

# The 1918–19 influenza pandemic revisited

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**ABSTRACT** The worldwide influenza outbreak of 1918–19 was a medical catastrophe, causing the deaths of around 50 million people. There is evidence however that the major wave, in November 1918, was not part of the pandemic that started in the summer of 1918. The virus responsible for the major wave has been isolated but the structural features responsible for its severity remain incompletely understood. In 1918–19 influenza was an infection so little understood that the government was unsure of what action to take. In contrast, during the pandemic starting in 2009, international and national bodies used many means of communication to keep the public fully informed, with beneficial results. In addition, antiviral agents, a vaccine and antibiotics to treat secondary infection were available. Such a response is possible only with appropriate funding and a comprehensive medical infrastructure, making the potential outbreak of severe influenza in a poor part of the world a matter of grave concern.

**KEYWORDS** Influenza, virus, pandemic, wave, 1918, 2009

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## INTRODUCTION

In Flanders fields the poppies blow  
 Between the crosses, row on row

In 1915 John McCrae, a Canadian physician, wrote these words as he gazed out over the thousands of crosses on the battlefields of Flanders, giving us in the poppy a lasting symbol of remembrance still in use today. Sadly he died of complications following a disease that was largely forgotten by the general public for many decades, the dreaded 'Spanish' flu. Why it was forgotten has been addressed in a previous article.<sup>1</sup> In this paper we discuss why interest in the 1918–19 influenza pandemic has been revived and compare it with the influenza pandemic of 2009. The earlier pandemic probably caused the deaths of over 50 million people worldwide,<sup>2</sup> while far fewer died in 2009. Was the striking difference due solely to the advanced and varied interventions of 2009 or was there something special about the influenza virus of 1918–19 that meant that the number of deaths was inevitable?

Influenza is not a disease of modern times. Hippocrates<sup>3</sup> described a condition with symptoms characteristic of influenza and there have been accounts throughout the centuries of an illness that must, in some instances, have been influenza. Tommasino de' Bianchi described an outbreak in 1510 that left the sufferer with a 'terrible cough that lasts maybe eight days ... [and] they do not perish'.<sup>4</sup> There were several pandemics around the end of the nineteenth century but none garnered much public attention or official concern. What happened in

1918–19 was dramatically worse than anything that had occurred before. Although the severity occasioned only limited concern at the time, the fear that something similar could happen again has troubled medical authorities ever since. That concern extended into the twenty-first century, almost 100 years later when the pandemic of 2009 occurred and health authorities looked to what happened in 1918–19 as a model of what might happen.

## SEQUENCING THE 1918 VIRUS

Almost nothing was known about the specifics of the influenza virus in 1918 and some of the horror of the pandemic was heightened by the mystery surrounding its cause. The influenza virus was not finally isolated until 1931<sup>5</sup> and now, with modern techniques, it is not only readily isolated but it is possible to sequence all the viral ribonucleic acid (RNA) segments. Because of its virulence there has been particular interest in sequencing the influenza virus responsible for the 1918–19 pandemic. The initial problem was obtaining a sample of this version of the virus. In 1997 the Swedish-American virologist Johan Hultin set out for Brevig Mission in Alaska where an Inuit woman, who had died of influenza in 1918, was buried in the permafrost. Digging up such a grave not only raised the possibility of acquiring the infection but also of releasing it more generally. However, four days later the cadaver was found at a depth of seven feet, and the virus, frozen in time, had survived. A sample of lung tissue was shipped back to the USA and no harm came to Hultin.<sup>6</sup>

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The virus was extracted and subjected to sequencing studies by Taubenberger and colleagues.<sup>7</sup> In 2005, after a nine-year effort, the structure of the 1918 viral genome was completed and in a collaborative, multicentre effort, the 1918 virus was reconstructed by plasmid-based reverse genetics.<sup>8</sup> Its severity in an animal model was confirmed.<sup>9</sup> The unique structural feature appears to be a peculiar configuration of the haemagglutinin, affecting receptor binding and membrane fusion.<sup>10</sup> The study, in spite of its significant breakthroughs, did not clarify the relationship between the virus's severity and its structural uniqueness. The matter was discussed in detail by Qi et al.<sup>11</sup>

Non-structural factors may have contributed to its dramatic effect. Most deaths occurred not from the influenza itself but from a bacterial infection (such as pneumonia), as a consequence of the influenza infection. It has been suggested<sup>12,13</sup> that a symbiotic relationship may have existed between the virus and bacterial pathogens. The virus was possibly able to damage the epithelial layer of the respiratory tract, increasing exposure of binding sites for the bacteria to attach themselves. In addition, the poor general health of those involved in the war, both combatants and civilians, as a consequence of four years of privation, may have exacerbated the effect of the virus and, without those factors, the effect might have been less dramatic.

