of the ATS of Milan.

We defined visits due to pneumonia according to the International Classification of Diseases, Ninth Revision (ICD-9)<sup>15</sup> as viral pneumonia (ICD-9 480), bacterial pneumonia (ICD-9 481–482), pneumonia due to other specified organism (ICD-9 483), pneumonia in infectious diseases classified elsewhere (ICD-9 484), bronchopneumonia organism unspecified (ICD-9 485), pneumonia organism unspecified (ICD-9 486), pneumonia in

influenza (ICD-9 487.0), unspecified alveolar and parietoalveolar pneumonopathy (ICD-9 516.9), acute respiratory failure (ICD-9 518.81), other pulmonary insufficiency not elsewhere classified (ICD-9 518.82) and congenital pneumonia (ICD-9 770.0). Aggregated daily data were collected using current ED databases. To evaluate the total burden of the epidemic in the territory, a patient visiting an ED on two different days was counted twice. No individual-level data were used and patients cannot be identified from aggregated data which do not contain low counts (ie, days with less than five visits). For this reason, and according to the Italian legislation, this study was not submitted for ethics approval.<sup>16</sup>

The number of COVID-19 cases by province of residence, as defined on 17 August 2020, was collected from the ATS of Milan through a web-based platform, specifically developed since the beginning of the outbreak, to trace positive and negative cases as well as related contacts. Prevalence was calculated as the number of cases over the number of residents on 1 January 2020 per 1000 inhabitants.<sup>17</sup>

## Patient and public involvement

Patients were not involved in this research.

## Statistical methods

Aggregated data on daily ED visits were analysed using a Poisson regression model adjusted for seasonality and influenza epidemics.<sup>18</sup> Seasonality was controlled for by including Fourier terms, a series of sine-cosine functions able to approximate periodicity.<sup>19 20</sup> Fourier terms specification does not depend on original data. They are particularly useful because they can be easily integrated in postsample forecasting equations.<sup>19</sup> Weekly data on ILI notifications were taken from the National Health Service Sentinel System (InfluNet).<sup>21</sup> Weekly incidence rates of ILI were expressed as the number of cases per 1000 inhabitants per week. The model was specified as the following:

$$\ln(\lambda_i) = \beta_0 + \beta_1 \times \sin \theta_i + \beta_2 \times \cos \theta_i + \beta_3 \times \text{ILI}_i$$

where  $\lambda_i$  is the expected value of the Poisson variable  $Y_i$  (the number of visits on day  $i$ ),  $\sin \theta_i$  and  $\cos \theta_i$  are the Fourier terms where  $\theta_i = 2 \times \pi \times i/365$ , and  $\text{ILI}_i$  is the weekly incidence rate of ILI for day  $i$ . The ILI rate was provided on a weekly basis; thus, in the model above,  $\text{ILI}_i$  is repeated seven times, for each day of the week.

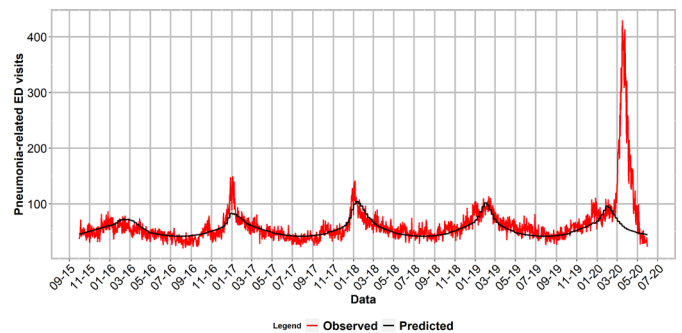
Data sets were divided into training (data from 1 October 2015 to 30 September 2019) and validation (data from 1 October 2019 to 31 May 2020) sets. We first estimated the parameters in the training set and then predicted the outcome in the validation set. This projection represents a counterfactual situation where COVID-19 had not happened. The number of excess visits was calculated as the difference between observed and predicted values between 1 October 2019 and 31 May 2020. We calculated 95% prediction interval (PI) by sampling from the uncertainty distributions of the

estimated model parameters.<sup>18 22</sup> Results were displayed overall and by province of residence: in the city of Milan, in the province of Milan, in the province of Lodi (the province of the first COVID-19 case) and outside the ATS of Milan. In order to evaluate pneumonia excess attributed to COVID-19 adjusting for natural fluctuations in the number of visits, we performed a sensitivity analysis dividing the data set into training (from 1 October 2015 to 30 September 2018), validation set 1 (from 1 October 2018 to 30 September 2019) and validation set 2 (from 1 October 2019 to 31 May 2020). We performed, on these three data sets, the same analyses described above and compared the pneumonia excess found in validation set 2 with those found in validation set 1 according to t-test statistics and number of statistically significant excesses.

All analyses were performed with R software (V.4.0.2; R Core Team, Vienna, Austria) and Fourier terms were calculated using the Fourier function in the R package forecast<sup>23</sup> after specifying the daily count as a time series with annual periodicity.

## RESULTS

Between 1 October 2015 and 31 May 2020 (amounting to 1704 days), we observed 105 651 pneumonia-related visits, of which 80 086 (76%) were in the training set and 25 565 (24%) were in the validation set. Influenza epidemics were stronger in the epidemic periods of 2015–2019 compared with 2019–2020, with a maximum ILI rate of 14.7 and 12.6 new cases per 1000 inhabitants per week, respectively. In the overall territory of the ATS of Milan we found a COVID-19 prevalence of 14.6 cases per 1000 inhabitants (table 1), similar to the city of Milan and to the province of Milan, but approximately half of that found in the province of Lodi, with 26.3 cases per 1000 inhabitants.



**Figure 1** Daily observed and predicted emergency department (ED) visits due to pneumonia between 1 October 2015 and 31 May 2020. Predictions were obtained by a Poisson regression model adjusted for seasonality and influenza epidemics. Time series in the overall territory of the Agency for Health Protection of Milan (ATS of Milan).

