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Title: Excess pneumonia and influenza death as herald wave of COVID-19 in England and Wales, United Kingdom

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Highlights

- Excess pneumonia and influenza death showed a herald wave ahead of the wave of COVID-19 deaths in England and Wales, United Kingdom.
- We argue that this could be a death coding issue. Namely in the early phase, a proportion of COVID-19 deaths were classified as pneumonia of unknown type.
- Before and after the herald wave, the weekly pneumonia and influenza deaths were lower than the average of the previous five years (by 550 deaths per week)

Dear Editor:

We read with interest Gosce et al's modelling on COVID-19 in London, United Kingdom (UK) [1], concerning approaches to lift the lockdown. Their work utilized

notified cases, deaths, contacts, and mobility data. The authors pointed out "the recent observed increase in all-cause mortality during lockdown, which is in part due to individuals dying from other causes warrants investigation." In this work, we analyse the impact of COVID-19 on all-cause mortality and pneumonia and influenza (P&I) deaths in England and Wales (E&W), UK with the aim to show that these data could embed useful information. Compared with confirmed COVID-19 cases, the reported COVID-19 deaths may be relatively more reliable as an index since deceased patients are more likely to be hospitalized, and thus more likely to be tested and ascertained than the general infected population [2,3]. All-cause deaths were also used to reconstruct the course of the pandemic, often through implementing the well-known Serfling's method [4]. Weinberger et al. (2020) found that the all-cause deaths are 28% higher than the reported number of COVID-19 deaths from March 1 to May 30, 2020, in the United States [5]. For comparison, we found that the excess all-cause mortality is 23.4% higher than the reported number of COVID-19 deaths over the same period in the United Kingdom.

However, the impact of COVID-19 on P&I deaths is complex. On the one hand, both COVID-19 and influenza may contribute to the mortality risk of pneumonia at the populational scale. On the other hand, pneumonia deaths, as one of the major clinical outcomes of COVID-19, due to unascertained COVID-19 may be recorded as an unknown type of pneumonia especially during the early stages of the outbreak.

In this work, we analysed the P&I mortality, all-cause mortality, and COVID-19 mortality in E&W, UK [6]. The reason we chose E&W, UK as an example is largely due to the availability of the data (COVID-19 deaths, P&I deaths and all-cause mortality). However, we only have daily COVID-19 cases and weekly influenza positives for the whole UK. Since the E&W population accounts for 89% of the UK population, it is reasonable to assume COVID-19 cases and influenza positives in UK are good proxy for that of E&W.

The first two cases of COVID-19 were reported in the UK on February 1, 2020, and the number of reported cases has been increasing since then. Up until August 6, 2020, 307,188 confirmed COVID-19 cases were reported in the UK, including 46,364 deaths due to COVID-19, with a raw case fatality rate of 15%. These are shown as timeseries in Figure 1A. In the same figure we also show the weekly laboratory confirmation of influenza. Seasonal influenza and COVID-19 could compete for patients, deaths, and medical resources. However seasonal influenza should have a

smaller basic reproductive number than that of COVID-19, and thus is more sensitive to social distancing. According to the weekly influenza positives timeseries in Figure 1A, across the UK the number of influenza positives in the first half year was significantly lower overall than previous years, except for a brief peak in January, 2020. Weekly influenza positives fell rapidly to a low level when social distancing was in place in the UK. Figure 1A shows data for UK, but we suppose the same trends would be apparent for E&W.

We first noticed that the P&I mortality in the first half year of 2020 was unusually aligned with the previous five-year baseline average in E&W, UK, as seen in Figure 1B. In this figure we have in fact plotted the P&I mortality after applying a small constant vertical shift (amounting to 550 deaths per week) to help emphasise the correspondence. The alignment is astounding. We plotted the differences in alignment as a histogram by subtracting the actual P&I mortality of this year from the baseline. The histogram shows that there is a peak difference of 550 deaths (Figure 1C).

In the period week-11 to week-24 in 2020, some 59,138 excess all-cause deaths were reported in E&W, UK. Over the same period, there were 48,218 laboratory confirmed COVID-19-associated deaths (Figure 1D). If we denote the true number of COVID-19 related deaths as A, we have $A > 48{,}218$ presumably [7-9]. The excess all-cause mortality may be denoted as $A - B$, where B is the reduced death of other causes due to the city lockdown (for instance traffic accident deaths, improved air conditioning or suppression of influenza). While we can easily calculate excess mortality $A - B$ from the data, we can never find A without knowledge of B.

Interestingly, but unsurprisingly, the time series of excess all-cause deaths is similar to that of COVID-19 deaths (Figure 1D). There is a seemingly irrational phenomenon in the time series of excess all-cause mortality in Fig.1D which reached negative values in the first few months of 2020. Harrison et al. (2020) suggested this may have resulted from the public having learnt about the severity of COVID-19 elsewhere and having taken a series of precautionary measures which may have led to fewer deaths from other diseases before the outbreak [10]. These negative values are a manifestation of the aforementioned B value. Figure 1A also shows that influenza epidemics were more severe in 2018 and 2019 than in 2020 at the beginning of the year, and thus possibly another reason for the lower number of overall excess deaths.

