Mortality Risk Factors During the 1918–1919 Influenza Pandemic in the Australian Army

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Background. Understanding the risk of mortality during the 1918–1919 influenza pandemic could inform preparations for a future pandemic.

Methods. Prospectively collected demographic, hospitalization, and death data from all individuals who served in the Australian Imperial Force from 1914 through 1919 in Europe and the Middle East were abstracted from archived records. Analyses were conducted to determine mortality risk factors.

Results. Hospitalization with a respiratory illness during the spring-summer of 1918 protected soldiers from death (odds ratio, 0.37 [95% confidence interval, 0.25–0.53]; P < .001) but not from hospitalization during the fall-winter of 1918–1919. During the fall-winter of 1918–1919, there was a strong inverse relationship between risk of dying of pneumonia-influenza and time in military service. The pneumonia-influenza death rate among men who enlisted in 1918 (6.33 deaths per 100 person-years) was 9 times higher than that among the 1917 enlistment cohort (0.72 deaths per 100 person-years) and >14 times higher than that among the 1916 cohort (0.43 deaths per 100 person-years), 1915 cohort (0.29 deaths per 100 person-years), and 1914 cohort (0.28 deaths per 100 person-years).

Conclusion. There was a strong inverse relationship between length of service in the Australian Imperial Force and mortality risk from pneumonia-influenza during the fall-winter of 1918–1919. The protective effect of increased service likely reflected increased acquired immunity to influenza viruses and endemic bacterial strains that caused secondary pneumonia and most of the deaths during the 1918–1919 influenza pandemic.

During the influenza pandemic of 1918–1919, there were an estimated 40 million pandemic-related deaths worldwide. An equivalent pandemic today could cause 51–81 million deaths [1]. Understanding the determinants of the risk of dying during the 1918–1919 pandemic may inform preparations for future influenza pandemics [2].

The 1918–1919 pandemic killed many more people than subsequent pandemics (in 1957 and 1968). The mechanisms of its extraordinary lethality include the inherent pathogenicity of [3, 4] and dysregulated immune responses to the pandemic influenza A/H1N1 virus strain and the effects of secondary bacterial coinfections [5, 6]. Influenza typically kills individuals at the extremes of age; however, in 1918–1919, young adults died in numbers and at rates that were unprecedented and not adequately explained [7, 8]. Details regarding the origin of the pandemic strain of the virus, its evolution within the human population, and the pathophysiological mechanisms that produced the unprecedented mortality among young adults are of interest to influenza pandemic response planners.

Because the 1918–1919 pandemic predated the ad-
vent of virology, insights regarding the pandemic influenza A/H1N1 virus have been largely obtained from laboratory studies of archived autopsy and permafrost-preserved specimens [9–11]. The comparative molecular biology of the few available specimens indicates that the pandemic virus evolved its surface hemagglutinin binding characteristics during 1918; evolution of the hemagglutinin of the pandemic strain likely enabled the epidemic waves [12–14]. However, the origin of the pandemic strain and the timing and location of its emergence in humans remain unclear; prominent hypotheses implicate the central plains of the United States (in March 1918) [15, 16] and large military camps in France (in the winter of 1916–1917) [17, 18].

Many military organizations maintain detailed administrative and medical information on all of their members for long periods. Because the 1918–1919 influenza pandemic coincided with the end of the First World War, we investigated the use of prospectively collected information from the military records of all members of the First Australian Imperial Force (AIF). Specifically, we summarized the experience of all Australian soldiers during the times they were deployed to serve in Europe or the Middle East. The original personnel and medical records of all individuals who served in the AIF were digitized and made accessible to the public by the National Archives of Australia [19, 20].

For this report, we used standard epidemiological methods to analyze administrative and medical records abstracted from a database that was assembled by the AIF Project of the University of New South Wales at the Australian Defence Force Academy [20, 21]. Our objectives were to characterize the effects of the 1918–1919 pandemic on a large, well-defined, dynamic cohort of young adults and define the determinants of mortality risk during the fall-winter of 1918–1919.

