American Journal of Epidemiology

Vol. 187, No. 12
DOI: 10.1093/aje/kwy191
Advance Access publication:
September 7, 2018

Epidemiology in History

Reassessing the Global Mortality Burden of the 1918 Influenza Pandemic

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Initially submitted April 13, 2018; accepted for publication August 20, 2018.

Mortality estimates of the 1918 influenza pandemic vary considerably, and recent estimates have suggested that there were 50 million to 100 million deaths worldwide. We investigated the global mortality burden using an indirect estimation approach and 2 publicly available data sets: the Human Mortality Database (13 countries) and data extracted from the records of the *Statistical Abstract for British India*. The all-cause Human Mortality Database was used to estimate mortality annually for 1916–1921 for detailed age groups. Three different calculation methods were applied to the data (low, medium, and high scenarios), and we used a multilevel regression model to control for distorting factors (e.g., war and the underlying time trend in mortality). Total pandemic mortality was an estimated 15 million deaths worldwide in 1918 ($n =$ 2.5 million in 1919) after including the rates for British India and controlling for wars and the underlying mortality trend. According to our validity analysis, simulations of total number of deaths being greater than 25 million are not realistic based on the underlying mortality rates included in Human Mortality Database and in British India. Our results suggest the global death impact of the 1918 pandemic was important ($n =$ 17.4 million) but not as severe as most frequently cited estimates.

1918; influenza; mortality; pandemic; smallpox; vital statistics

In this article, we estimate the global death burden of the 1918 influenza pandemic. The burden has been estimated many times over the past 100 years, and the estimated burden gradually has increased. One of the oldest estimates was made by Jordan in 1927 (1), who estimated the global burden to be approximately 21.6 million deaths. Patterson and Pyle (2), in 1991, estimated the burden to be 30 million (ranging from 24.7 million to 39.3 million). In 2002, Johnson and Mueller (3) reported a range of 50 million to 100 million deaths, with 50 million closer to the results from the studies they cited, and 100 million being the upper limit, because they believed 50 million to be an underestimate (3).

The 1918 pandemic occurred in 3 or 4 waves and the spatiotemporal spread has been described in several studies (2, 4, 5). The first wave occurred around spring 1918 and was considered mild. The second wave, which was global, started in August and lasted until the end of December 1918, and is considered to have been, by far, the most deadly wave. The third wave was only seen in some countries in early 1919, and some authors think there may have been a fourth wave in 1920 (3).

Interestingly, there was a strong similarity between the 1918 and 2009 pandemics in the northern hemisphere (first wave in spring/summer, second global (and more deadly) wave in the last 4 months of 2009). In the southern hemisphere in 2009, the second wave occurred in July and August (the same period as the seasonal epidemic). The timing of the pandemic waves indicates the speed of spread around the world is surprisingly similar, except the 2009 pandemic reached the southern hemisphere more quickly.

Methods to estimate the death burden at a global level can be divided approximately into 2 approaches. The first is a direct estimation method based on cause-specific deaths. The second approach is to use an indirect estimation method, which is based on all-cause mortality only. The main problem with both approaches is that a reference death rate is needed to calculate the excess, because the deviation from this reference is the estimate of excess mortality. That both methods have their problems if they are used to estimate the pandemic death burden has long been recognized (6–10). Estimates vary a lot; therefore, our objective in this study was to re-estimate the global mortality rate of the 1918–1919 pandemic by 1) using data based on the total population (vital statistics); 2) including the death rates in the years before and after the pandemic; 3) taking into account the death rate in different age groups; and 4) taking into account other factors that influence death rates, such as war and the underlying time trend in mortality.

METHODS

Data sources

The data used in our analysis mainly were from the Human Mortality Database (11), which has population and death data for several countries by age by year. The death counts come from national registries, and the population counts come from periodic censuses and/or official population estimates (vital statistics). We used 10 age classes (grouped in years): 0, 1–4, 5–9, 10–14, 15–19, 20–29, 30–39, 40–49, 50–59, and 60 or older). A total of 13 countries had sufficient data for our study period (1916–1921); the total combined population of these 13 countries was 159 million in 1918.

