

J'accuse: difference between the two Covid-19 episodes in Italy, what is the cause?

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J'accuse: the difference between the two Covid-19 waves in Italy. What is its cause?

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Abstract

Background: The COVID-19 pandemic appears to have struck Italy in two waves.

Objective: To analyse the differences between the first (W1) and the second wave (W2).

Methods: Our analysis was based on weekly data retrieved from the Official Bulletin of the Italian Civil Protection Department from 1 March 2020 to 21 January 2021.

Results: W1 lasted about 23 weeks, from March to 15 August 2020. W2 started on 16 August and was still under way on 21 January 2021.

W2 is much more severe than W1 in terms of positive cases and deaths, and its decay is much slower.

We have identified at least six different causes of these differences: the colder season, the impact of seasonal influenza, viral mutation, the lack of a plan to tackle viral resurgence, poor care of elderly people, and lack of oral hygiene as an important preventive measure. Moreover, in an attempt to give the best possible information through the media, the experts have instead caused feelings of uncertainty and fear.

Conclusions: There are several reasons for the differences between W1 and W2: the start of the colder season during W2, poor care of elderly people, the delay in providing seasonal influenza vaccination, the lack of a national plan against COVID-19 resurgence, confusion over the lockdown measures, lack of information about oral hygiene, and confusing information given through the media.

Key words: COVID-19: COVID-19 positive cases: Covid-19 deaths

Introduction

The number of positive cases of Covid-19 on 21 January was about 97 million people worldwide, and there had been more than 2,077 million deaths [1]. It can be considered one of the most dramatic pandemics in recent history.

Table 1 shows the mortality rates in some of the most affected countries.

Table 1. Number of positive cases of Covid-19 in relation to the population; number of deaths, and death/population ratio updated to 21 January

Country	Population 10 ³	Covid-19 positive N	Deaths N	Death/population 10 ³
USA	318885	24438721	406147	1.27
Brazil	202768	8638249	212831	1.05
France	63290	3023661	71792	1.12
UK	64658	3515796	93469	1.45
Spain	46344	2412318	54637	1.18
Italy	60796	2414166	84161	1.42
Germany	80822	2100818	50017	0.62
Belgium	11150	685256	20572	1.84
Slovenia	2081	152851	3257	1.58
WHO countries	7834000	96938729	2077005	0.265

The lowest values recorded in Europe are in Germany, while Italy has among the highest.

The average values for WHO countries are significantly lower than those listed in table 1 because the number of deaths in many countries were limited to a few dozen (e.g. Iceland and New Zealand) or a few hundred cases (e.g. Finland, Estonia and Norway), or did not exceed 0.003×10^3 , as in China.

In Italy, the trend in number of deaths seems to show two different waves (W1 and W2). The aim of this study is to describe these two different curves and discuss their respective causes.

Material and methods

Source of data

The Italian data was taken from the Official Bulletins [2] and all the other data from the John Hopkins Coronavirus Resource Center [1]. The number of positive cases depends on the number of swabs taken, and positive subjects are normally tested more than three times. This leads to a bias, particularly as concerns W2, where the number of swabs taken has been much higher. Number of deaths is a more reliable variable to measure the difference

between W1 and W2, even though it can be influenced by delays in regional notifications. In order to reduce this bias, weekly data were used.

The bounds of the two waves were chosen arbitrarily: W1 started on 1 March and lasted up to 15 August, while W2 started on 16 August and was still under way on 21 January.

A total of 45 weeks was considered in this analysis, where week 1 corresponds to 1 to 7 March (from Sunday to Saturday).

Statistical methods

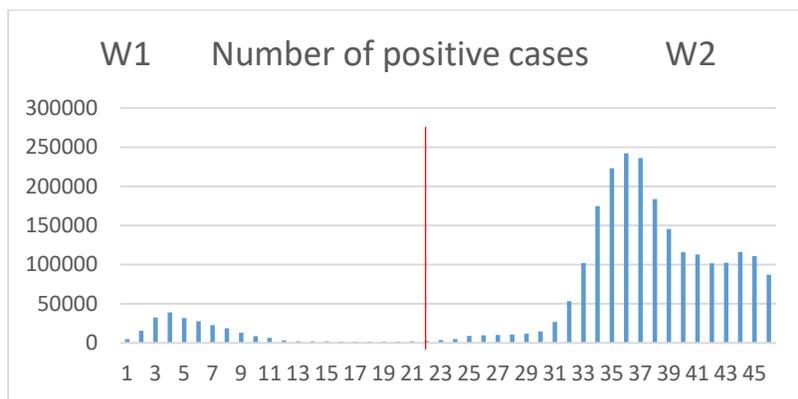
Time series analysis was used to obtain simple moving seven-day averages which describe the observed phenomena better and make it possible to calculate more realistic trends. Regression analysis was also used to evaluate the types of curves. SAS Institute JMP14 software was used for the calculations.