METHODS

A cohort analysis of the full AIF was undertaken. In addition, a case-control study and unit-specific analyses were performed on smaller data sets. These smaller studies enabled detailed analysis of soldiers’ medical records. The study design for each of these analyses is detailed in this section. Formal institutional clearance was provided from the University of Queensland Human Research Ethics Committee (report no. 2007001146), dated 29 August 2007.

Cohort analysis of the AIF. Cohort analyses were conducted to document temporal changes in the rates of all-cause and pneumonia-influenza–specific mortality—overall, in different enlistment cohorts, and in various military occupational subgroups of the study population. The study period was 1 January 1915 through 31 March 1919. The study population included all individuals who served in the AIF and embarked from Australia for Europe or the Middle East any time during the study period.

The AIF database includes near-complete listings by name and regimental number of all individuals who served in the AIF during the First World War. Each member of the study population was considered to be at risk of dying from pneumonia-influenza (the endpoint of analyses) from the date of embarkation from Australia until the date of death from any cause, termination of AIF service, or the end of the study period (whichever was earlier). Royal Australian Navy sailors (~6000) were not included because they had different and more limited records than their Army and Flying Corps counterparts. Soldiers whose embarkation dates could not be determined or whose service was exclusively in New Guinea as part of the Australian Naval and Military Expeditionary Force were also excluded [20]. Of 336,503 records of AIF members maintained in the National Archives of Australia, 6361 (1.9%) duplicates and 52,632 (15.6%) records that contained missing, uninterpretable, and/or out-of-range information required for analysis (eg, start, embarkation, and/or termination dates of AIF service) were excluded.

The records in the AIF database were linked with death records from the Roll of Honour database [22]. The Roll of Honour database is the official archive of all AIF members who died in military service. Dates and causes of death were ascertained from casualty cards, death notifications, and/or death certificates. Records of deaths due to disease were examined in detail to identify those due to pneumonia and/or influenza. Of 63,666 death records in the Roll of Honour database, 9914 (15.6%) were excluded because they did not match a record on the AIF personnel roster or contained missing and/or out-of-range information required for analysis. Of deaths excluded, 148 (1.5%) were reportedly caused by pneumonia-influenza and 9766 (98.5%) were battle-related, due to other illnesses, or had unknown causes.

For retrospective cohort follow-up analyses, the study population was divided into 5 enlistment cohorts on the basis of dates of assignment to the AIF: the 1914 enlistment cohort began their AIF service between 15 August 1914 and 30 June 1915, the 1915 enlistment cohort began their AIF service between 1 July 1915 and 30 June 1916, the 1916 enlistment cohort began their AIF service between 1 July 1916 and 30 June 1917, the 1917 enlistment cohort began their AIF service between 1 July 1917 and 30 June 1918, and the 1918 enlistment cohort began their AIF service between 1 July 1918 and 31 March 1919. Because the risk of dying from pneumonia-influenza varied from year to year and across seasons, days of AIF service were apportioned among the calendar years and seasons in which the service occurred. For analysis purposes, the winter season was considered to be December through February, the spring-summer season was considered to be March through...
August, and the fall season was considered to be September through November. For the cohort analyses, exposure to risk was quantified by days of AIF service, and mortality rates were expressed as the number of deaths (from all causes or pneumonia-influenza) per 100 person-years of deployed AIF service. The Kaplan-Meier method was used to estimate the cumulative probabilities of dying from pneumonia-influenza over the duration of deployed service of members of various enlistment cohorts and military occupational subgroups of the AIF.