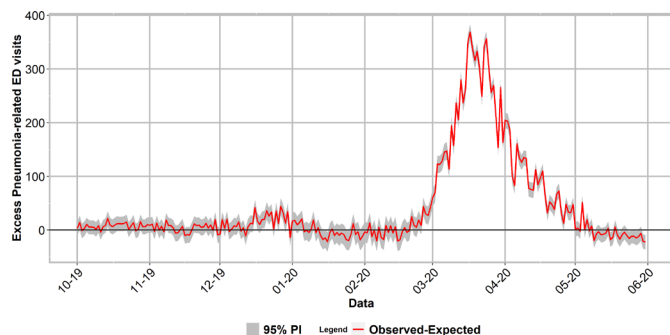
In figure 1 we present the daily observed and predicted ED visits due to pneumonia in the overall period and in the overall territory of the ATS of Milan (time series by province of residence can be found in online supplemental figure 1A–D). Daily visits showed a typical seasonal pattern over the years, well captured by seasonality and influenza epidemics (black line in figure 1). The demographic characteristics of patients by province of residence and period of comparison are described in table 1. Between 1 October 2015 and 31 May 2020, 38 972 (37%) pneumonia-related visits were from residents of the city of Milan, 48 678 (46%) from the province of Milan, 7609 (7%) from the province of Lodi and 10 392 (10%) from residents outside the territory of the ATS of Milan. Majority of visits were attributed to residents of Milan and the province of Milan, with daily time series (online supplemental figure 1A,B) resembling that of the overall territory of ATS (figure 1). Overall, excess pneumonia

**Table 1** Demographic characteristics of patients who visited the emergency departments of the ATS of Milan for pneumonia, by province of residence, between 1 October 2015 and 31 May 2020

	Overall territory	City of Milan	Province of Milan	Province of Lodi	Outside the ATS of Milan
	N=105 651	n=38 972 (37%)	n=48 678 (46%)	n=7609 (7%)	n=10 392 (10%)
Missing demographic information	16	6	5	–	5
Sex: male (%)	56 911 (54)	20 170 (52)	26 645 (55)	4178 (55)	5918 (57)
Age, mean (SD)	63 (28)	64 (29)	63 (27)	65 (25)	58 (27)
Age class (years) (%)					
<17	13 082 (12)	5234 (13)	6030 (12)	618 (8)	1200 (12)
17–40	6762 (6)	2225 (6)	2816 (6)	529 (7)	1192 (11)
40–70	27 590 (26)	8913 (23)	12 831 (26)	2301 (30)	3545 (34)
≥70	58 201 (56)	22 594 (58)	26 996 (56)	4161 (55)	4450 (43)
COVID-19 prevalence per 1000 inhabitants	14.6	13.2	13.1	26.3	–

ATS of Milan, Agency for Health Protection of Milan.





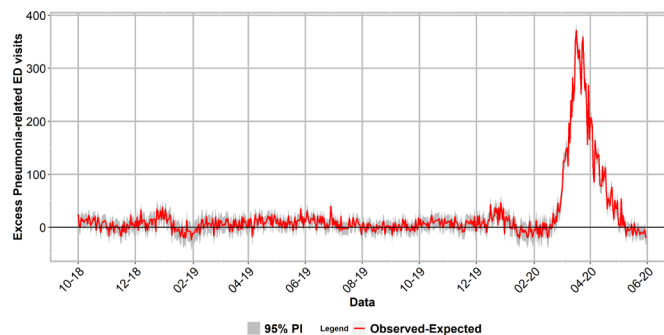
**Figure 2** Daily excess visits and 95% prediction interval (PI) between 1 October 2019 and 31 May 2020 in the territory of the Agency for Health Protection of Milan (ATS of Milan). ED, emergency department.

visits (figure 2) were statistically not different from the preceding years up to 15 December, and then significantly higher in the last 2 weeks of 2019. The number of ED visits due to pneumonia, excesses and PIs between 1 December 2019 and 31 May 2020 can be found in online supplemental data ('Results on validation set' columns). In January and in the beginning of February, pneumonia excesses were not statistically significant. The trend increased rapidly since 26 February, reaching a peak on 17 March 2020, with 369 additional ED visits compared with the expected (95% PI 353–383). The estimated excesses ended in May 2020 (the administrative end of the Italian lockdown). Early circulation of the virus was found in the province of Lodi, where the excesses started on 21 February 2020, while in the remaining territory of the ATS of Milan excesses started more than 10 days later, in March. Similar trends to those found for the overall territory of the ATS were found in the time series of Milan and the province of Milan (online supplemental figure 2A–D), with statistically significant pneumonia excesses in the last 2 weeks of December 2019.

The number of ED visits due to pneumonia, excesses and PIs in validation set 1 (on the subset from 1 December 2018 to 31 March 2019) and validation set 2 (on the subset from 1 December 2019 to 30 March 2020) can be found in online supplemental data ('Sensitivity Analysis Results' column). In late December 2018 we found similar excesses to those found in the same period of 2019 (figure 3). Comparing the months of December and January, we found no statistically significant differences between the two validation sets (t-test for mean difference,  $p=0.77$ ). However, in December 2019 and January 2020 there were 18 days with statistically significant pneumonia excesses (of which 5 consecutive days from 19 to 23 December 2019) compared with 11 days with statistically significant pneumonia excesses in December 2018 and January 2019.

## DISCUSSION

In this work, we evaluated whether the administrative health data of the ATS of Milan supported the hypothesis on the early presence of the virus in Italy, before the



**Figure 3** Daily excess visits and 95% prediction interval (PI) between 1 October 2018 and 31 May 2020 in the territory of the Agency for Health Protection of Milan (ATS of Milan): sensitivity analysis. ED, emergency department.

first COVID-19 case in Italy was actually diagnosed in the Lombardy region. Because some symptoms of COVID-19 and influenza are similar,<sup>12</sup> it has been suggested that influenza could mask early COVID-19 cases during the 2019–2020 season.<sup>24</sup>

Here we estimated the expected number of ED visits due to pneumonia by Poisson regression, including as predictors seasonality and influenza epidemics. Results showed a lack of excess in January 2020. The starting date of the excesses corresponded to what was already known on the territory: early circulation of the virus was found in the province of Lodi where the excess started on 21 February 2020, while the excess in the remaining territory of the ATS of Milan appeared with a delay of more than 10 days compared with the province of Lodi. Overall, the peak of excess was found on 17 March 2020. Accounting for a median incubation period of 5.1 days,<sup>25</sup> the hypothetical starting date of the epidemic in the territory of the ATS of Milan was on 16 February for the province of Lodi and on 25 February for the province of Milan.