Because most countries in the data set are in Europe and, according to the literature, the burden in some parts of Asia was much larger (3), we added data for British India (which we call India in the rest of the article, although it represents a larger geographical area than the current state of India (see Web Figure 1, available at https://academic.oup.com/aje)). These data, which are available for the same 10 age categories, were taken from the *Statistical Abstract for British India* (12). Considering the Indian population was 243 million people in 1918, the combined total population covered by our sample of 14 countries is 402 million, which was approximately 20% of the world population in 1918.

Measurement procedure

Given that we used all-cause mortality data, we took an indirect calculation approach. We created a sample of yearly total death rates for the 14 countries and, based on this assessment, the yearly average pandemic excess death burden for the sample was estimated. Next, we assumed the sample average could be viewed as a valid estimate of the global pandemic mortality rate and, using the total world population, we estimated the total number of deaths.

We used 3 scenarios to assess the pandemic burden, with each scenario differing in the choice of mortality rate as the reference value. The reference values are derived from the 2 years before (1916, 1917) and the 2 years after (1921, 1922) the pandemic. The excess was estimated as the death rate in the pandemic year (1918 or 1919) minus the reference death rate. We chose the reference values such that we have expected high, medium, and low pandemic burden scenarios. To explain, we provide a fictitious example for which death rates, per 100,000, for each year from 1916 through 1921 are as follows: 1916 = 3,700; 1917 = 3,500; 1918 = 5,800; 1919 = 4,600; 1920 = 4,500; and 1921 = 4,400. In this example, the reference year in the high scenario is 1917, this is the reference year with the lowest mortality rate. This choice maximizes the difference in mortality rate between the pandemic year (1918) and the reference year and produces the highest excess mortality rate. The underlying idea is that we assumed the variation between the reference years was mostly due to variation in seasonal influenza. Other causes are constant, meaning they cause no variation between the reference years. In the low scenario, we did the opposite: We selected the reference year closest to the pandemic year (note: reference years with higher values than the pandemic year are ignored), which is 1920 in our example. Now we assumed most of the variation between reference years was due to other causes (e.g., war, famine, other diseases). It is important to note that the choice of reference year differs between countries and also between age groups within a country. In the medium scenario, the reference value is the average mortality rate over the 2 years before and after the pandemic. In this scenario, we assumed variation between reference years was due to seasonal influenza and other causes.

Statistical model

Although calculations can be done directly using the sample data, we developed a multilevel regression model to estimate the average excess mortality rate. An important advantage of using a multilevel regression model is that it is possible to correct for distorting factors (e.g., wars or famines). In 1918, several of the sampled countries were at war, leading to excess mortality rates (e.g., England and civil war in Finland). Ignoring this factor would lead to an overestimation of the pandemic burden. This approach also allowed us to correct for long-term trends in the series within a country (controlling for the time series being nonstationary).

Within the multilevel regression model, yearly mortality rates, the dependent variable, are nested within countries; level 2 is the country level and level 1 is the 6 years within a country. The independent variables are measurement procedure indicators and correction variables (for a more elaborate discussion of the model, see Web Appendix 1).

Validity tests

To test the robustness of our model, several tests were performed. 1) We tested the sensitivity of the method by using different subsets of the data; 2) we explored the India data in more detail (by region); 3) we looked at the estimated death rate per age group to find out which scenario (low, medium, high) best fit the pandemic age signature (13); 4) we simulated the effect of several fictitious pandemic excess rates on a year with a normal global mortality rate (1922) to explore the credibility of those excess rates; and 5) we applied the methods to other pandemics.

RESULTS

Overview of the available data

If one looks at the total population mortality rates for the 14 countries in our study over a range of years (see Web Figure 2A–2K), in almost all countries there was a clear spike in mortality in 1918, except in Denmark (however, this does not mean that Denmark did not have any deaths due to the pandemic). In general, India had a higher mortality rate and there was a very high spike in 1918. For the European countries that experienced a war in 1918, the spike was substantially higher in Finland, France, England, and Italy; the only exception was Spain.