**Case-control analysis.** A case-control analysis was conducted to investigate the relationship between hospitalization for respiratory illnesses prior to the fall of 1918 and risk of dying from pneumonia-influenza between October 1918 and March 1919. Case subjects were defined as deployed members of the AIF who died from pneumonia-influenza during the fall-winter of 1918–1919. Case subjects were identified from reviews of records of hospitalizations, causes of death, death notifications, and death certificates. Specifically, a single physician (G.D.S.) reviewed all death records to identify case-defining diagnoses (as recorded by medical officers in 1918–1919); the case ascertainment process identified 1238 soldiers who died of pneumonia-influenza from October 1918 to March 1919. From all deployed members of the AIF who survived the epidemic period of the fall-winter of 1918–1919 and returned to Australia, 1237 control subjects were randomly selected. Control subjects were selected to match case subjects who were alive on 1 October 1918. Seven Royal Australian Navy personnel were excluded from the case group because Navy records were more limited in detail than those of the other services. For all case subjects and control subjects, dates of previous hospitalizations for acute respiratory illnesses were identified from handwritten or typed service records and casualty cards. Univariate and multivariate logistic regression analyses used acute respiratory illness–related hospitalizations during the epidemic periods of November 1916 through April 1917 and of April 1918 through July 1918 as independent predictors of risk of death from pneumonia-influenza during the epidemic period of the fall-winter of 1918–1919. Multivariate analyses adjusted for length of service on 1 October 1918 (categorical variable).

**Unit-specific studies.** Analyses of 6 military groups were designed to determine whether hospitalization for a respiratory illness during the epidemic period of the spring-summer of 1918 (April through July 1918) modified the risk of hospitalization for a respiratory illness during the epidemic period of the fall-winter of 1918–1919 (September 1918 through March 1919). The records of all soldiers who were assigned to the groups of interest and known to be alive on 1 October 1918 were examined to identify dates of and diagnoses during their hospitalizations (as recorded on individual casualty cards). On 1 October 1918, 1363 and 1243 soldiers were assigned to the 49th and 50th Infantry Battalions, respectively, of the 13th Brigade. Similar methods were used to identify medical officers (n = 1416) and nursing officers (n = 896), Flying Corps officers and enlisted men (n = 2365), and enlisted members of the Engineer Corps (n = 1557) who were alive and deployed overseas on 1 October 1918. For these analyses, the events of primary interest were respiratory illnesses sufficient to require holding at a field medical station or admission to a hospital (such illnesses were not necessarily life-threatening; eg, soldiers unable to march were often evacuated from their units for convalescence). Cumulative incidence percentages of respiratory illness–related hospitalization between 1 September 1918 and 31 March 1919 were compared between subjects with and without respiratory illness–related admissions during the previous spring-summer (1 April 1918 through 31 July 1918). In addition, Cox proportional hazards modeling was used to estimate the relative risks of respiratory illness–related inpatient medical treatment between 1 September 1918 and 31 March 1919 across enlistment cohorts and in relation to respiratory illness–related experience during the preceding spring-summer.

**RESULTS**

The base population for the cohort analysis consisted of 277,510 AIF members who provided 593,801 person-years of service after embarkation from Australia and during the study period. Characteristics of the population overall are summarized in Table 1. During the study period, 19.8% of all study subjects (n = 55,059 deaths, all causes) died in military service. The crude mortality rate (all causes) was 9.27 deaths per 100 person-years. More than 90% of all deaths were combat-related (including deaths from accidents, in prison camps, and at sea); of non–combat-related deaths with known causes, approximately three-fourths (77%) were caused or complicated by infections; and of infectious disease deaths, approximately three-fourths (78%) were due to pneumonia-influenza.

Frequency distributions of weekly non–combat-related and pneumonia-influenza–related deaths in the AIF overall reveal 2 distinct bimodal epidemic periods—the winter of 1916–1917 and the fall-winter of 1918–1919 (Figure 1A). During each major campaign of the AIF (spring-summer-fall of 1915 [Galipoli], summer of 1916 [Somme], fall of 1917 [Passchendaele], and spring-summer of 1918 [second Somme]) there were concurrent peaks in all-cause mortality rates among all of the enlistment cohorts that were in military service at the respective times (Figure 1B).