Furthermore, we found excesses in late December 2019 that could be caused by other stressors than seasonality and influenza epidemics. However, sensitivity analysis showed similar excesses in December 2018, thus ascribing those found in December 2019 as not COVID-19-related. Further work needs to be done in order to explain the double peak found in December 2018 and 2019, while previous years were characterised by one higher peak only. On the other hand, in December 2019 and January 2020 we found a greater number of days with statistically significant excesses compared with the same period of the preceding year. This seems in line with the findings of December traces of COVID-19 in sewer water samples in Milan, as reported by the ISS.<sup>10</sup> However, further evidence has to be provided to strengthen the conclusion of an early circulation of the virus in December 2019, for example by testing those patients for the presence of SARS-CoV-2. In fact, pneumonia excesses were mostly found among residents of the province of Milan rather

than among residents of the province of Lodi, where the outbreak started in February 2020.

The city of Milan, considering the bulk of trade and human movements with China, the population density and the characteristics of urban transportation, would have been an ideal contender to be the first Italian area to be interested by the spread of the virus.

Instead, surprisingly, the city of Milan had a lower prevalence of PCR-positive cases from nasal swab and also a much lower general mortality than many adjacent areas.<sup>26</sup>

This could be explained by an early immunisation of residents in the province of Milan, which was indeed reached by the outbreak later than the province of Lodi. To date, the proportion of asymptomatic carriers is estimated around 15%,<sup>27 28</sup> but it may likely be underestimated and close to one-third of the total infected population.<sup>29</sup> On the other hand, after the first pandemic wave, studies in Europe found a low seroprevalence<sup>30</sup> (5% in Spain, 2.5% in Italy and 7.5% in Lombardy). It is hard to think that an early circulation in December, apparently related to a small excess of pneumonias, could produce immunisation of a significant proportion of the population.

A major limitation of this study is the possibility that unmeasured variables, other than seasonality and influenza epidemics, can affect the outcome, for example differences in the population structure that may modify the baseline time series. Another possible limitation is that this system is not able to differentiate the diagnosis of viral pneumonia from other diagnoses of pneumonia, in particular due to a potential misclassification of the ICD-9 codes. However, this information system based on routinely collected ED data can be a potential low-cost surveillance system for an early alert on the spread of the epidemic in the population, not only for COVID-19 but also for other respiratory pathogens. This would be critical for the early implementation of measures of prevention and containment, such as social distancing, by public health authorities and hospitals.

**Contributors** All authors have made substantial contributions to the conception and design of the work, interpretation of data, definition of methodology and revision of the paper. RM and AGR conceptualised the study and defined the methodology. RM analysed the data set. AD supervised the methodologies and revised the paper. AGR supervised and administered the project.

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**Patient consent for publication** Not required.

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information.

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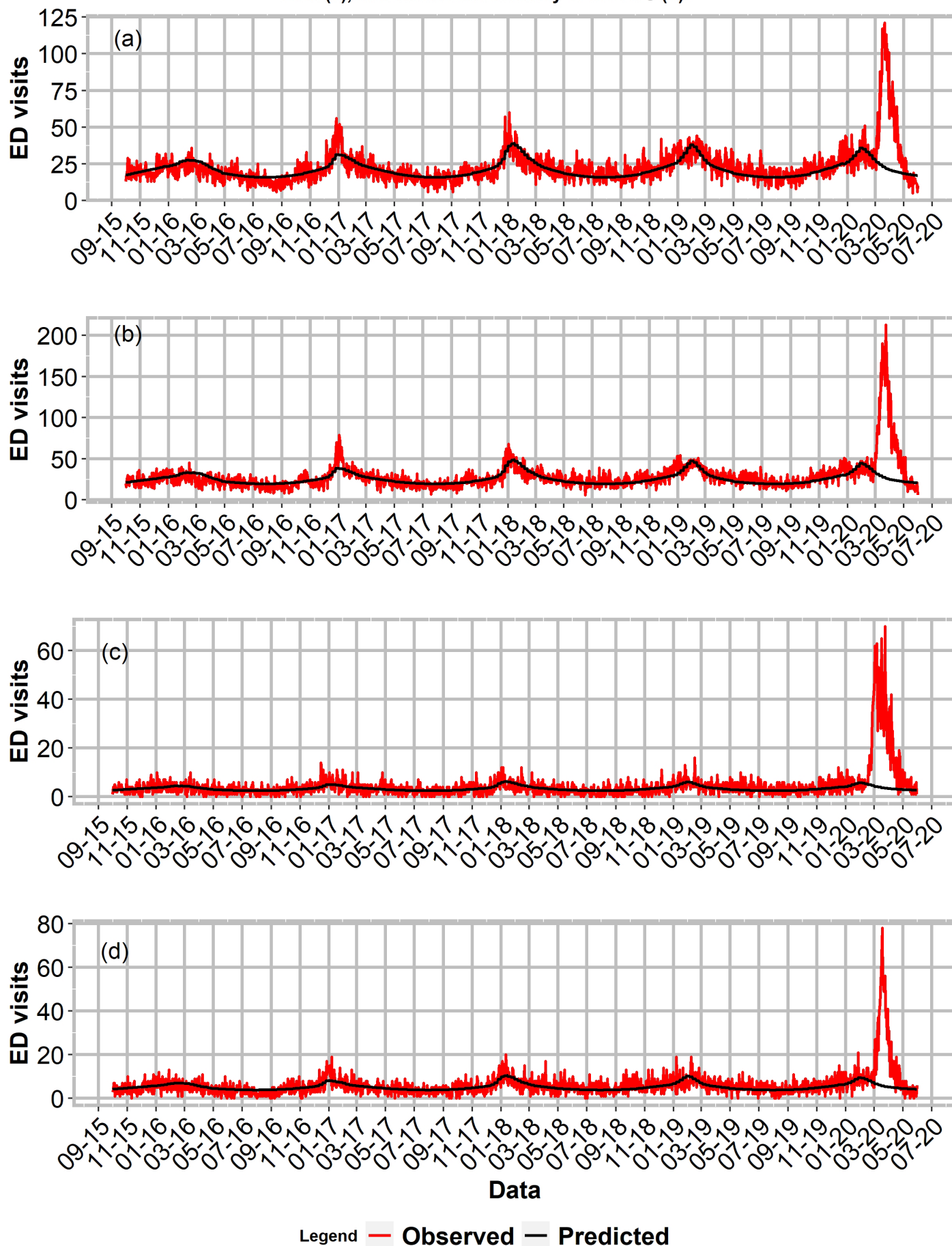
#### REFERENCES