In Web Figure 2A–2K, we present the same graphs for the different age groups. If one looks at the younger age groups (i.e., 0, 1–4), there was not a clear overall spike in 1918 for all countries. In the middle age groups, from 15 to 59 years, the spike in 1918 was present in all countries (including Denmark).

And in the group age 60 years or older, there was no clear pattern. What these graphs indicate is that it is important to assess the burden from age-specific data and that assessments using total population data can introduce large errors (e.g., Denmark). The importance of age differences in a pandemic was recognized very early on: "This epidemic presented a sudden and very remarkable change in the behaviour of influenza. It destroyed not the very young or the old, but the adolescent and the adult" (10, p. xiv), and differences in mortality rate by age group have become a signature of an influenza pandemic (13, 14).

Results of the 3 scenarios

Table 1 gives the 1918–1919 results for the 3 scenarios. First, the model-based results without correction are presented, then the model in which the underlying time trend in mortality was corrected for, and, finally, the model in which war in 1918 in Finland, Italy, France, England and Wales together, and Scotland also was corrected for.

The choice of the reference value had a profound influence on the pandemic impact in the different scenarios. The medium scenario in all models had a lower total mortality estimate compared with the low scenario. Correcting for war deaths also substantially reduced the estimated pandemic excess burden. Adding the trend did not have such a strong effect in 1918.

Validity analysis

Our first validity test used different subsets of the data. Ignoring the India data resulted in a reduction of more than 5 million deaths globally in 1918 in all 3 scenarios; the difference was much smaller in 1919 (see Web Table 1A and 1B). Using 20 age categories instead of 10 did not have a strong effect. This analysis was run without the India data because these data were only available for 10 age categories (see Web Table 1A and 1B).

Second, we explored the very high death rate in India (compared with the other 13 countries in the sample) in more detail (see Web Figure 2A–2K), and the crucial question was whether the mortality in India was driven by influenza or other factors (e.g., famine or other illnesses). If we look at the yearly death rates for 1912–1933 for the total population (see Web Figure 2A–2K), the death rate in India was very high in 1917 compared with the previous years (1912–1916), suggesting that other factors affected the death rates in India. If we look at the different age groups in India, there was a spike in 1918 in all these groups (see Web Figure 2A–2K). In the other countries, only in those at war was there a clear spike in these age groups, but the spikes are much smaller. The only exception was Spain. This difference in age effects is contrary to the age signature of influenza pandemics and suggests that other factors caused the high spike in India in 1918.

We also reviewed data for India by month and year. Using the medium calculation procedure, we compared 1918–1919 mortality rates with the average over the reference years per month (see Web Table 2). It is well documented that the second wave peaked in India in September, October, and November (5, 10, 13, 14). For the other months, one would expect that, in 1918 and 1919, compared with the average of the 4 reference years, the excess mortality would be positive sometimes and sometimes negative. In our analysis, however, excess mortality is always positive, suggesting that other factors affected the mortality rate. If we average the excess over the first 8 months of 1918, the monthly mortality rate was 77 per 100,000. This monthly mortality rate is equal to a yearly excess for 1918 of 924 per 100,000 due to other causes, which is substantial.

India had a strong regional variation in death rates in 1918 that had an odd pattern (10, 14). In the western provinces, the excess rates varied between 4,000 and 6,660; in the United Provinces, the excess dropped to 2,290; and in the east (Burma and Bengal), the excess mortality dropped to 600 and 470, respectively—values seen in many other countries. The Statistical Abstract (12) from which we derived our data also reported deaths resulting from other causes. One might expect that influenza would be recorded as respiratory disease, but looking at the different years, there appeared to be hardly any increase in 1918. The strong increase is seen within the death cause "fevers," so the influenza excess mortality is recorded under the same heading that also includes, for example, malaria.