Pneumonia-influenza mortality rates sharply varied across enlistment cohorts, seasons, and years (Figure 1C). In general, pneumonia-influenza mortality rates were higher in 1918 and 1919 than in earlier years and in fall and winter than in spring-summer seasons. Of particular note, the pneumonia-influenza mortality rate in the 1918 enlistment cohort overall (6.33 deaths per 100 person-years) was ~9 times higher than in the 1917...
enlistment cohort (0.72 deaths per 100 person-years) and >20 times higher than in the 1914 cohort (0.28 deaths per 100 person-years) and 1915 cohort (0.29 deaths per 100 person-years).

Figure 2 summarizes cumulative mortality rates (Kaplan-Meier method) in various subgroups of the AIF in relation to various causes of death—that is, mortality from all causes (Figure 2A), from pneumonia-influenza by enlistment cohort (Figure 2B), and from pneumonia-influenza by military occupational group (Figure 2C). Notably, the cumulative probability of dying from pneumonia-influenza during AIF service was >2 times higher for the 1918 enlistment cohort (3.7%) than for the 1914 enlistment cohort (1.7%), even though the latter had ~8 times longer duration of AIF service than the former. Across occupational groups, the lowest and highest cumulative pneumonia-influenza mortality rates were observed among medical and nursing personnel (0.19 deaths per 100 person-years) and among tunnelers and miners (0.74 deaths per 100 person-years), respectively (Figure 2C).

In case-control analyses, hospitalization for a respiratory illness in the fall-winter of 1916–1917 did not protect soldiers from death during the influenza epidemic in the fall-winter of 1918–1919 (Table 2). However, soldiers who were hospitalized with a respiratory illness in the spring-summer of 1918 had a statistically significantly lower risk of death during the fall-winter epidemic period (odds ratio, 0.37 [95% confidence interval, 0.25–0.53]; P < .001). Also, soldiers with the least duration of military service in the fall-winter of 1918–1919 had significantly higher risk of dying from pneumonia-influenza, compared with that of their more seasoned counterparts (Table 2). When time in military service was controlled, association with rank (data not shown) was not an independent correlate of risk of dying from pneumonia-influenza; however, age was a significant correlate of pneumonia-influenza–related mortality risk (Table 2). Diarrheal disease was also tested as a non-respiratory cause for hospitalization and showed no difference between case subjects and control subjects.

In the AIF, infantry units of similar types (eg, battalions and brigades) had similar organizational structures and numbers of men. Of note, however, pneumonia-influenza–related mortality rates widely varied (by >20-fold) across AIF infantry battalions. For example, 2 infantry battalions colocated in the 13th Infantry Brigade had widely different pneumonia-influenza mortality experiences during the epidemic period of the fall-winter of 1918–1919 (cumulative mortality of the 49th Battalion, 7.0 deaths per 1000 men; cumulative mortality of the 50th Battalion, 0.8 deaths per 1000 men).

Among members of these infantry battalions, as well as among officers of the Medical, Nursing, and Flying Corps and enlisted members of the Engineer and Flying Corps, hospitalization for a respiratory illness during the fall-winter of 1916–1917 did not decrease the risk of hospitalization during the fall-winter of 1918–1919 (data not shown). Nurses who were hospitalized during the spring-summer of 1918 were less likely to be hospitalized during the fall-winter of 1918–1919. However, soldiers who were hospitalized during the spring-summer of 1918 were more likely to be hospitalized during the fall-winter of 1918–1919 (data not shown).
Figure 1. Epidemic curves of mortality in the Australian Imperial Force from 1914 through 1919. A. Histogram of weekly non–combat-related and pneumonia-influenza (P&I)–related deaths. B. All-cause mortality rates by enlistment year cohort, by season and year. C. Mortality rates for pneumonia-influenza by enlistment year cohort, by season and year.
Figure 2. Kaplan-Meier survival curves for the entire Australian Imperial Force from 1914 through 1919, as described in Table 1. Enlistment year cohorts are defined by the year in which the soldier joined the Army. Military occupation consists of type of unit (infantry, artillery, mounted, or all other). By 1918, the infantry were primarily located in Europe and the cavalry were largely restricted to the Middle East. A, Survival curve for mortality due to all causes by enlistment year cohort. B, Survival curve for mortality due to pneumonia-influenza by enlistment year cohort. C, Survival curve for mortality due to pneumonia-influenza by military occupation.
Table 2. Case-Control Study of Death from Influenza from 1 October 1918 through 31 March 1919 among the Australian Imperial Force