Results

Positive cases

Covid-19 infection in Italy is consistent with two waves (W1 and W2). A cut-off point was fixed arbitrarily between W1 and W2 at the 23rd week after the first cases appeared. As regards positive cases, W1 started on 1 March and lasted up to 15 August (from the 1st to the 23rd week), while W2 started on 16 August and was still continuing on 21 January (from the 24th to the 46th week). Figure 1 shows the positive case data.

Figure 1. Number of positive cases/week during W1 and W2

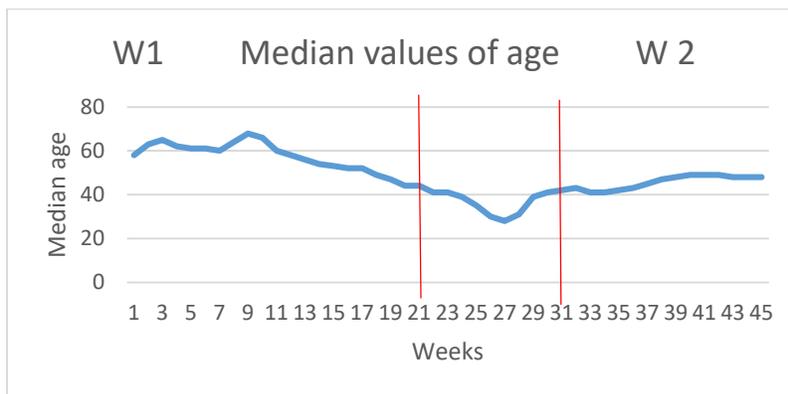


The red line shows the arbitrary limit between W1 and W2, fixed at the 23rd week

W2 is characterized by a much larger number of cases, about 8.7 times higher than during W1 (2,116,281 and 243,232 respectively), but about four times as many swabs have been taken during W2. These differences mean the two periods cannot be properly compared.

However, one interesting aspect is that the median age trends of the positive cases during W1 and W2 are different [3], as shown in figure 2.

Figure 2. Median age of cases with COVID-19 positive swabs [6] during the two waves (W1 and W2)



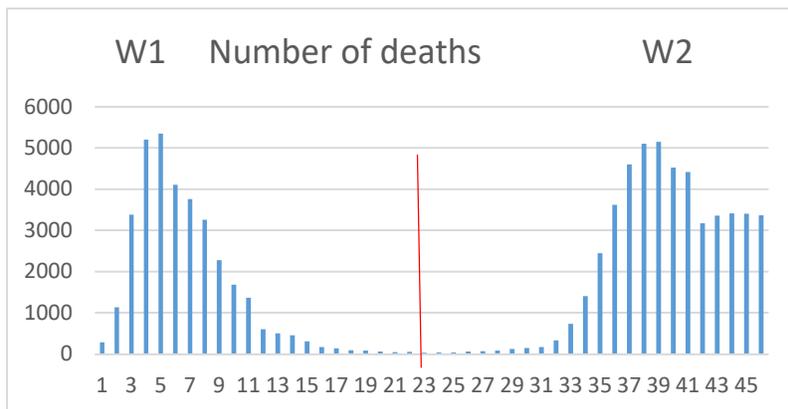
Week 1= 17 - 24 February; week 45 = 7 - 14 December: the two red lines correspond to the summer vacation period

Figure 2 shows that during W1, up to the 11th week, the median age was > 60 years most of the time; from the 12th to the 27th week, this age progressively dropped to 28 years; and the lowest values correspond to the summer holidays. After the 29th week, the median age stabilized at between 40 and 50 years.

Deaths

As for positive cases, the number of deaths also showed a two-wave pattern, as can be seen in figure 3.

Figure 3. Number of deaths/week during W1 and W2



The red line shows the arbitrary limit between W1 and W2, fixed at the 23rd week

The number of deaths during W1 was 34,367, while there were 46,424 deaths during W2 up to 21 January. The growth was faster during W1 and the peak (5349 deaths/week) was reached four weeks after the start, whereas it took 7 weeks to reach the W2 peak (5251 deaths/week). Similarly, the decay was more rapid in W1, reaching a 90% reduction in 8 weeks (Figure 4), while during W2, the decay was only 35% after 8 weeks (figure 5).