Figure 1 shows how the excess mortality rates behave for different age groups under the 3 scenarios (the rates were controlled

Table 1. Estimated Average Global Mortality Rates Under the 3 Scenarios Using Different Correction Models, Influenza Pandemic, 1918–1919

Estimation Strategy and Year	Low		Medium		High	
	Rate per 100,000	Death Count, millions	Rate per 100,000	Death Count, millions	Rate per 100,000	Death Count, millions
Model-based calculation						
1918	906.0	17.31	839.8	16.04	1,068.4	20.41
1919	147.6	2.84	89.1	1.72	309.2	5.96
Model corrected for time trend						
1918	872.8	16.67	821.6	15.69	1,022.2	19.52
1919	152.5	2.94	103.6	2.00	278.8	5.37
Model corrected for war in 1918 and time trend						
1918	813.4	15.34	761.5	14.54	964.4	18.42
1919	152.7	2.94	103.6	2.00	279.6	5.39

for war and time trend). For the middle age groups, the difference between the scenarios is smallest. The difference is greatest for the oldest and especially in the youngest age groups. If the theory that pandemic excess mortality was smallest in the old and young, the medium and low scenario behave the best, although the low scenario for the young also leads to some overestimation of excess mortality. Web Figure 3A–3E shows how the scenarios behave without corrections and with a correction for the time trend only. We conclude that correcting for war and the time trend helped control for the overestimation in the young and elderly. For 1919, this picture was similar, with the biggest difference in the young (see Web Figure 3A–3E).

In the fourth validity analysis, we assessed the impact of different, fictitious, total influenza mortality estimates on the global death rate in a normal year (1922) and compared these with the observed 1918 total death rates for the countries in the sample (Web Figure 4A and 4B). Generally, when our model was applied to a fictitious excess of 10 million deaths, the results resembled the excess number of deaths in the nonwar sample of European countries in the pandemic years: 20–30 million deaths resembles the numbers in the European countries with war (including the war casualties), 50 million resembles the excess rates in India, and 100 million means that India would be a country below the average excess mortality rate and would not be the hardest hit country by the 1918 pandemic (as it is often described in the literature).

Last, we tested the robustness of our method by checking what excess mortality would be estimated for other influenza pandemics or infectious diseases worldwide that had a spike in incidence in 1–2 years (e.g., smallpox). We selected the other 3 known influenza pandemics in the 20th and 21th century (i.e., 1957–1958, 1968–1969, and 2009–2010), the potential pandemic in 1889–1890, and the smallpox pandemic from 1871 to 1872. Results are presented in the Web Appendix 2, Web Tables 3 and 4, and Web Figure 5A–5T. The results for the 3 other influenza pandemics were reasonably in line with what is reported in the literature (15–17). The burden in 1969 was higher than the burden in 1968, which is also confirmed by the literature. But if we look at the excess mortality per age group (see Web Appendix 2, Web Tables 3 and 4, and Web Figure 5A–5T), the eldest and youngest age groups had a large contribution. Because pandemics appear to have affected mainly the ages groups encompassing 20–60 years (13), a high mortality excess in the oldest and youngest age groups suggests that the estimates might be too high, although it may be that the numbers given in the literature might be too high.

The basic assumption of our assessment is that the average excess mortality rate of a sample of country excess mortality rates is a reasonable approximation of the global excess mortality rate. An important strength of our approach is that each country estimate is based on real data from population registries (vital statistics). The use of total death rates makes underestimation highly unlikely; theoretically, underestimation could only occur if the number of deaths resulting from other causes in 1918 was much lower than that seen in the other years, and this would have had to occur in most countries in our sample. Another way our approach could lead to an underestimation would be that we have unusual reference years, meaning that in 1 year, the mortality was exceptionally high and this had to happen in many countries in the sample. However, this would mainly affect the low scenario; the high scenario would be unaffected. Another possibility that would mostly affect the high scenario would be if the mortality rate for all 4 reference years was exceptionally high, but this would also have to have occurred in many countries in the sample. We have no reason to assume that any of these possibilities occurred in the Human Mortality Database sample data.