More surprisingly, excess P&I deaths showed an almost perfect exponential increasing trend from week 6 until its peak at week 14 and then quickly fell back to a

normal level (i.e., zero excess; Figure 1D). This pattern seen in the P&I excess deaths indicates the arrival time of COVID-19 and its spreading. We crudely estimated the basic reproductive number to be approximately R_0=1.66 (95% confidence interval: 1.58-1.74) (see Supplementary Materials).

The excess P&I deaths in Fig.1D, could be seen as a "herald-wave" of COVID-19 in that it has the appearances of an outbreak that peaks several weeks in advance of COVID-19. Before and after the "herald wave", the P&I deaths matched the previous five years average astonishingly well. Upon consideration, the "herald wave" is most likely an identification and coding issue, namely, when a new disease emerges, there will be a transition from "coding the new disease related deaths with the closest existing code" to "coding them with the newly created specific code". But importantly, these timeseries illuminate how important quality real-time disease surveillance that detect anomalies can predict major disease outbreaks that might otherwise go undetected for significant time periods. Also our observation may provide a signal for commencing enhanced population protection [1].

Declaration

Ethical Approval and Consent to participate

The ethical approval and individual consents were exempted as the aggregated data were used in this study.

Availability of data and materials

All data used are from public domain.

Conflict of interest:

DH was supported by an Alibaba (China) Co. Ltd. Collaborative Research project. Other authors declare no conflict of interest.

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Authors' contributions

All authors conceived and conducted the research and wrote the draft. All authors critically revised the manuscript, and all authors approved the submission.

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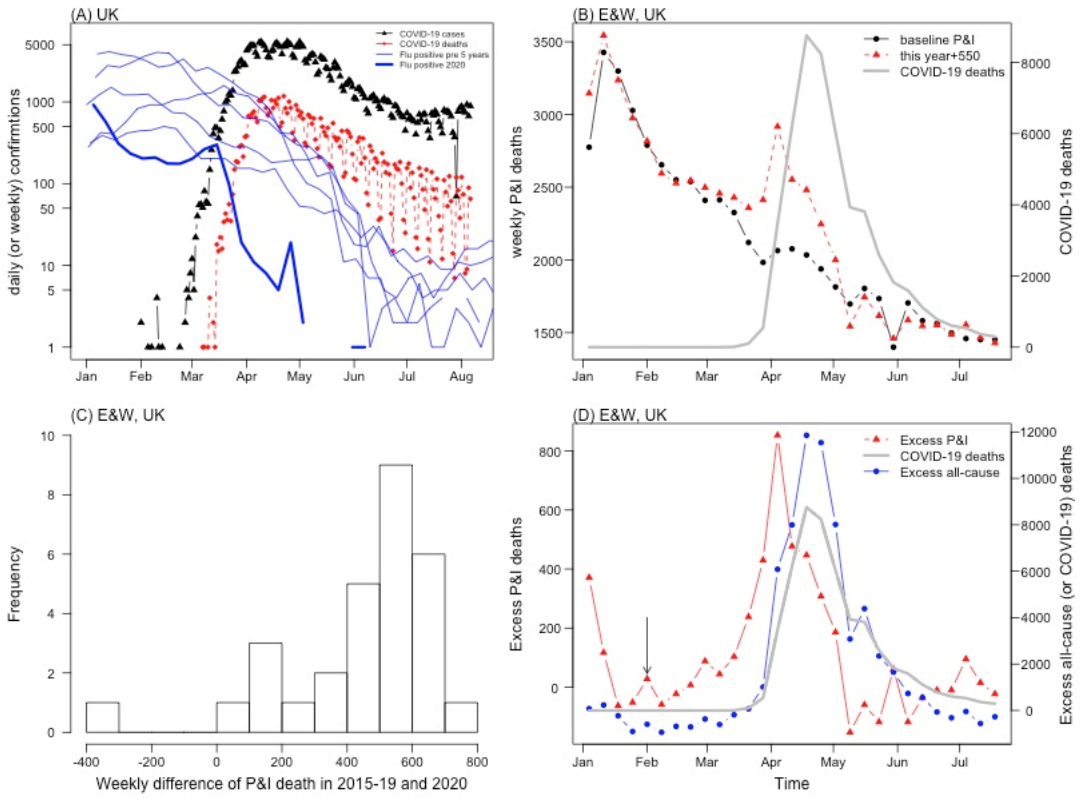

Figure 1. Time series plots of daily confirmed COVID-19 cases (in black), COVID-19 deaths (in red), and influenza positive cases in 2015-2019 (in light blue) and in 2020 (in dark blue) in the UK (panel A). The comparison between COVID-19 and P&I deaths in E&W, UK (panel B). Frequency distribution of the difference between weekly P&I deaths in 2020 and the baseline of previous five years (panel C). The comparison among excess P&I, COVID-19 and excess all-cause deaths in E&W, UK (panel D). In panel D, the arrows indicate the time that the first two confirmed case of COVID-19 were reported.