Figure 4. Number of deaths during the last eight weeks of W1



Figure 5. Number of deaths during the last eight weeks of W2



In summary, the data shows that W2 is more severe than W1, and will last longer.

Discussion

One of the frequent characteristics of pandemics is the presence of waves. This was true for the Spanish flu, which was characterized by three waves, and also during the Hong Kong flu, where two waves were described [4].

There is no clear explanation for this phenomenon in the literature, but in the case of Italy and COVID-19 there are several reasons that might explain the differences between the two waves.

W2 is characterized by about nine times more positive cases than W1, but this value is affected by the number of swabs taken, which has been at least 3.8 times higher (7.5 million vs. 28.5 million) during W2. Furthermore, the false negative cases may theoretically range from between 20 and 67% [5]. For these reasons, the data relating to deaths seem to be a sounder variable for comparing the two periods.

As regards deaths, the number of cases in W2 has been much higher than during W1 (46,424 and 34,367 respectively), and by the time the asymptote of the decay curve is reached, many more deaths will be added, though it is difficult to estimate a figure.

The triggers

The official data available [6-8] do not separate W1 and W2 and simply report the cumulative values at different periods between May and December 2020.

The data regarding the median age of positive cases [8] updated to 28 December (see Figure 2) are consistent with the following observations:

- 1) Besides during the first 11 weeks, the median age was lower than 60 years during W1.
 - 2) During W2 the median age seems to have stabilized at < 50 years.
 - 3) During the summer holidays (weeks 23-29), corresponding to the period between 20 June and 7 September, the median age reached its minimum values.
- This suggests that elderly people do not spread the virus, and those responsible for its circulation are people < 60 years, i.e. the more active part of the population.
- Lastly, elderly people bear the brunt of the virus since 95% of deaths are reported in patients > 60 years old [8,9].

The positive cases/death ratio

The high number of asymptomatic cases and false negatives makes the calculation of the positive cases/death ratio very difficult. The official records report that death occurs 12 days after the symptoms appear [8], and these take an average of 5 days (up to 11.5 days in 97.5% of cases) to become clinically evident after the viral infection [5]. On this basis, it is reasonable to assume that there is a period of from 17 to 32 days between the positive swab and death.

Figure 2 shows the lowest median age of positive swabs was in the period between 10 and 17 August, still during the first wave and when there was no lockdown. It should be borne in mind that most of the positive swabs were taken on symptomatic subjects during this period. As regards the deaths which occurred from 2 to 5 weeks later (14 to 35 days), the positive swabs/death ratio ranged from 0.80% to 0.92%.

During W2, the positive swabs/deaths ratio in the week between 7 and 14 December which occurred from 2 to 5 weeks later was between 3.84% and 4.01%. Despite underestimation of the W1 figures, because many more swabs have been taken during W2, these data confirm that W2 is several times (4 to 5) more severe.

The trends

The second wave is causing many more deaths and the decay trend is delayed compared to W1. There are several reasons for this which can be summarized in the following points.

- 1) The first cause might be the season. W1 started just before the spring, while W2 exploded in the autumn/winter period. Cold weather provides the virus with more suitable conditions and, at the same time, subjects are more sensitive to viral aggression [10]. During the colder season people tend to aggregate in crowded places, such as shopping centres, bars, and restaurants.

We cannot rule out that the increase in air pollution due to heating, in terms of PM_{2.5} and NO₂, could be instrumental in facilitating viral aggression [11] particularly in heavily industrialized regions.

- 2) The second cause may be seasonal influenza which is usually found in Italy from October to March. In the past, influenza has been seen to cause up to 25,000 cases of death [12].

The simultaneous circulation of more than one virus may have a combined effect on death, and - although it is difficult to determine the extent [13] - it is known that elderly people will be more affected.

While awaiting a specific vaccine for COVID-19, the seasonal influenza vaccine should have at least been administered since there was already documentary evidence that it could have been beneficial against COVID-19 deaths in Italy [14].

However, seasonal influenza vaccine distribution was delayed in some Italian Regions owing to logistic problems, and this may have determined an increase in deaths.

- 3) The third cause may be viral mutation. Mutations are extremely common during viral infection and many thousands of them have already been found for COVID-19 [15, 16].