Considering we used population registry data, our estimates have a clear and well-defined denominator, which makes the excess mortality rates between countries comparable. Another stabilizing effect on the sample country excess mortality rates is that each country has a sample size of more than 1 million people (except Iceland). Studies on the epidemiology of pandemic influenza have shown that an epidemic takes 2–3 months to sweep homogenously through a country and that case fatality follows a general, not country-specific, age pattern (9, 10, 13, 15). This pattern does not mean that in every part of a country, or between countries, the incidence and excess mortality rates are

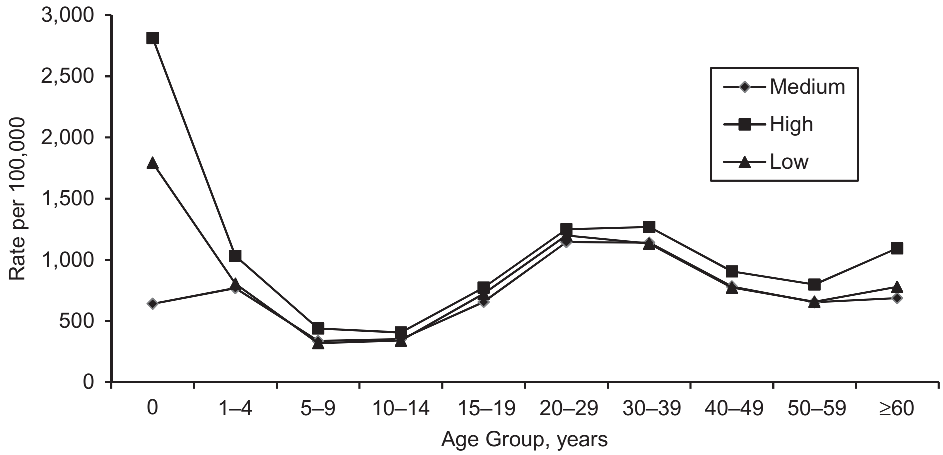

Figure 1. Estimated average excess mortality rate for 1918, per scenario, for the 10 age groups, corrected for war and time trend in mortality.

the same, but by using age-specific estimates, we can prevent under- or overestimation due to different age patterns.

Another aspect that limits under- and overestimations is the high similarity among influenza pandemics, which leads to the assumption that the country-specific excess mortality rates would follow a unimodal distribution. In our sample, most countries had similar corrected excess mortality rates; the only exception was India, which was an outlier at the high end of the distribution. The data from India, in turn, resulted in a much higher average (global) excess mortality rate compared with the situation if India was not included in the sample (Table 2). Even if most of the countries not included in our sample had excess mortality rates higher than the European (corrected) rates but lower than that of India, the effect on the overall global average would be limited (probably a few million more deaths globally). The effect would mainly influence the variance of the distribution. If the countries not in the sample had mortality estimates that resembled or were higher than the excess mortality rate (and also followed India's different age mortality pattern), we would have a bimodal distribution, which suggests the excess mortality age pattern would be different in these countries. It is also important to note that an estimate of 25 million deaths or more for the global burden requires such a bimodal distribution, which would mean that the relation between pandemic excess mortality and age is completely different (the highest mortality would be expected to be in those younger than 14 years and older than 60 years), and that other causes of death besides pneumonia (or, more broadly, respiratory diseases) play a larger role.

To illustrate this latter point, we performed an age analysis of the Indian excess mortality rates by dividing the population into 4 age categories (0–14, 15–24, 25–59, and 60 years or older) and comparing the relative contribution of each age group to the total population in each year. The age group with a relatively lower proportion (and so, on a graph, would show a dip) in 1918 and 1919 compared with the other years would be the age group with the highest relative death rate in the pandemic years. According to this analysis (see Web Figure 6), the age group with the highest relative mortality in India was the age group 0–14 years, which is very unexpected because it means the expected excess mortality age pattern in India was different than that in all other countries in the sample, in which that age group had the lowest relative excess mortality years (see Figure 1 and Web Figure 3A–3E) (9). An explanation for this finding is that changes in other, unknown causes of death not related to the pandemic influenza virus explain the pattern in India. As discussed previously, we think this is more likely than a different mortality age pattern due to pandemic influenza. This oddity was also noted by Hill (18), who decided to remove the mortality rate for the age group younger than 5 years. The change from respiratory cause to other causes was discussed previously for India.