<table>
<thead>
<tr>
<th>Exposure variable</th>
<th>Case subjects (n = 1231)</th>
<th>Control subjects (n = 1237)</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory illness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>April 1918 through July 1918</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>41</td>
<td>105</td>
<td>0.37 (0.25–0.53)</td>
<td>0.39 (0.27–0.57)</td>
</tr>
<tr>
<td>No</td>
<td>1190</td>
<td>1124</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
</tr>
<tr>
<td>November 1916 through April 1917</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>93</td>
<td>96</td>
<td>0.96 (0.72–1.30)</td>
<td>1.12 (0.83–1.51)</td>
</tr>
<tr>
<td>No</td>
<td>1138</td>
<td>1133</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
</tr>
<tr>
<td><strong>Type of military unit</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infantry</td>
<td>467</td>
<td>676</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
</tr>
<tr>
<td>Artillery</td>
<td>189</td>
<td>87</td>
<td>3.14 (2.38–4.16)</td>
<td>3.17 (2.39–4.20)</td>
</tr>
<tr>
<td>Light horse</td>
<td>71</td>
<td>147</td>
<td>0.70 (0.51–0.95)</td>
<td>0.71 (0.52–0.97)</td>
</tr>
<tr>
<td>Other</td>
<td>504</td>
<td>327</td>
<td>2.23 (1.86–2.68)</td>
<td>1.86 (1.53–2.25)</td>
</tr>
<tr>
<td><strong>Age on 1 October 1918</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15–19 years</td>
<td>56</td>
<td>46</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
</tr>
<tr>
<td>20–24 years</td>
<td>389</td>
<td>437</td>
<td>0.73 (0.48–1.11)</td>
<td>1.91 (1.15–3.14)</td>
</tr>
<tr>
<td>25–29 years</td>
<td>426</td>
<td>396</td>
<td>0.88 (0.58–1.34)</td>
<td>2.53 (1.52–4.20)</td>
</tr>
<tr>
<td>30–34 years</td>
<td>213</td>
<td>191</td>
<td>0.92 (0.59–1.42)</td>
<td>2.50 (1.48–4.22)</td>
</tr>
<tr>
<td>&gt;34 years</td>
<td>145</td>
<td>162</td>
<td>0.74 (0.47–1.15)</td>
<td>2.15 (1.26–3.69)</td>
</tr>
<tr>
<td><strong>Time from enlistment up to 1 October 1918</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;4 months</td>
<td>83</td>
<td>8</td>
<td>11.19 (5.35–23.40)</td>
<td>...</td>
</tr>
<tr>
<td>4–8 months</td>
<td>78</td>
<td>26</td>
<td>3.24 (2.04–5.14)</td>
<td>...</td>
</tr>
<tr>
<td>8–12 months</td>
<td>42</td>
<td>27</td>
<td>1.68 (1.02–2.77)</td>
<td>...</td>
</tr>
<tr>
<td>1–2 years</td>
<td>211</td>
<td>225</td>
<td>1.01 (0.80–1.27)</td>
<td>...</td>
</tr>
<tr>
<td>2–3 years</td>
<td>396</td>
<td>492</td>
<td>0.87 (0.72–1.05)</td>
<td>...</td>
</tr>
<tr>
<td>&gt;3 years</td>
<td>420</td>
<td>453</td>
<td>1 (Reference)</td>
<td>...</td>
</tr>
</tbody>
</table>