Besides modifying virulence, the sensitivity of tests may also change, and this may lead to a greater number of false negatives. A variant has been described in the UK [17] which already seems to be present in many countries,

including Italy. This mutation has been reported to be 70% more transmissible [18] and cause a higher number of deaths.

4) The fourth cause can be attributed to the lack of a plan in case of COVID-19 resurgence.

Very confusing information was given to people concerning prevention since each Region decided on its own anti-COVID-19 measures in terms of lockdown and school opening. In some cases, each province was also acting independently, and one would expect some people to take their own initiatives owing to this.

5) The fifth cause was the poor care of elderly people, and this is one of the most important. A total of 95% of the deaths caused by COVID-19 is reported in people > 60 years, and 1/3 of the deaths are in people aged between 60 and 80 years of age. Regarding the latter, the majority occurred at home or in nursing homes, i.e. outside hospitals, where the care was not as good as it should have been.

6) The sixth cause was lack of oral hygiene recommendations. Although the viral infection is spread through the mouth, no virologists, immunologists, epidemiologists, or the media (TV and magazines) explained that oral hygiene [19, 20] is the primary barrier against the virus spreading. It is much more efficient than the protection from masks, particularly when the viral concentration is expected to increase, as in the cold season.

We should not forget that the virus is not only transmitted in restaurants, supermarkets and on public transport, but it also spreads during working hours when people are wearing masks. Therefore, oral hygiene is important for prevention. The extremely high frequency of viral infection in the most industrialized areas of Italy (e.g. Lombardy, Veneto and Piemonte) means that workplaces should be considered with more care and all possible barriers against COVID-19 should be implemented [21].

We should also mention the media. In the attempt to focus on the pandemic, a lot of fear and uncertainty was stirred up, driven by the different - and sometimes opposite - opinions of the virologists, epidemiologists and immunologists who invaded the TV and magazines.

In this way, information was transformed into a sort of promotion. The result was that family doctors were plagued by phone calls from their patients, and had to spend hours and hours answering questions at the expense of their daily practice. The consequence was that many doctors did not answer the phone and patients went directly to hospitals, clogging up the emergency rooms and concentrating the virus. A better solution would have been to organize care at home, in homes for the elderly, and in the medical surgeries of family doctors. This was not done properly, and it is clear that the entire medical care system in Italy should be revised.

Conclusions

From the analysis of the curves that represent the two different waves of COVID-19 in Italy (W1 and W2), it is evident that W2 is much more severe. This could be put down to several reasons such as the cold season, the impact of seasonal influenza, viral mutation, the lack of a plan to tackle the pandemic, and poor care of elderly people.

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Aknowlegdegments

We would like to offer our condolences to the families of Cov19 victims, and express our closeness to the people suffering from this viral infection.

UC conceived the trial; UC, GB, MRC, RC collected the data; MR was in charge of statistical evaluation, and UC wrote the text.

Conflict of Interest

There is no conflict of interest

Ethical statement

This manuscript is original, has not been published before and is not being considered for publication elsewhere. All the authors mentioned in the manuscript have agreed on its authorship, read and approved it, and given consent for its submission and subsequent publication.

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There is no financial support

