Estimating Parameters of the 1918-19 Influenza Epidemic on U.S. Military Bases

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Occasional shifts in the influenza virus generates a new variant, posing potential threat of a deadly epidemic. This type of shift occurred with the 1918-19 flu with devastating consequences in the U.S. and worldwide. Using newly developed data from 18 U.S. military establishments during the 1918-19 flu epidemic, we estimate parameters of the Susceptible-Exposed-Infectious-Asymptomatic-Removed epidemic model. Our estimates show considerable variation in the value of the infectivity parameter across bases. This variation is uncorrelated with base size or beginning date of the epidemic. Results indicate that the epidemic on U.S. military bases was more infectious than those of in England and Wales.

INTRODUCTION

Occasional shifts in the flu virus generates a new variant. As individuals have little immunity to this new variant or the new strain is vaccine resistant, there is potential for a deadly pandemic. In 1918-1919, a new flu subtype killed at least 675,000 people in the United States and perhaps 40 million people worldwide (Brainerd and Siegler, 2003).

Formal epidemic models help to identify the factors influencing the pace of epidemics and the proportion of the population to be infected without intervention. They also provide tools for analyzing the effects of strategies to combat disease, including identification of disease outbreaks, evaluating treatments, and estimating the impacts of quarantines and vaccination programs. There are several studies using these models to investigate strategies for responding to pandemic influenza (Meltzer, et al. 1999; Patel, et al. 2005; Longini, et al. 2005; Gani, et al. 2005; Ferguson, et al. 2007; Medlock and Galvani, 2009). In this study, we use new data from 18 U.S. military establishments during the 1918-1919 flu epidemic to estimate parameters of the Susceptible-Exposed-Infectious-Asymptomatic-Removed (SEIAR) epidemic model.

There have been a number of recent attempts to estimate parameters of the 1918-1919 influenza epidemic. Unfortunately, historical data generally do not provide the richness of contemporary notification systems. The studies (Gani, et al., 2005; Ferguson, et al., 2006; Viboud, et al., 2006; and Chowell, et al., 2008) rely on weekly rather than daily data. The data represents counts of deaths rather than cases of influenza. So, one must make very strong assumptions about the case fatality rate and the lag between the onset of the disease and subsequent mortality to identify the time patterns of influenza cases needed for estimating epidemic model parameters.

MATERIALS AND METHODS

Epidemic (SEIAR) Model
   The authors use Susceptible-Exposed-Infectious-Asymptomatic-Removed (SEIAR) epidemic model for the estimation following Chowell, et al. (2006a, b). In the model, the population is divided into the following groups: the susceptibles, the infectives, the exposed, and the removed. Susceptibles (*S*) are individuals who are at risk of catching the disease. Exposed (*E*) are individuals who have been infected but are not yet infectious. Infectives have the disease and can transmit it. The infectives include two groups: the fully infectious (*I*) and asymptomatics (*A*). Removed (*R*) are individuals who had the disease, but have recovered and can no longer transmit it. Deceased (*D*) represents the number of individuals who have died.
   The total size of the population at time t equals the sum of these groups:

$$N(t) = S(t) + E(t) + I(t) + A(t) + R(t) + D(t). \tag{1}$$

   In SEIAR model, the number of infections among the susceptible population in a period of time depends on the rate at which the susceptibles contact the infectious (δ) and the transmissibility of the disease given contact (τ). After contact, some proportion of the susceptibles becomes exposed and there is an incubation period before the exposed become infectious. A compartmental SEIAR model diagram of influenza transmission is presented in Figure 1.

FIGURE 1
COMPARTMENTAL SEIAR MODEL DIAGRAM OF INFLUENZA TRANSMISSION
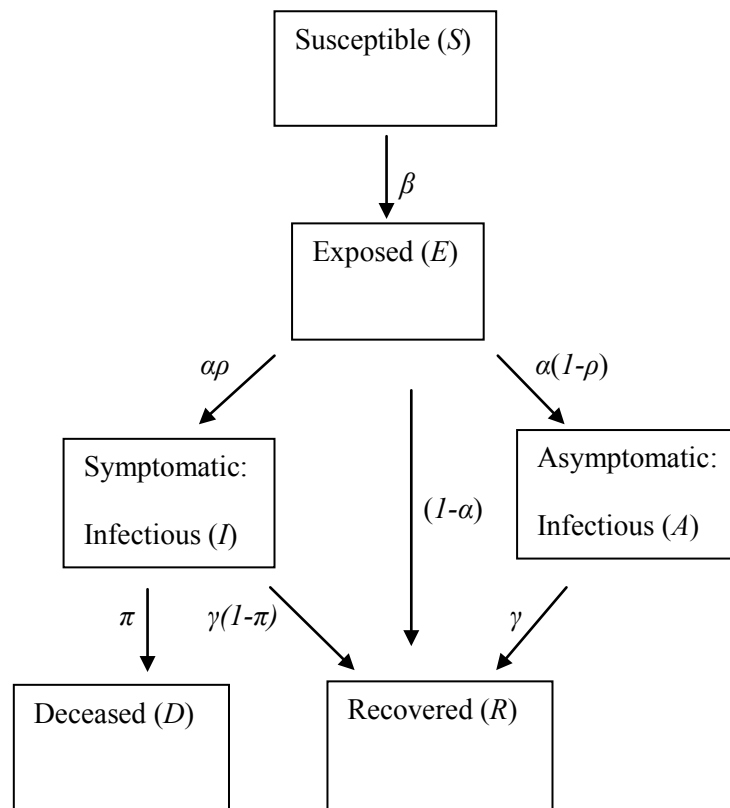
Assuming the probability that an asymptomatic individual transmits the disease is a fraction (q) of the probability that a fully infectious individual transmits the disease, and contacts among members of the population are random, the reduction in the number of the susceptibles due to infection per period is given by:

$$\frac{dS}{dt} = -\delta\tau\frac{S(t)[I(t)+qA(t)]}{N(t)} = -\beta\frac{S(t)[I(t)+qA(t)]}{N(t)}, \tag{2}$$

where β is called the infectivity parameter.