**NOTE.** Column subtotals may not equal the number of persons because of missing records. CI, confidence interval; OR, odds ratio.

a Adjusted for time from enlistment up to 1 October 1918.

than their counterparts to be hospitalized during the fall-winter of 1918–1919 (20% vs 29%). However, in all other groups (eg, 50th Infantry Battalion), the risk of hospitalization during the fall-winter of 1918–1919 was similar to or higher than the risk among those treated in a medical facility for a respiratory illness during the spring-summer of 1918 (Table 3). Finally, Cox proportional hazards analyses revealed that subjects with the longest military service (ie, those with the earliest enlistment dates) had the lowest risk of hospitalization for a respiratory illness during the fall-winter of 1918–1919 (Table 4).

**DISCUSSION**

These results document the experiences of Australian soldiers who were deployed overseas for wartime service. Among them, there were epidemic peaks of pneumonia-influenza–related mortality in the spring-summer of 1915, the winter of 1917, and the fall-winter of 1918–1919. During each epidemic period, mortality rates were highest among the soldiers who were newest to military service. It is implausible that soldiers who were deployed for different durations were exposed to different respiratory infectious agents. It is likely that after exposure to the same respiratory infectious agents, relatively recent soldiers were more immunologically susceptible than were more seasoned soldiers to more circulating infectious agents and/or had more virulent clinical expressions of infections with those agents. This finding suggests that individuals who are new members of dynamic, congregated groups (such mobilization camps, recruit camps, and deployed military units) are likely to be more susceptible to and may have more severe clinical expressions of acute respiratory infections in general [23, 24].

Among deployed Australian soldiers, pneumonia-influenza–related mortality during the fall-winter of 1918–1919 was lower among those in medical and nursing occupations than among those in any other major occupational group. Undoubtedly, by September 1918, soldiers with the longest durations of military service and those in medical and nursing occupations (groups with relatively low mortality during the lethal period during the fall-winter of 1918–1919) had been exposed to more and
produced protective immunity against the pandemic influenza could not have been caused by an influenza virus strain that epidemics (the first wave of the pandemic by many accounts) from illness in the fall-winter, the widespread spring-summer individuals affected in the spring-summer were not protected much lower mortality from pneumonia-influenza. Because in-

through July 1918) had similar rates of hospitalization for but 

counterparts, soldiers who had been hospitalized for a respi-

There is no evidence (and no reason to expect) that a wider variety of endemic viral and bacterial respiratory pathogens. There is no evidence (and no reason to expect) that these groups were less frequently or intensively exposed to the influenza A/H1N1 virus that caused the widespread epidemics of the fall-winter of 1918–1919. On the contrary, during the pandemic period, many medical and nursing personnel were continuously exposed to high concentrations of influenza virus and other viral and bacterial respiratory infectious agents [25–27].

During the fall-winter of 1918–1919, compared with their counterparts, soldiers who had been hospitalized for a respiratory illness during the preceding spring-summer (April through July 1918) had similar rates of hospitalization for but much lower mortality from pneumonia-influenza. Because individuals affected in the spring-summer were not protected from illness in the fall-winter, the widespread spring-summer epidemics (the first wave of the pandemic by many accounts) could not have been caused by an influenza virus strain that produced protective immunity against the pandemic influenza A/H1N1 virus strain. However, respiratory illnesses during the spring-summer were associated with increased survival of acute respiratory illnesses during the fall-winter. Perhaps individuals affected during the spring-summer acquired antibodies or cell-mediated immune responses to an influenza virus (eg, A/HxN1) that prevented death but not infection with the pandemic influenza A/H1N1 virus strain. In addition, acute respiratory illness in the spring-summer may have caused a (nonspecific) decrease in the intensity of the immune response to influenza A/H1N1 virus infection in the fall-winter (thus, lowering the risk of lethal damage from cytokine storm).