Figures

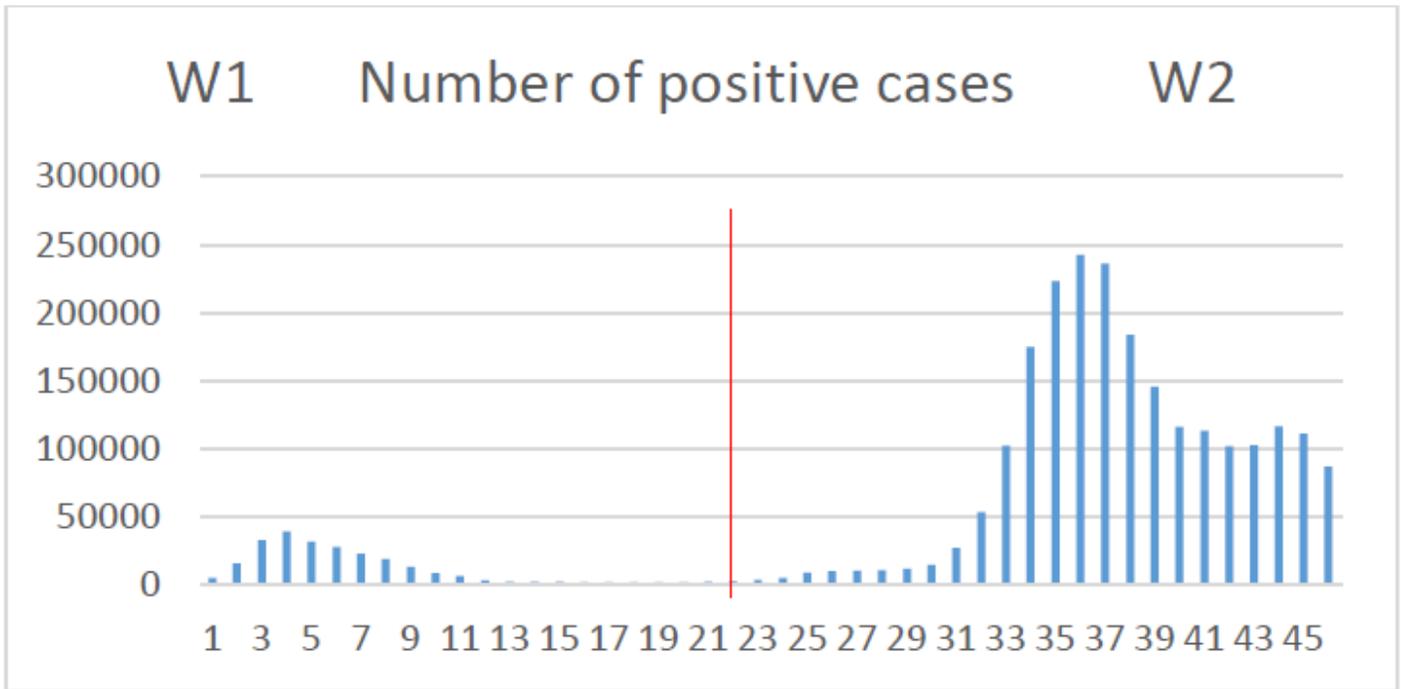


Figure 1

Number of positive cases/week during W1 and W2. The red line shows the arbitrary limit between W1 and W2, fixed at the 23rd week