DISCUSSION

We assessed the impact of deaths during the 1918–1919 pandemic using an indirect estimation method that included data for 14 countries, including India, and controlled for wars and the underlying trend in deaths. Our best estimates are the medium and low estimates. The low estimate is closer to the expected estimate for the young and old, and the medium is closer to the expected estimate for the middle age groups. Therefore, our final estimate is the average of the 2 scenarios, which is an estimate of 15 million deaths in 1918 and 2.5 million in 1919 (see Table 2).

Although our results seem to conflict with those reported in the literature, this is mainly the case with more recent articles that give a global burden estimate. For instance, in a study in which a similar method was used to compare data from Japan, the United States, and the United Kingdom (19) (i.e., the reference value is based on averaging over a few years before and after the pandemic), the all-cause excess mortality rate per 100,000 was 970 for Japan, 280 for the United Kingdom. and 590 for the United States. The authors also made the comparison on the basis of cause-specific rates (i.e., pneumonia and influenza), resulting in excess rates of 760 for Japan, 400 for the United Kingdom, and 600 for the United States. These excess mortality rates are in line with our results.

The large variation in the literature between different regions of the same country also is surprising. For instance, in India, the excess mortality rates varied between districts from 470 to 6,660 per 100,000 (14). In US cities, excess mortality rates varied less, from 150 to 800 per 100,000 (for pneumonia and influenza) (20). If we look at the variation between countries, the differences were even larger, from 120 up to 44,500 per 100,000 (3). Are these large differences reasonable? In the 2009 pandemic, the differences between countries were much smaller (14). The reasons for the between-country variation in 2009 has been studied (21) and the most important factor was the difference in the population distribution (a pyramid), with younger populations had a higher burden of death, and, to a much lesser extent, the variation in death rates due to other respiratory

Table 2. Best Estimate for the Global Influenza Pandemic Excess Mortality and Death Toll, 1918–1919[a,b]

Year	HMD Without British India		HMD and British India	
	Rate per 100,000	Death Count, millions	Rate per 100,000	Death Count, millions
1918	487	9.29	787.5	14.94
1919	101.1	1.95	128.2	2.47
Total		11.24		17.41

Abbreviation: HDM, Human Mortality Database.
[a] Model corrected for war in 1918 and time trend for mortality.
[b] Average of the low and medium scenarios is reported.

infectious diseases. Differences in the population pyramid and infectious diseases were smaller in 1918; thus, the between-countries variation in 1918 should be smaller than that in 2009. Large variations in 1918 could be an indication that other causes of death played a role in the number of excess deaths during the pandemic years.

We also show that the estimation method (i.e., a large difference between high and low) can partly explain variation in the overall estimates. For India, estimates have been made that differ by 10 million using similar methods (18). Finding a good method is difficult, which has been recognized for a long time (6, 8). Also, the choice of the reference period can have a profound influence on the estimates. It is generally believed that the highest mortality rate across countries occurred in 1918 during the studied period, but this was not always the case. In British Malaya, for example, during 1911–1920, the death rates in most years was a little greater than 2,000; in 1918, the rate was 5,380, but in 1911, the death rate was 6,510, and this was attributed to a malaria epidemic (22). Such local epidemics would probably not only occur in reference years but also in 1918, resulting in an overestimation of the pandemic burden.

An important advantage of using age-specific, all-cause mortality and comparing the findings with those from reference years is that underestimation is less likely. Overestimation might be more of an issue because we only corrected for war casualties and the time series being nonstationary. A potential important weakness of our sample is that most countries in the sample are in the same part of the world (mainly western Europe). But this is less of a problem for the representativeness of the sample, because pandemic influenza spreads homogenously through a population and excess mortality occurred mostly in the middle age groups and was caused by pneumonia, a pattern seen in all countries globally (10).