- 1 Patel M, Chaubey AK, Pittman CU, *et al*. Coronavirus (SARS-CoV-2) in the environment: occurrence, persistence, analysis in aquatic systems and possible management. *Sci Total Environ* 2020;142698.
- 2 Jafferli MH, Khatami K, Atasoy M, *et al*. Benchmarking virus concentration methods for quantification of SARS-CoV-2 in RAW wastewater. *Sci Total Environ* 2021;755:142939.
- 3 La Rosa G, Mancini P, Bonanno Ferraro G, *et al*. SARS-CoV-2 has been circulating in northern Italy since December 2019: evidence from environmental monitoring. *Sci Total Environ* 2021;750:141711.
- 4 Mao K, Zhang H, Yang Z. An integrated biosensor system with mobile health and wastewater-based epidemiology (iBMW) for COVID-19 pandemic. *Biosens Bioelectron* 2020;169:112617.
- 5 Randazzo W, Cuevas-Ferrando E, Sanjuán R, *et al*. Metropolitan wastewater analysis for COVID-19 epidemiological surveillance. *Int J Hyg Environ Health* 2020;230:113621.
- 6 Street R, Malema S, Mahlangeni N, *et al*. Wastewater surveillance for Covid-19: an African perspective. *Sci Total Environ* 2020;743:140719.
- 7 Mohapatra S, Menon NG, Mohapatra G, *et al*. The novel SARS-CoV-2 pandemic: possible environmental transmission, detection, persistence and fate during wastewater and water treatment. *Sci Total Environ* 2020;142746.
- 8 Kogan NE, Clemente L, Liautaud P. An early warning approach to monitor COVID-19 activity with multiple digital traces in near real-time, 2020. Available: <http://arxiv.org/abs/2007.00756> [Accessed 3 Nov 2020].
- 9 Wang L, He W, Yu X, *et al*. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *J Infect* 2020;80:639–45.
- 10 La Rosa G, Iaconelli M, Mancini P, *et al*. First detection of SARS-CoV-2 in untreated wastewaters in Italy. *Sci Total Environ* 2020;736:139652.
- 11 Chavarria-Miró G, Anfruns-Estrada E, Guix S. Sentinel surveillance of SARS-CoV-2 in wastewater anticipates the occurrence of COVID-19 cases. *medRxiv* 2020.
- 12 CDC. Similarities and differences between flu and COVID-19. centers for disease control and prevention, 2020. Available: <https://www.cdc.gov/flu/symptoms/flu-vs-covid19.htm> [Accessed 10 Aug 2020].
- 13 Manzanares-Meza LD, Medina-Contreras O. SARS-CoV-2 and influenza: a comparative overview and treatment implications. *Bol Med Hosp Infant Mex* 2020;77:262–73.
- 14 Krammer F, Smith GJD, Fouchier RAM, *et al*. Influenza. *Nat Rev Dis Primers* 2018;4:1–21.
- 15 ICD - ICD-9-CM - International Classification of Diseases, Ninth Revision, Clinical Modification, 2019. Available: <https://www.cdc.gov/nchs/icd/icd9cm.htm> [Accessed 10 Mar 2020].
- 16 Italia. Provvedimento del Garante n. 2 del 16 giugno. *Codice di deontologia e di buona condotta per I trattamenti di dati personali per scopi statistici e scientifici*, 2004.
- 17 Demo-Geodemo. - Mappe, Popolazione, Statistiche Demografiche dell'ISTAT. Available: <http://demo.istat.it/> [Accessed 21 Jan 2019].
- 18 Weinberger DM, Chen J, Cohen T, *et al*. Estimation of excess deaths associated with the COVID-19 pandemic in the United States, March to May 2020. *JAMA Intern Med* 2020;180:1336.
- 19 Marcilio I, Hajat S, Gouveia N. Forecasting daily emergency department visits using calendar variables and ambient temperature readings. *Acad Emerg Med* 2013;20:769–77.
- 20 Hyndman RJ, Athanasopoulos G. *Forecasting: principles and practice*. OTexts, 2018.