In summary, military and medical records of Australian soldiers during the First World War document that those who had been serving the longest, those in medical and nursing occupations, and those who had been hospitalized with respiratory illnesses during the previous spring-summer were relatively protected from death during the lethal fall-winter influenza epidemics. Because the influenza A/H1N1 virus strain was novel, nearly all Australian soldiers were likely immuno-

### Table 3. Unit-Specific Risk of Hospitalization for Pneumonia-Influenza among the Australian Imperial Force, by Epidemic Period

<table>
<thead>
<tr>
<th>Variable</th>
<th>49th Battalion</th>
<th>50th Battalion</th>
<th>Medical officers</th>
<th>Nurses</th>
<th>Engineers</th>
<th>Flying Corps</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>1208 (89)</td>
<td>144 (11)</td>
<td>1054 (85)</td>
<td>184 (15)</td>
<td>1280 (91)</td>
<td>842 (94)</td>
</tr>
<tr>
<td>Yes</td>
<td>1435 (93)</td>
<td>114 (7)</td>
<td>126 (9)</td>
<td>40 (80)</td>
<td>126 (9)</td>
<td>842 (94)</td>
</tr>
</tbody>
</table>

**NOTE.** Column and row subtotals may not equal the number of persons because of missing records.

### Table 4. Unit-Specific Risk of Hospitalization for Pneumonia-Influenza between 1 September 1918 through 31 March 1919 among the Australian Imperial Force, by Enlistment Date

<table>
<thead>
<tr>
<th>Variable</th>
<th>49th Battalion</th>
<th>50th Battalion</th>
<th>Nurses</th>
<th>Engineers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization for respiratory illness, April 1919 through July 1918</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
<td>1 (Reference)</td>
</tr>
<tr>
<td>Yes</td>
<td>0.90 (0.61–1.34)</td>
<td>1.29 (0.87–1.91)</td>
<td>0.69 (0.37–1.31)</td>
<td>1.05 (0.66–1.66)</td>
</tr>
</tbody>
</table>

**NOTE.** Results are of a Cox proportional hazards model. Members of the Medical and Flying Corps are not included because the assumption of proportional hazards did not hold for these models. All subjects were still serving on 1 October 1918. Follow-up starts on 1 September 1918 or on the date of enlistment (if the date of enlistment is between 1 September 1918 and 30 September 1918). The event of interest is hospital admission for respiratory illness between 1 September 1918 and 31 March 1919. Follow-up ends on the date of hospital admission for respiratory illness, the date of death, the date of return to Australia, or 31 March 1919, whichever is earlier. Only hospital admissions during deployment are known; subjects are assumed to have had no hospital admissions in the intervals before enlistment date. CI, confidence interval.

a Adjusted hazard ratios from model containing enlistment cohort and previous hospitalization indicator.
logically susceptible to it; and because influenza A/H1N1 virus epidemics were widespread, most soldiers were likely exposed during the fall-winter of 1918–1919. Still, there were significant differences across subgroups in pneumonia-influenza–related mortality; the findings suggest that decreased lethality of infection with the pandemic strain likely resulted from nonspecific immunological protection, which was perhaps related to previous infections with another influenza virus strain and/or other respiratory infectious agents.