The graph in Web Figure 4A is a simple but powerful way to put the global total deaths into context. The graph clearly makes the point that global death burden values of 25 million or more are unlikely, because these values result in average death rates that are above the actual average death rate and, as discussed, a burden of 100 million deaths is highly unlikely because, in that case, there would have been many countries that had even much higher mortality rates than India. Another important point is that researchers should argue how they dealt with potential overestimation in the young and elderly, other causes of increases in the number of deaths (e.g., war, famine, other infectious epidemics), and how they corrected for time trends.

In the present study, the best estimate (including India) for global influenza pandemic deaths is 15 million, with an excess death rate of 788 per 100,000, in 1918; and 2.5 million deaths, with an excess death rate of 128 per 100,000, in 1919. The reader should be aware that this estimate may be too high because of limited possibilities for corrections. If one assumes that, especially for India, the results are a clear overestimation, it is probably better to use the results excluding data from India, which results in an estimate for 1918 of 9.3 million deaths (a rate of 487 per 100,000), and of 2 million deaths (a rate of 101 per 100,000) for 1919. Especially for western India, these problems should be studied in further detail, but it is crucial that information about other causes of death that led to higher mortality rate are included in the analysis and time trends in mortality are also taken into account.

Another way to improve the estimates would be to add population-based, age-specific total death data from other parts of the world. For instance, there is a discussion that China was hit mildly by the 1918–1919 pandemic (23). If this is the case, we may have overestimated the true burden.

To put the global mortality burden for the 1918 pandemic in perspective, one can compare the burden with the other influenza pandemics. Doing so shows the 1918 burden was very high. Interestingly, other aspects of the influenza pandemics are quite similar: The spread around the world was comparable and most deaths occurred in over 6 weeks and spared the young and elderly. But comparing the death burden with that of the 1871 smallpox epidemic (24) indicates the global burden also was higher. This was probably due to the nature of the diseases, with influenza spreading equally through all parts of a country and the mortality rate mostly independent of environmental circumstances. For smallpox, environmental factors (e.g., dirty environment, population density, crowded housing conditions) played an important role, and isolation of infected people had a strong impact on the spread of the disease.

This can be clearly shown with the example of the Netherlands. The smallpox (1871–1872) and influenza (1918) pandemics had a similar nationwide excess mortality rate of approximately 550 per 100,000 people for the country as a whole. But if we look at the rates per province ($n = 11$ in total), we see large differences between the 2 pandemics. For the 1918 influenza pandemic, most provinces had similar mortality rates (although the province with the smallest population size had a rate twice as high). Mortality rates were much higher in the smallpox epidemic in the western part of the country (per 100,000 people, the numbers for the provinces of Noord-Holland, Zuid-Holland, and Utrecht were 638, 1,315, and 1,351, respectively), which includes the most densely populated areas of the country and the 4 largest cities. Here, the smallpox excess mortality was twice that of the 1918 influenza pandemic. In the rest of the country, the opposite occurred: The 1918 influenza excess mortality was twice that of the smallpox epidemic (10, 25).

In conclusion, we have developed an indirect estimation method using vital statistics population data. Our best estimate (a total of 15 million deaths in 1918) is lower than recent estimates (50–100 million) and shows that researchers need to be careful with the methods they choose to make their estimates. For example, researchers must take into account wars and other possible causes of increases in numbers of deaths, and the underlying time trends in mortality. We also show that it is important to test the theoretical feasibility of estimates (e.g., 100 million deaths), because results of such tests suggest the true estimate is very unlikely to be higher than 25 million and probably closer to our final estimate of 17.4 million deaths (1918 and 1919 combined).

ACKNOWLEDGMENTS

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Conflict of interest: none declared.