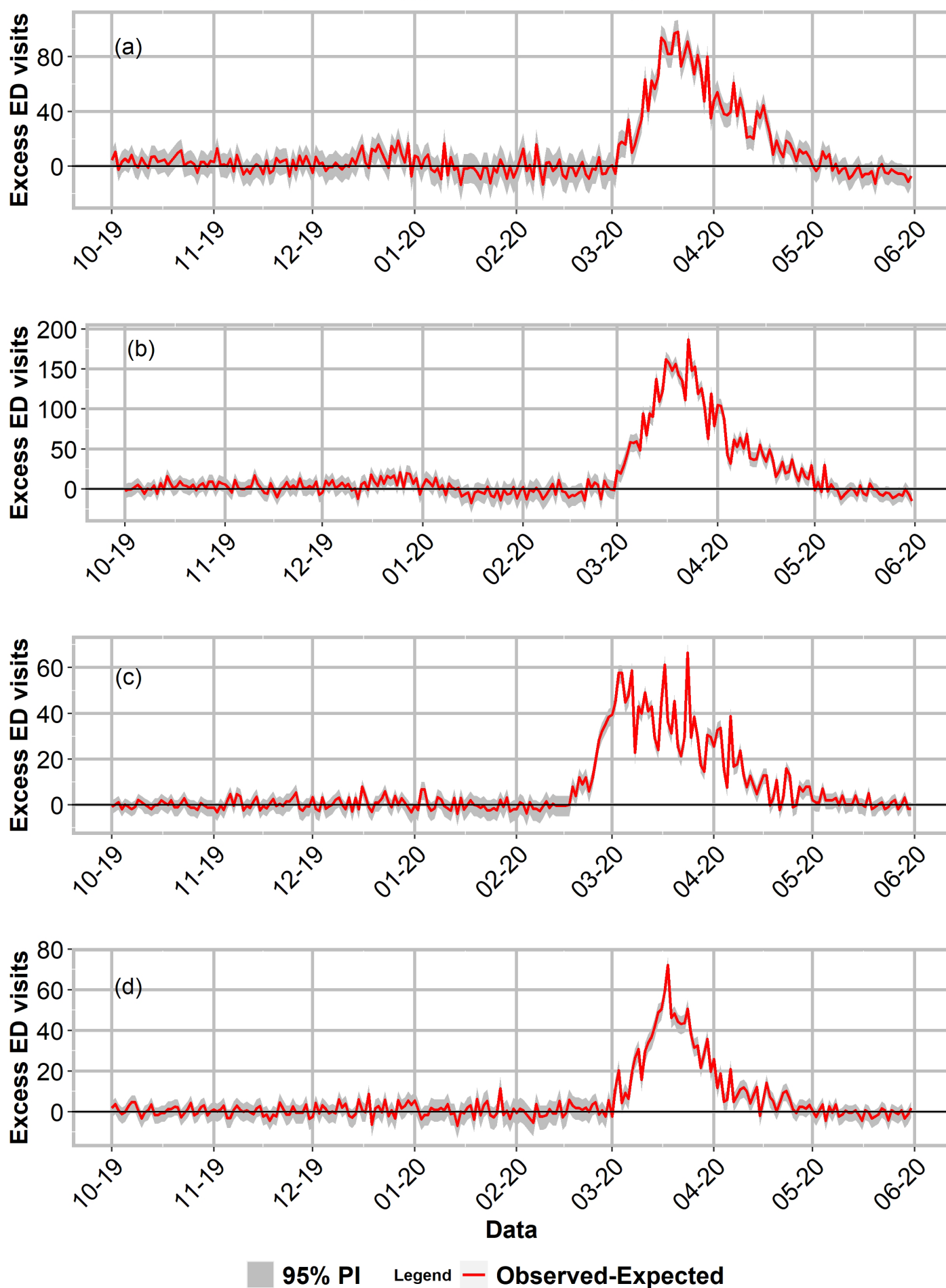
- 21 Ministero della Salute. Influenza. Available: <http://www.salute.gov.it/portale/influenza/homeInfluenza.jsp> [Accessed 10 Mar 2020].
- 22 Lauer SA, Sakrejda K, Ray EL, *et al.* Prospective forecasts of annual dengue hemorrhagic fever incidence in Thailand, 2010-2014. *Proc Natl Acad Sci U S A* 2018;115:E2175-82.
- 23 Forecast: Forecasting functions for time series and linear models, 2020. Available: <https://CRAN.R-project.org/package=forecast> [Accessed 14 Nov 2020].
- 24 Coma Redon E, Mora N, Prats-Urbe A, *et al.* Excess cases of influenza and the coronavirus epidemic in Catalonia: a time-series analysis of primary-care electronic medical records covering over 6 million people. *BMJ Open* 2020;10:e039369.
- 25 Lauer SA, Grantz KH, Bi Q, *et al.* The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann Intern Med* 2020;172:577-82.
- 26 ATS di Milano. Valutazione degli eccessi di mortalità nel corso dell'epidemia COVID-19 nella popolazione della ATS di Milano, 2020. Available: <https://www.ats-milano.it/portale/Epidemiologia/Valutazione-dellepidemia-COVID-19>
- 27 Zhao H, Lu X, Deng Y, *et al.* COVID-19: asymptomatic carrier transmission is an underestimated problem. *Epidemiol Infect* 2020;148:e116.
- 28 He J, Guo Y, Mao R, *et al.* Proportion of asymptomatic coronavirus disease 2019: a systematic review and meta-analysis. *J Med Virol* 2021;93:820-30.
- 29 Pollán M, Pérez-Gómez B, Pastor-Barriuso R, *et al.* Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet* 2020;396:535-44.
- 30 Primi risultati dell'indagine di sieroprevalenza sul SARS-CoV-2, 2020. Available: <https://www.istat.it/it/archivio/246156> [Accessed 24 Nov 2020].

**Supplementary Figure 1. Daily observed and predicted ED visits due to pneumonia between 1st of October 2015 and the 31st of May 2020, predictions were obtained by a Poisson regression model adjusted for seasonality and influenza epidemics. Time series among residents: in the city of Milan (a), in the hinterland of the city of Milan (b), in the province of Lodi (c), and outside the territory of the ATS (d).**





Supplementary Figure 2. Daily excess visits and 95% prediction intervals between 1th of October 2019 and the 31th of May 2020, among residents: in the city of Milan (a), in the hinterland of the city of Milan (b), in the province of Lodi (c), and outside the territory of the ATS (d).





Supplementary Data. Number of ED visits due to Pneumonia and excesses between 2018-2019, 2019-2020. Results on validation set and from Sensitivity analysis.

\*Sensitivity Analysis Results, dividing the dataset into training (from the 1th of October 2015 to the 30th of September 2018) and validation set one (from the 1th of October 2018 to the 30th of September 2019) and validation set two (from the 1th of October 2019 to the 31th of May 2020) \*\* Original results dividing the dataset into training (from the 1th of October 2016 to the 30th of September 2019) and validation sets (from the 1th of October 2019 to the 31th of May 2020).

Sensitivity Analysis Results		
Date 2018_2019	Number of ED visits due to Pneumonia (2018-2019)	Excess 2018-2019 (95% PI)*
01 December 2018	69	12 (-4,26)
02 December 2018	58	1 (-15,15)
03 December 2018	78	19 (4,34)
04 December 2018	53	-6 (-21,8)
05 December 2018	71	12 (-4,27)
06 December 2018	63	4 (-11,19)
07 December 2018	92	33 (17,48)
08 December 2018	66	7 (-8,21)
09 December 2018	72	13 (-3,27)
10 December 2018	75	14 (-2,29)
11 December 2018	74	13 (-2,28)
12 December 2018	54	-7 (-23,8)
13 December 2018	69	8 (-8,23)
14 December 2018	56	-5 (-21,10)
15 December 2018	67	6 (-10,20)
16 December 2018	69	8 (-8,23)
17 December 2018	78	15 (0,30)
18 December 2018	78	15 (-1,30)
19 December 2018	67	4 (-12,19)
20 December 2018	78	15 (-1,30)
21 December 2018	79	16 (0,31)
22 December 2018	78	15 (-1,30)
23 December 2018	55	-8 (-24,7)
24 December 2018	99	34 (17,50)
25 December 2018	95	30 (14,45)
26 December 2018	80	15 (-1,30)
27 December 2018	85	20 (4,35)
28 December 2018	96	31 (14,46)
29 December 2018	80	15 (-1,30)
30 December 2018	103	38 (21,53)
31 December 2018	87	17 (0,33)
01 January 2019	85	15 (-1,31)
02 January 2019	104	34 (18,50)
03 January 2019	92	22 (5,38)
04 January 2019	78	8 (-8,24)
05 January 2019	85	15 (-2,31)
06 January 2019	85	15 (-2,31)
07 January 2019	101	24 (7,41)