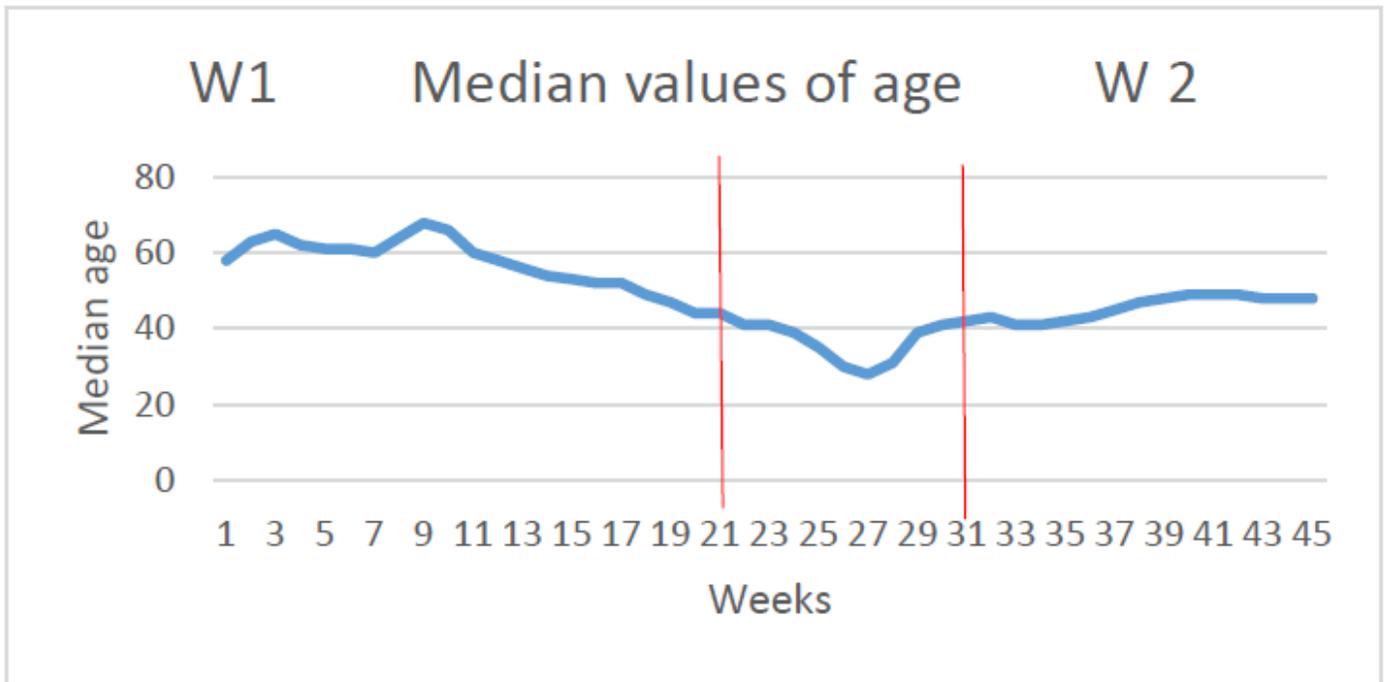


Figure 2

Median age of cases with COVID-19 positive swabs [6] during the two waves (W1 and W2). Week 1= 17 - 24 February; week 45 = 7 - 14 December: the two red lines correspond to the summer vacation period

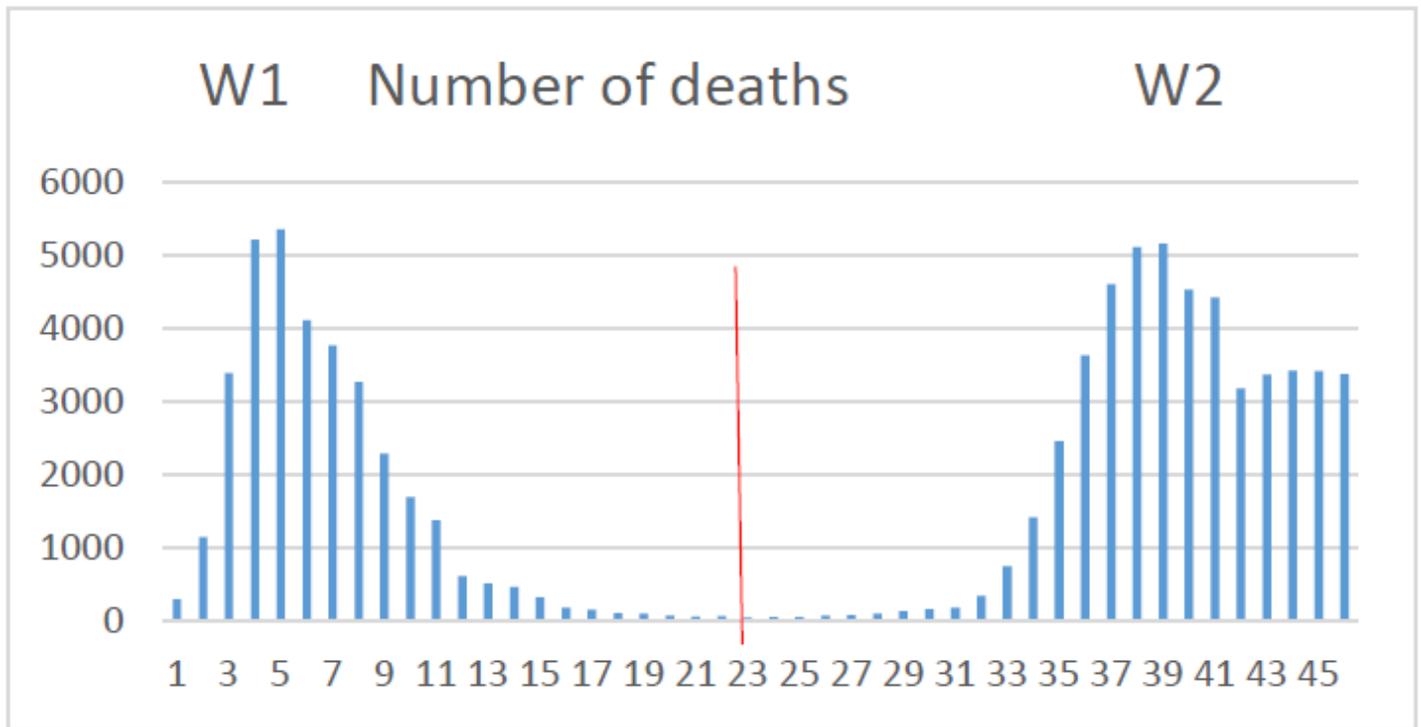


Figure 3

Number of deaths/week during W1 and W2. The red line shows the arbitrary limit between W1 and W2, fixed at the 23rd week



Figure 4

Number of deaths during the last eight weeks of W1



Figure 5

Number of deaths during the last eight weeks of W2