### UNIQUE FEATURES OF THE 1918–19 INFLUENZA PANDEMIC

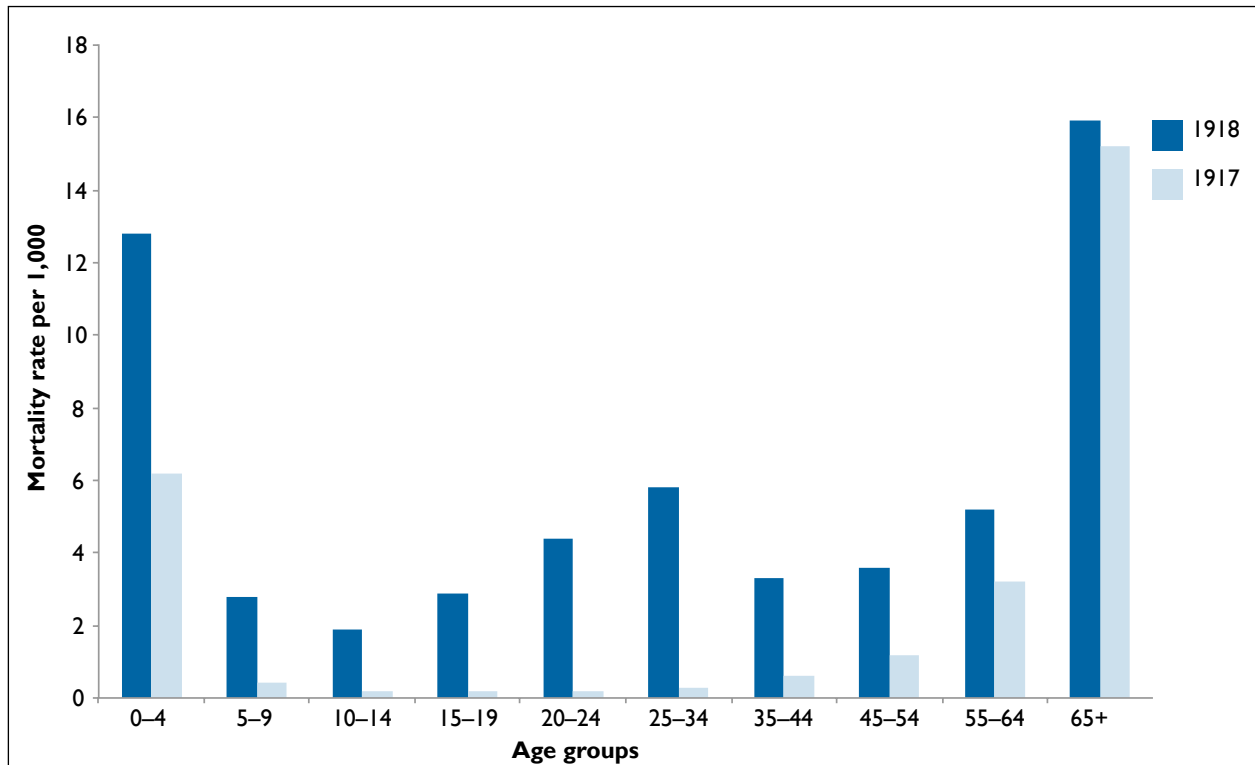
As well as its severity there are other features of the 1918 pandemic that demand attention and, if possible, explanation. Firstly, influenza generally causes greatest mortality among the very young and the elderly, giving rise to a U-shaped graph for the distribution of deaths against age.<sup>14</sup> However, in 1918 the graph was W-shaped.<sup>15</sup> Not only were the very young and the very old affected but there was an even higher mortality among those between the ages of 20 and 40 (Figure 1). The excess mortality seen in the healthy, middle-aged population is explained by a generally accepted effect described as a 'cytokine storm' that occurs with a robust immune system.<sup>1</sup>