08 January 2019	95	18 (1,35)
09 January 2019	62	-15 (-32,2)
10 January 2019	78	1 (-16,18)
11 January 2019	90	13 (-4,30)
12 January 2019	68	-9 (-26,8)
13 January 2019	76	-1 (-18,16)
14 January 2019	80	-6 (-24,12)
15 January 2019	78	-8 (-27,10)
16 January 2019	84	-2 (-21,16)
17 January 2019	80	-6 (-25,12)
18 January 2019	68	-18 (-37,0)
19 January 2019	76	-10 (-29,8)
20 January 2019	87	1 (-17,19)
21 January 2019	80	-16 (-36,2)
22 January 2019	76	-20 (-40,-2)
23 January 2019	86	-10 (-30,8)
24 January 2019	76	-20 (-40,-1)
25 January 2019	109	13 (-6,32)
26 January 2019	89	-7 (-26,12)
27 January 2019	89	-7 (-27,11)
28 January 2019	96	-7 (-27,12)
29 January 2019	95	-8 (-28,11)
30 January 2019	80	-23 (-44,-4)
31 January 2019	92	-11 (-32,8)
01 February 2019	91	-12 (-33,7)
02 February 2019	93	-10 (-31,9)
03 February 2019	98	-5 (-25,14)
04 February 2019	97	-2 (-22,17)
05 February 2019	90	-9 (-29,10)
06 February 2019	100	1 (-19,20)
07 February 2019	105	6 (-14,25)
08 February 2019	86	-13 (-33,6)
09 February 2019	98	-1 (-21,18)
10 February 2019	113	14 (-7,33)
11 February 2019	104	14 (-5,32)
12 February 2019	88	-2 (-20,16)
13 February 2019	93	3 (-16,21)
14 February 2019	96	6 (-12,25)
15 February 2019	110	21 (1,38)
16 February 2019	89	0 (-19,18)
17 February 2019	97	8 (-11,25)
18 February 2019	88	7 (-11,25)
19 February 2019	87	6 (-12,23)
20 February 2019	81	0 (-17,18)
21 February 2019	90	10 (-8,27)
22 February 2019	97	17 (-2,34)
23 February 2019	64	-16 (-34,1)
24 February 2019	82	2 (-16,19)
25 February 2019	91	20 (3,36)
26 February 2019	70	-1 (-18,15)

27 February 2019	67	-4 (-21,12)
28 February 2019	86	15 (-3,31)
01 March 2019	70	-1 (-18,15)
02 March 2019	83	12 (-5,28)
03 March 2019	83	12 (-5,28)
04 March 2019	68	3 (-14,18)
05 March 2019	69	4 (-12,19)
06 March 2019	71	6 (-10,22)
07 March 2019	69	4 (-12,19)
08 March 2019	80	15 (-1,31)
09 March 2019	76	11 (-5,27)
10 March 2019	81	17 (1,32)
11 March 2019	63	2 (-14,17)
12 March 2019	53	-8 (-24,7)
13 March 2019	67	6 (-10,21)
14 March 2019	64	3 (-12,17)
15 March 2019	52	-9 (-24,6)
16 March 2019	74	13 (-2,28)
17 March 2019	61	1 (-16,15)
18 March 2019	73	15 (-1,29)
19 March 2019	60	2 (-13,17)
20 March 2019	61	3 (-12,18)
21 March 2019	52	-6 (-21,9)
22 March 2019	71	13 (-2,28)
23 March 2019	59	1 (-14,16)
24 March 2019	54	-3 (-19,11)
25 March 2019	76	20 (5,34)
26 March 2019	53	-3 (-18,11)
27 March 2019	74	18 (3,32)
28 March 2019	65	9 (-6,24)
29 March 2019	66	11 (-5,25)
30 March 2019	57	2 (-14,16)
31 March 2019	54	-1 (-16,13)

Sensitivity Analysis Results		
Date 2019_2020	Number of ED visits due to Pneumonia (2019-2020)	Excess 2019-2020 (95% PI)*
01 December 2019	51	-6 (-21,8)
02 December 2019	80	21 (5,35)
03 December 2019	64	5 (-11,20)
04 December 2019	81	22 (6,36)
05 December 2019	58	-1 (-17,13)
06 December 2019	63	3 (-12,18)
07 December 2019	69	9 (-6,24)
08 December 2019	68	8 (-7,23)
09 December 2019	78	17 (1,32)
10 December 2019	61	0 (-16,15)
11 December 2019	67	6 (-10,21)
12 December 2019	52	-10 (-26,5)
13 December 2019	69	7 (-8,23)
14 December 2019	76	14 (-2,29)
15 December 2019	75	13 (-3,28)
16 December 2019	107	43 (27,58)
17 December 2019	82	18 (2,33)
18 December 2019	76	12 (-4,27)
<b>19 December 2019</b>	<b>85</b>	<b>21 (5,36)</b>
<b>20 December 2019</b>	<b>86</b>	<b>22 (5,37)</b>
<b>21 December 2019</b>	<b>102</b>	<b>38 (22,53)</b>
<b>22 December 2019</b>	<b>92</b>	<b>28 (11,42)</b>
<b>23 December 2019</b>	<b>99</b>	<b>35 (19,50)</b>
24 December 2019	68	4 (-12,20)
25 December 2019	101	37 (21,52)
26 December 2019	78	14 (-2,29)
27 December 2019	110	46 (30,61)
28 December 2019	98	34 (17,49)
29 December 2019	79	15 (-1,30)
30 December 2019	103	36 (19,51)
31 December 2019	55	-12 (-29,3)
01 January 2020	86	19 (2,34)
02 January 2020	87	20 (3,35)
03 January 2020	79	12 (-5,27)
04 January 2020	83	15 (-1,31)
05 January 2020	90	22 (6,38)
06 January 2020	71	-2 (-19,14)
07 January 2020	74	1 (-16,17)
08 January 2020	70	-3 (-20,13)
09 January 2020	76	3 (-14,19)