REFERENCES

1. Jordan EO. *Epidemic Influenza: A Survey*. Chicago, IL: American Medical Association; 1927.
2. Patterson KD, Pyle GF. The geography and mortality of the 1918 influenza pandemic. *Bull Hist Med*. 1991;65(1):4–21.
3. Johnson NP, Mueller J. Updating the accounts: global mortality of the 1918–1920 "Spanish" influenza pandemic. *Bull Hist Med*. 2002;76(1):105–115.
4. Vaughan WT. Influenza: an epidemiologic study. Monographic series no. 1. *Am J Hyg*. 1921;1(5-6):1–260.
5. Frost WH, Sydenstricker E. Epidemic influenza in foreign countries. *Public Health Rep (1896–1970)*. 1919;34(25): 1361–1376.
6. Pearl R. Influenza studies: 1. On certain general statistical aspects of the 1918 epidemic in American cities. *Public Health Rep (1896–1970)*. 1919;34(32):1743–1783.
7. Christian HA. Incorrectness of the diagnosis of death from influenza. Presence of bronchopneumonia in practically all persons severely ill with pneumonia. *JAMA*. 1918;71(19): 1565–1566.
8. Sydenstricker E, King ML. Difficulties in computing civil death rates for 1918, with especial reference to epidemic influenza. *Public Health Rep (1896–1970)*. 1920;35(7): 330–345.
9. Frost WH. Statistics of influenza morbidity: with special reference to certain factors in case incidence and case fatality. *Public Health Rep (1896–1970)*. 1920;35(11):584–597.
10. United Kingdom, Ministry of Health. *Report on the Pandemic of Influenza 1918–19*. London, UK: His Majesty's Stationary Office; 1920.
11. Human Mortality Database. University of California, Berkeley (USA), and Max Planck Institute for Demographic Research (Germany). www.mortality.org. Accessed December 9, 2016.
12. *Statistical Abstract for British India 1915–16 to 1924–25*. London, UK: His Majesty's Stationary Office; Series 59; 1926.
13. Miller MA, Viboud C, Balinska M, et al. The signature features of influenza pandemics – implications for policy. *N Engl J Med*. 2009;360(25):2595–2598.
14. Influenza in India, 1918. *Public Health Rep*. 1919;34(30): 1624–1625.
15. Simonsen L, Spreeuwenberg P, Lustig R, et al. Global mortality estimates for the 2009 influenza pandemic from the GLaMOR project: a modeling study. *PLoS Med*. 2013;10(11):e1001558.
16. Viboud C, Grais RF, Lafont BA, et al. Multinational impact of the 1968 Hong Kong influenza pandemic: evidence for a smoldering pandemic. *J Infect Dis*. 2005;192(2):233–248.
17. Viboud C, Simonsen L, Fuentes R, et al. Global mortality impact of the 1957–1959 influenza pandemic. *J Infect Dis*. 2016;213(5):738–745.
18. Hill K. Influenza in India 1918: excess mortality reassessed. *Genus*. 2011;67(2):9–29.
19. Richard SA, Sugaya N, Simonsen L, et al. A comparative study of the 1918–1920 influenza pandemic in Japan, USA and UK: mortality impact and implications for pandemic planning. *Epidemiol Infect*. 2009;137(8):1062–1072.
20. Deaths from influenza and pneumonia in cities. *Public Health Rep*. 1919:34(11):505.
21. Morales KF, Paget J, Spreeuwenberg P. Possible explanations for why some countries were harder hit by the pandemic influenza virus in 2009 – a global mortality impact modelling study. *BMC Infect Dis*. 2017;17:642.
22. Liew KK. Terribly severe though mercifully short: the episode of the 1918 influenza in British Malaya. *Mod Asian Stud*. 2007; 41(2):221–252.
23. Cheng KF, Leung PC. What happened in China during the 1918 influenza pandemic? *Int J Infect Dis*. 2007;11(4):360–364.
24. Körösi J. *Statistique Internationale des Grand Villes, Mouvement de la Population*. Budapest, Hungary: Maurice Rath; 1876.
25. Departement van Binnenlandsche Zaken. *De Pokken-Epidemie in Nederland in 1870–1873*. 's Gravenhage, The Netherlands: van Weelden en Mingelen; 1875.