Secondly, pandemic influenza normally occurs in waves. The so-called Russian Influenza of 1889–94 came in four waves<sup>16</sup> and the pandemic starting in 1957 in the Far East had its third wave in 1962. However in 1918–19 the waves closely followed one another; the third was only ten months after the first. Thirdly, the normal pattern for a pandemic is as follows: the first wave is the most severe, the second less so and the third the weakest of all. In 1918–19 the most severe by far was the second or 'major' wave in November 1918. It has been suggested that the major wave was caused by a different virus from the original pandemic one, possibly resulting from a

particularly significant genetic mutation. This view was supported by the epidemiologist Dr Rosalind Eggo, who wrote '...the summer wave [of 1918] was so unlike normal flu and more characteristic of the pandemic form. To have another and more severe wave right on its heels [November 1918] is very unusual and suggests that the virus may have genetically altered to escape population immunity.' (Dr Rosalind Eggo, 26 November, 2012.) Another possibility is that the major wave was caused not by a virus characteristic of pandemic influenza but by a seasonal one. There is evidence that from 1915 onwards there was present throughout Europe a particularly virulent form of seasonal influenza which was not given much publicity because of the exigencies of war. Oxford et al.<sup>17</sup> chronicled the outbreaks of severe influenza in France, Norway, Germany and the USA during the years 1915–17 that they considered to be heralds of the major wave in November 1918. This seasonal influenza virus could have spread among the troops at the fighting front and those returning home, and there were soldiers and contract workers from all over the world including India and China, who carried it to places remote from Europe. The onset of winter, normally the trigger for activation of the influenza virus, precipitated the November wave. The spread of influenza throughout England and Wales (the data for Scotland have yet to be considered) indicated a fairly predictable pattern fitting with the normal mathematical model used to describe the spread of an infectious disease.<sup>18</sup> There is further evidence of a virulent influenza virus in 1915 in Scotland contained in this excerpt from letters in the RCPE College Library archives written by a doctor from Golspie concerning a cottage that was functioning as a hospital:<sup>19</sup> 'Influenza has broken out and the men have temperatures and sore throats. The sick men were lying in rooms with several other men, clothes and food lying about. Two men were so bad she got permission from Dr Macaulay to take them into Hospital but there was no room for more...'

As with normal seasonal influenza, the effect of this particularly virulent pathogen was short-lived and had died out before the second wave of pandemic influenza in March 1919. The situation was possibly compounded by the poor health of the population due to the privations of four years of war, making the March wave of the pandemic more severe than it might otherwise have been.

The idea that the virus causing influenza in November 1918 was not the same as that causing the first wave of influenza earlier in the year could be given a more scientific rationale if it were known that the viral RNA of the virus in the major wave was different from that of the other waves. However, it is extremely unlikely that the structure of the virus in the first wave will ever be elucidated in the same way as the major wave. The



**FIGURE 1** The 'W-shaped' graph showing age and mortality in the 1918–19 influenza outbreak (data<sup>14</sup>).

suggestion given for the greater severity of the second wave is, of course, speculative and further complications, which make certainty in this matter impossible, are reviewed by Morens and Taubenberger in a recent publication.<sup>20</sup> The final sentence of that review, based on a remark by the Danish philosopher Søren Kierkegaard about life, is a comment that sums up the situation well: 'influenza epidemics are lived forward and understood backwards'.<sup>20</sup> The recent resurgence of interest in the 1918–19 outbreak of influenza has been partly caused by the threat of global pandemic. In view of what has been suggested about the major wave, how far what happened in 1918–19 is a good model for what might happen in a future pandemic (as was assumed in 2009) is open to question.

## PREPARING FOR ANOTHER PANDEMIC

The possibility that an outbreak of influenza as severe as that in November 1918 could occur again was taken seriously by both national and international health authorities. By 2002 the Chief Medical Officer of England had published *Getting Ahead of the Curve: A Strategy for Combating Infectious Diseases*, assessing influenza as a potent threat, and a Ministerial Committee on Pandemic Influenza Planning (MISC 32) met for the first time in December 2000, 'to guide the preparations for a potential influenza pandemic and related international activity'.<sup>21</sup> In early 2007 an exercise named 'Winter Willow' was undertaken to test the UK's ability to

manage a pandemic. There were 5,000 participants from every level of the government hierarchy, public health authorities and NHS bodies. The aim was to familiarise people with the planned central response and with simulated drug distribution. It tested the speed and flow of information and identified gaps in preparedness. The lessons learned included the value of clear and concise communication with the public and how to manage the surge in demand for medical supplies, including masks, antivirals and antibiotics. Following the exercise the Government published *Pandemic Flu: A National Framework for Responding to a Pandemic*. The main, but not the only, objective in the response was to give pharmaceutical companies, with which the government had 'sleeping contracts', time to develop and manufacture a vaccine, specific for that pandemic virus, in sufficient quantity to immunise the majority of the population.<sup>22</sup> The UK appears to be in the vanguard of countries worldwide in preparing for a pandemic.