10 January 2020	93	20 (2,36)
11 January 2020	70	-3 (-20,13)
12 January 2020	79	6 (-11,22)
13 January 2020	71	-9 (-27,8)
14 January 2020	63	-17 (-35,0)
15 January 2020	66	-14 (-32,3)
16 January 2020	59	-21 (-39,-4)
17 January 2020	77	-3 (-21,14)
18 January 2020	83	3 (-15,20)
19 January 2020	71	-9 (-27,8)
20 January 2020	84	-5 (-23,13)
21 January 2020	79	-10 (-28,8)
22 January 2020	83	-6 (-24,13)
23 January 2020	80	-9 (-27,9)
24 January 2020	71	-18 (-37,0)
25 January 2020	69	-20 (-39,-2)
26 January 2020	80	-9 (-28,10)
27 January 2020	108	11 (-8,30)
28 January 2020	88	-9 (-29,10)
29 January 2020	93	-4 (-24,16)
30 January 2020	78	-19 (-38,0)
31 January 2020	85	-12 (-31,7)
01 February 2020	93	-4 (-23,15)
02 February 2020	91	-6 (-26,13)
03 February 2020	107	13 (-7,31)
04 February 2020	82	-12 (-32,6)
05 February 2020	94	0 (-19,18)
06 February 2020	74	-20 (-40,-2)
07 February 2020	99	5 (-14,23)
08 February 2020	80	-14 (-33,5)
09 February 2020	76	-18 (-37,1)
10 February 2020	97	9 (-10,27)
11 February 2020	84	-4 (-23,14)
12 February 2020	96	8 (-11,26)
13 February 2020	83	-5 (-24,13)
14 February 2020	94	6 (-13,24)
15 February 2020	68	-20 (-38,-2)
16 February 2020	70	-18 (-36,1)
17 February 2020	80	-1 (-20,16)
18 February 2020	87	6 (-12,23)
19 February 2020	78	-3 (-21,14)
20 February 2020	81	0 (-18,18)
21 February 2020	107	26 (8,43)
22 February 2020	91	10 (-8,27)
23 February 2020	87	6 (-12,23)
24 February 2020	94	20 (3,37)
25 February 2020	84	10 (-7,27)
26 February 2020	119	46 (28,62)
27 February 2020	105	32 (14,48)
28 February 2020	102	29 (11,45)

29 February 2020	117	44 (27,60)
01 March 2020	135	62 (45,78)
02 March 2020	139	72 (56,88)
03 March 2020	192	125 (109,141)
04 March 2020	191	124 (108,140)
05 March 2020	197	130 (114,145)
06 March 2020	214	147 (131,163)
07 March 2020	216	150 (133,165)
08 March 2020	182	116 (100,131)
09 March 2020	259	197 (180,212)
10 March 2020	222	160 (143,175)
11 March 2020	301	239 (223,254)
12 March 2020	270	208 (192,223)
13 March 2020	344	282 (266,297)
14 March 2020	301	239 (223,254)
15 March 2020	324	262 (247,277)
16 March 2020	411	353 (337,367)
17 March 2020	429	371 (355,385)
18 March 2020	399	341 (326,356)
19 March 2020	376	318 (303,332)
20 March 2020	393	335 (320,350)
21 March 2020	363	306 (290,320)
22 March 2020	309	252 (237,266)
23 March 2020	399	345 (330,358)
24 March 2020	413	359 (344,373)
25 March 2020	357	303 (288,317)
26 March 2020	313	259 (244,273)
27 March 2020	326	272 (257,286)
28 March 2020	269	215 (201,229)
29 March 2020	210	156 (142,170)
30 March 2020	320	268 (253,281)

Results on validation set		
Date 2019_2020	Number of ED visits due to Pneumonia (2019-2020)	Excess 2019-2020 (95% PI)**
01 December 2019	51	-8 (-23,6)
02 December 2019	80	20 (4,34)
03 December 2019	64	3 (-13,18)
04 December 2019	81	20 (5,35)
05 December 2019	58	-3 (-19,12)
06 December 2019	63	2 (-14,17)
07 December 2019	69	8 (-8,23)
08 December 2019	68	7 (-9,22)
09 December 2019	78	15 (0,30)
10 December 2019	61	-2 (-18,13)
11 December 2019	67	4 (-11,19)
12 December 2019	52	-11 (-27,4)
13 December 2019	69	6 (-10,21)
14 December 2019	76	13 (-3,28)
15 December 2019	75	12 (-4,27)
16 December 2019	107	42 (25,57)
17 December 2019	82	17 (0,32)
18 December 2019	76	11 (-6,26)
19 December 2019	85	19 (3,35)
20 December 2019	86	20 (4,35)
21 December 2019	102	36 (20,51)
22 December 2019	92	26 (9,42)
23 December 2019	99	34 (18,49)
24 December 2019	68	3 (-13,18)
25 December 2019	101	36 (19,51)
26 December 2019	78	13 (-4,28)
27 December 2019	110	44 (28,60)
28 December 2019	98	32 (16,48)
29 December 2019	79	13 (-3,29)
30 December 2019	103	34 (18,50)
31 December 2019	55	-14 (-30,2)
01 January 2020	86	17 (0,33)
02 January 2020	87	18 (1,34)
03 January 2020	79	10 (-6,26)
04 January 2020	83	14 (-3,30)
05 January 2020	90	21 (5,37)
06 January 2020	71	-3 (-20,13)
07 January 2020	74	0 (-18,16)
08 January 2020	70	-4 (-22,12)
09 January 2020	76	2 (-16,18)