The First World War and its associated influenza pandemic occurred at an epidemiological transition point from intermittent to annual influenza virus infections [11, 25]. During the 1918–1919 pandemic, for the first time in history, many individuals were infected for the second time in their lives with pandemic strains of influenza A virus (from the pandemics of 1890–1892 and 1918–1919). We hypothesize that lethal cytokine storms (and the resulting mortality peaks) among young adults in 1918–1919 may have resulted from sequential infections—years apart from each other—with heterosubtypic strains of influenza A virus that shared 1 or more immunodominant epitopes of internal proteins; and that previous infections with multiple and varied other respiratory infectious agents modulated the intensity of immune responses to influenza A/H1N1 virus—and, in turn, decreased the clinical severity of influenza A/H1N1 virus–related illnesses. As a result, the Australian soldiers (most notably, medical workers) were relatively protected from the lethal pathological effects of excessive immune responses to influenza A/H1N1 virus.

Detailed genomic studies using all available influenza A/H1N1 viral sequences strongly suggest that 3 influenza A/H1N1 viral lineages (pandemic, seasonal, and swine) separated several years prior to 1918 [28, 29]. In turn, the events of 1918 may be manifestations of sequential pandemics with different influenza A/H1N1 viruses: the early to mid 1918 first wave was caused by a seasonal influenza A/H1N1 virus strain noted for its high transmissibility, and the fall-winter 1918–1919 second and third waves were caused by a pandemic influenza A/H1N1 virus strain noted for its lethality. Important immunological differences (resulting from the evolutionary separation of viral lineages) between the surface glycoproteins of the viruses are required to explain 2 sequential influenza pandemics during 1918.

The influenza virus of 1918 was not inherently or intrinsically lethal. Even without antivirals, antibiotics, or influenza virus vaccines, the vast majority of infected individuals had uncomplicated, self-limited clinical courses of disease; in most affected populations and settings, case fatality was <2%. The finding strongly suggests that host-specific factors, rather than virus-specific factors, were the key determinants of the clinical expressions of infections with the pandemic virus.

The current influenza pandemic is caused by an influenza A/H1N1 virus that is a direct descendent of the 1918–1919 pandemic strain; thus, in a sense, the current pandemic is a continuation of the 1918–1919 pandemic [30]. Given the relatively few deaths among massive numbers of individuals infected with essentially the same virus, it is clear again that host factors largely determine mortality risk. In the fall of 1918, soldiers who were new to military service were at the highest risk of dying after influenza virus infection; in the fall of 2009, individuals with immunity that was compromised by underlying diseases, pregnancy, obesity, and certain medications were at the highest risk of dying [31]. In many places of the world, antivirals, antibiotics, viral and bacterial vaccines, and state-of-the-art life-supporting care are available to counter the life-threatening effects of pandemic influenza. However, particularly in populations and settings in which modern countermeasures are not available, the identification and protection of the relatively few individuals at the highest risk of severe clinical manifestations after influenza virus infection should be high research priorities. The findings of this study suggest that individuals who have been exposed to multiple influenza A viruses and other respiratory pathogens may have relatively mild clinical expressions of infections with novel influenza A virus strains. If this is the case, then during the current and future influenza A virus pandemics, relatively few deaths would be expected among previously healthy members of most modern populations (eg, those exposed to annual epidemics of seasonal influenza). Although the pandemics of 1918–1919 and 2009 were caused by similar influenza viruses, they had very different mortality outcomes largely because of the sequence and timing of previous respiratory infections. We think that the reoccurrence of a highly lethal influenza pandemic that is similar to the 1918–1919 pandemic is a very unlikely event.

Acknowledgments

We have been privileged to access information concerning the Australian Imperial Force during 1914–1919 and recognize the extraordinary sacrifices made by these soldiers. The data that we report here were graciously provided from sources at the National Archives of Australia, the Australian War Memorial, and the Australian Imperial Force Database Project of the University of New South Wales. We thank Dr Jeffery Taubenberger for valuable discussions on influenza, Prof Tracy Hussell for discussions on immunology, and many medical librarians for help in locating references.

References

27. Eyre JWH, Lowe EC. Report upon the autumn influenza epidemic 1918 as it affected the NZEF in the United Kingdom. Lancet 1919; 553–560.