The possibility of pandemic became a reality when, in 2009 an influenza outbreak occurred in Mexico. Edgar Hernandez, a five-year-old boy, was shown to be infected by the pandemic H1N1 influenza virus. The World Health Organization (WHO) raised the alert.<sup>23</sup> The outbreak spread rapidly and 142 countries were affected with an estimated 20,000 deaths. The virus arrived in Britain with an outbreak in a school in Birmingham, with one in London following a few days later. The WHO issued strong warnings of what might occur but it soon

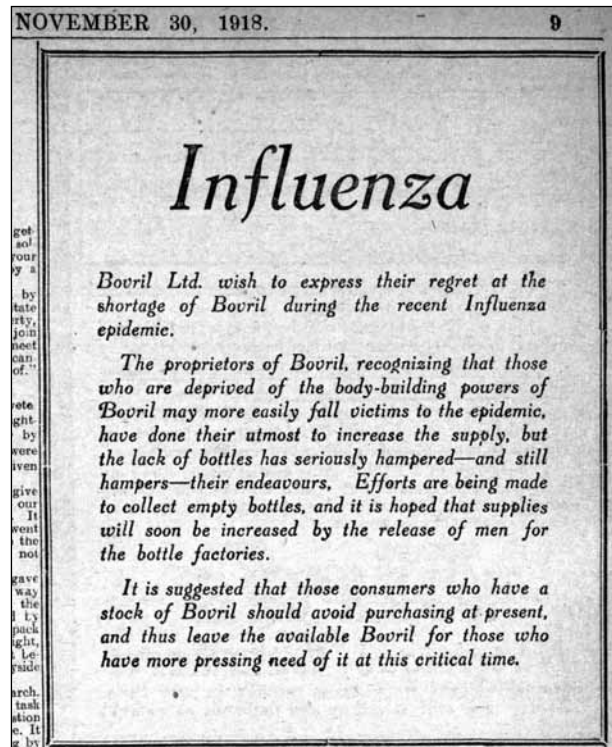
became clear that the effect was to be much less catastrophic than in 1918.<sup>23</sup> Whether this was because the virus was less virulent or due to the preparedness of the world community is not certain; it was possibly a combination of the two. The virulence of the virus was tested on animal models and appeared to be weaker than the 1918 virus but, as virulence is species-dependent, it is not certain that this effect would be the same in humans.

As well as the probable lower virulence of the virus, there was a marked difference in the response of the health authorities to the pandemic and the actions taken in 2009 may have had a profound effect on the consequences of the pandemic; they give a good indication of what may be needed in future outbreaks. Interventions by public authorities during a pandemic are of two kinds: medical and non-medical. Let us consider medical interventions first as, by 2007, every local authority had a detailed plan of medical action.

### MEDICAL THERAPY IN 2009 AND 1918 COMPARED

Medical science progressed so much between 1918 and 2009 that it is not surprising that the responses were very different. By 2009, to allow a specific vaccine to be produced rapidly, contracts had been signed with two pharmaceutical companies, both of which had already started testing 'mock-up' vaccines. The aim in prompt production of the vaccine was to ensure not only that 'key' members of the population were protected but also to ensure that 'herd' immunity was achieved.<sup>24</sup> By 30 March 2009, 37.6% of the at-risk population (those aged over 65, pregnant women and those with specified medical conditions) and 25% of all children had received a vaccine prepared for the prevention of seasonal influenza. Even higher vaccination rates had been achieved in Scotland and the nation was well-prepared for the pandemic. According to a mathematical model, the vaccination of children is the most cost-effective procedure,<sup>25</sup> a fact that may be of importance in poor countries where widespread vaccination is constrained by cost.

In 1918–19, antiviral agents were, of course, unknown but various over-the-counter palliatives were promoted, although not directly described as cures. These included inhalers for congestion, aspirin, quinine, opium, ammonia, iodine, turpentine, salt water, beef tea, Vick vaporub and Bovril. The last was one of the most favoured treatments – a notice about its 'special' properties appeared an issue of *The People's Journal* (a weekly paper circulating in Scotland) (Figure 2).<sup>26</sup> A rather surprising, and hazardous, remedy was drinking carbolic acid, as recommended in a letter to *The Scotsman* newspaper.<sup>27</sup> However a notice appeared subsequently warning patients that it was an



**FIGURE 2** Notice in *The People's Journal* concerning the shortage of Bovril during the 1918–19 influenza pandemic. Local History Centre, Dundee Central Library.

irritant poison and that the quantity suggested was sufficient to poison 250 people and cause 50 deaths.<sup>28</sup> Some prominence was given in the press to the shortage of whisky. Even in the absence of the influenza pandemic this might have been to many a newsworthy item and damaging to the social fabric of society but in 1918, whisky was believed to have a medical role and its scarcity was therefore a matter of medical concern.