10 January 2020	93	19 (2,35)
11 January 2020	70	-4 (-22,13)
12 January 2020	79	5 (-12,21)
13 January 2020	71	-9 (-27,7)
14 January 2020	63	-17 (-35,-1)
15 January 2020	66	-15 (-33,3)
16 January 2020	59	-22 (-40,-4)
17 January 2020	77	-4 (-22,13)
18 January 2020	83	2 (-16,19)
19 January 2020	71	-10 (-28,7)
20 January 2020	84	-4 (-24,14)
21 January 2020	79	-9 (-29,8)
22 January 2020	83	-5 (-24,12)
23 January 2020	80	-8 (-27,10)
24 January 2020	71	-17 (-36,1)
25 January 2020	69	-19 (-38,-2)
26 January 2020	80	-8 (-27,10)
27 January 2020	108	12 (-8,31)
28 January 2020	88	-8 (-28,11)
29 January 2020	93	-3 (-22,16)
30 January 2020	78	-18 (-38,1)
31 January 2020	85	-11 (-31,8)
01 February 2020	93	-3 (-22,16)
02 February 2020	91	-5 (-25,14)
03 February 2020	107	13 (-7,32)
04 February 2020	82	-12 (-31,7)
05 February 2020	94	0 (-19,19)
06 February 2020	74	-20 (-39,-1)
07 February 2020	99	5 (-14,24)
08 February 2020	80	-14 (-33,5)
09 February 2020	76	-17 (-36,1)
10 February 2020	97	9 (-10,27)
11 February 2020	84	-4 (-23,14)
12 February 2020	96	8 (-11,26)
13 February 2020	83	-5 (-23,13)
14 February 2020	94	6 (-14,24)
15 February 2020	68	-20 (-38,-2)
16 February 2020	70	-18 (-37,0)
17 February 2020	80	-2 (-21,15)
18 February 2020	87	5 (-13,22)
19 February 2020	78	-4 (-22,13)
20 February 2020	81	-1 (-19,16)
21 February 2020	107	25 (7,42)
22 February 2020	91	9 (-9,26)
23 February 2020	87	5 (-13,22)
24 February 2020	94	19 (1,35)
25 February 2020	84	9 (-8,26)
26 February 2020	119	44 (26,60)
27 February 2020	105	30 (12,47)
28 February 2020	102	27 (10,43)



29 February 2020	117	42 (25,59)
01 March 2020	135	60 (43,77)
02 March 2020	139	70 (53,86)
03 March 2020	192	123 (107,139)
04 March 2020	191	122 (105,138)
05 March 2020	197	128 (112,144)
06 March 2020	214	145 (129,162)
07 March 2020	216	148 (131,163)
08 March 2020	182	114 (97,129)
09 March 2020	259	194 (178,210)
10 March 2020	222	158 (142,173)
11 March 2020	301	237 (221,252)
12 March 2020	270	206 (190,221)
13 March 2020	344	280 (264,295)
14 March 2020	301	237 (221,252)
15 March 2020	324	260 (244,275)
16 March 2020	411	351 (335,365)
17 March 2020	429	369 (353,383)
18 March 2020	399	339 (323,353)
19 March 2020	376	316 (300,331)
20 March 2020	393	333 (318,348)
21 March 2020	363	303 (287,318)
22 March 2020	309	249 (234,264)
23 March 2020	399	342 (327,356)
24 March 2020	413	356 (341,371)
25 March 2020	357	300 (285,314)
26 March 2020	313	256 (241,271)
27 March 2020	326	270 (254,284)
28 March 2020	269	213 (197,227)
29 March 2020	210	154 (139,168)
30 March 2020	320	265 (250,279)

Results on validation set		
Date 2019_2020	Number of ED visits due to Pneumonia (2019-2020)	Excess 2019-2020 (95% PI)**
31 March 2020	218	163 (148,177)
01 April 2020	259	205 (190,219)
02 April 2020	257	203 (188,216)
03 April 2020	241	187 (172,201)
04 April 2020	155	101 (86,115)
05 April 2020	137	83 (68,97)
06 April 2020	214	161 (146,175)
07 April 2020	188	135 (121,149)
08 April 2020	179	126 (112,140)
09 April 2020	188	135 (121,149)
10 April 2020	186	134 (119,148)
11 April 2020	130	78 (63,91)
12 April 2020	128	76 (61,90)
13 April 2020	126	74 (60,88)
14 April 2020	164	112 (98,126)
15 April 2020	136	85 (70,98)
16 April 2020	149	98 (83,112)
17 April 2020	161	110 (95,123)
18 April 2020	119	68 (53,82)
19 April 2020	83	32 (18,45)
20 April 2020	103	53 (38,66)
21 April 2020	98	48 (34,61)
22 April 2020	89	39 (24,52)
23 April 2020	117	67 (53,80)
24 April 2020	123	73 (59,86)
25 April 2020	81	31 (17,44)
26 April 2020	63	13 (-1,27)
27 April 2020	97	48 (34,61)
28 April 2020	82	33 (19,47)
29 April 2020	81	33 (18,46)
30 April 2020	96	48 (34,61)
01 May 2020	50	2 (-12,15)
02 May 2020	52	4 (-10,17)
03 May 2020	46	-2 (-16,11)
04 May 2020	99	51 (37,64)
05 May 2020	48	0 (-14,13)
06 May 2020	67	19 (5,32)
07 May 2020	46	-1 (-16,11)
08 May 2020	55	8 (-6,20)
09 May 2020	28	-19 (-33,-6)

10 May 2020	40	-7 (-21,6)
11 May 2020	44	-3 (-17,10)
12 May 2020	38	-9 (-23,4)
13 May 2020	39	-8 (-22,5)
14 May 2020	41	-6 (-19,7)
15 May 2020	50	4 (-10,16)
16 May 2020	29	-17 (-31,-5)
17 May 2020	33	-13 (-27,-1)
18 May 2020	52	6 (-8,19)
19 May 2020	37	-9 (-23,4)
20 May 2020	29	-17 (-31,-4)
21 May 2020	37	-9 (-23,4)
22 May 2020	42	-4 (-18,9)
23 May 2020	36	-10 (-23,3)
24 May 2020	30	-15 (-29,-3)
25 May 2020	34	-11 (-25,1)
26 May 2020	34	-11 (-25,1)
27 May 2020	31	-14 (-28,-1)
28 May 2020	33	-12 (-26,1)
29 May 2020	39	-6 (-20,7)
30 May 2020	24	-21 (-34,-8)
31 May 2020	23	-22 (-35,-9)