By 2009 there were two antiviral agents available for the treatment of the symptoms of influenza: oseltamivir (Tamiflu) taken orally and zanamavir (Relenza) delivered by inhalation or intravenously. While both drugs are effective, they must be taken within 48 hours of being infected by the virus, a stipulation that poses problems for countries with a poor medical infrastructure. The UK had enough stockpiles of Tamiflu to treat 50% of the population, a figure based on the Winter Willow exercise. There were also smaller stockpiles of Relenza in case of a build-up of resistance. By April 2009, the Department of Health had increased the stockpiles to cover at least 80% of the population, more than any other developed nation.<sup>21</sup> Supplies of antibiotic to deal with any bacterial infections secondary to influenza were also available.

## COMMUNICATION TO THE PUBLIC: THE PANDEMICS COMPARED

In terms of non-medical interventions there is again a complete contrast between 2009 and 1918–19. In 1918 there appears to have been a definite policy agreed by the government and newspaper editors to play down the severity of the pandemic. In *The Scotsman* newspaper for the period October–November 1918 influenza was often mentioned but normally as an item at the bottom of the page. In *The People's Journal* for the same period, influenza is mentioned but often in a jocular manner in columns such as 'big truths in little nutshells', as an unfortunate intrusion into the life of the city.<sup>29</sup> All theatres and the La Scala opera house in Dundee remained open in spite of the fact that poor ventilation made these places ideal locations for person-to-person transmission of the virus. Some schools closed but on the choice of the headmaster rather than as the result of a directive from the authorities. In view of the fact that previously healthy people were being taken ill at breakfast time and were dead by evening makes the absence of reporting and an alarmed response difficult to understand. Juliet Barker's book entitled *The Great Silence* is a good account of the social history of the period.<sup>30</sup> The silence of which she writes includes not only the cessation of gunfire, the great silence of the Cenotaph ceremony and the silent grief of those who had lost husbands, other relatives and fiancés during the War but also the silence in the newspapers on the full extent of the seriousness of the influenza outbreak that was killing more than the war had.

In complete contrast, in 2009 communication was viewed as a central component of the Government's response. The WHO released weekly statements, hand washing was urged and helpful phone numbers and website addresses were publicised. The press also played an important role. There were 2,374 news articles in the UK alone between March 2009 and February 2010 concerning the impending pandemic.<sup>31</sup> Not only did these articles compare the current pandemic with those of the past, one in five reported modes of transmission and how to contain the spread. On balance, the press helped shape the public's understanding of the health issues involved.

## FUTURE PANDEMICS

Valuable lessons can be learned from the 1918 and 2009 pandemics. Firstly, and perhaps most importantly, is the value of transparency and communication. In 1918 non-medical intervention appears to have had little effect as the public had so little understanding of what was happening. People were tired after years of warfare and did not want to be informed of yet more tragic deaths about which nothing could be done. Barker has suggested that silence acted as an analgesic.<sup>30</sup> In 2009, however, greater public awareness, coupled with well-informed public health officials, allowed for the quick distribution of clear and concise messages concerning procedures to minimise the effect of the pandemic.

Secondly, it is crucial that every country in the world has a healthcare system with the capacity to tolerate the extra burden of a pandemic, despite its unpredictability. Not only was the influenza virus of 2009 different from what had been predicted, it came from Mexico rather than Asia, as was expected. This level of preparedness is possible for most industrialised countries but poses a significant challenge for countries of the Developing World. This is a particular cause for concern when we consider that with the vast increase in air travel in modern times, predicted to increase further, a newly emerged virus can be taken to the ends of the Earth in a matter of days; the challenge becomes one of vaccinating the population of the whole planet, rather than country by country. There are many countries in the world that do not have the infrastructure nor the financial resources to implement the procedures put in place by the British Government in 2009. The consequences of an influenza pandemic for the population of a poor country already blighted by bad health is a frightening one, for that country and for the rest of the world. The influenza virus is still a long way from being defeated.

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