The number of exposed is augmented by the decrease in the number of susceptibles from (2) and is reduced by the number who become fully infectious or asymptomatic:

$$\frac{dE}{dt} = \beta\frac{S(t)[I(t)+qA(t)]}{N} - \alpha E(t), \tag{3}$$

where α is the rate at which the exposed become infectious.

The number of individuals who are fully infectious depends upon the rate at which the exposed become infectious (α) and the fraction who become fully infectious (ρ) and decreases by those who recover or die:

$$\frac{dI}{dt} = \rho\alpha E(t) - (\gamma + \pi)I(t), \tag{4}$$

where γ is the recovery rate and π is the death rate among the fully infectious.

Asymptomatics are the remainder of individuals who convert from exposed to infectious.

$$\frac{dA}{dt} = (1-\rho)\alpha E(t) - \gamma A(t). \tag{5}$$

The change in the size of the removed population is given by:

$$\frac{dR}{dt} = \gamma[I(t)+A(t)]. \tag{6}$$

The change in the number of those who have D(t) is given by:

$$\frac{dD}{dt} = \pi I(t), \tag{7}$$

where the mortality rate π is given by $\pi = \gamma[\text{CFR}/(1 - \text{CFR})]$ and CFR is the average case fatality rate.

For epidemics of new strains of pandemic influenza, it is assumed that the population is wholly susceptible. In this case, the parameters of the model can be summarized by the basic reproductive ratio (R_0), which equals the average number of secondary cases arising from the introduction of a single infective when the population is wholly susceptible. If $R_0 > 1$ in a deterministic epidemic model, then the introduction of an infective into a population will generate an epidemic, whereas if $R_0 < 1$, it will not. The basic reproductive ratio in our model is given by

$$R_0 = \beta \left[\rho \frac{1}{\gamma + \pi} + (1 - \rho) \frac{q}{\gamma} \right]. \tag{8}$$

Data

There were at least two waves of the influenza in 1918. The first began in March of 1918 and spread sporadically across the US and Europe. The first and second waves were believed to be similar strains, but the relative mildness of the illness and the length of time the first wave took to spread suggest that it was not yet as perfectly adapted to humans as it would later become (Reid, et al. 2001). The first case of the second wave appeared on September 8 at Camp Devens, MA. It then spread to other military bases along the East coast and among civilians from Maine to Virginia, paralleling the pattern in military establishments (Crosby, 1976).

TABLE 1
DESCRIPTIVE STATISTICS OF THE 1918-19 FLU EPIDEMIC AT U.S. MILITARY BASES

Station	Average Base Population	No. of Infl. cases	No. of Deaths	Epidemic Infl. attack rate /1000	Epidemic death rate /1000	Case fatality/100	Duration and Epidemic in days
Cape May, NJ (N)	1,720	150	14	87.20	8.13	9.33	12 (9/23-10/4)
Gulfport, MS (N)	1,772	822	18	463.88	10.15	2.18	27 (9/28-10/24)
New Orleans, LA (N)	2,542	952	33	374.50	12.98	3.46	29 (9/26-10/24)
Seattle, WA (N)	4,158	724	34	174.12	8.17	4.69	15 (9/25-10/8)
Charleston, SC (N)	4,167	1,118	26	265.89	6.23	2.23	67 (9/11-11/16)
Boston, MA (N)	4,454	804	52	180.46	11.67	6.46	35 (8/28-10/1)
San Diego, CA (N)	4,932	628	19	127.34	3.85	3.02	23 (9/8-9/30)
Pensacola, FL (N)	5,418	1,393	24	257.10	4.42	1.72	31 (9/15-10/15)
Puget Sd., WA (N)	6,370	568	60	89.16	9.41	10.55	24 (9/17-10/10)
Philadelphia, PA (N)	6,434	1,246	78	193.96	12.12	6.26	29 (9/11-10/9)
Norfolk, VA (N)	7,994	991	69	123.96	8.63	6.96	21 (9/16-10/6)
Quantico, VA (N)	8,244	3,056	117	370.69	14.19	3.82	75 (9/9-11/22)
Newport, RI (N)	9,493	1,449	113	152.63	11.9	7.79	15 (9/10-9/24)
Hampton Rd., VA(N)	11,104	3,005	175	270.62	15.76	5.82	25 (9/15-10/9)
Lewis, WA (A)	13,031	5,033	177	386.23	13.58	3.52	61 (9/16-11/15)
Pelham, NY (N)	14,200	2,399	145	168.94	10.21	6.04	29 (9/23-10/21)
Upton, NY (A)	44,000	6,947	438	157.87	9.95	6.30	79 (9/13-11/30)
Great Lakes, IL (N)	44,605	9,623	924	215.73	20.71	9.60	30 (9/12-10/11)
Combined Total (Avg)	**194,638**	**40,908**	**2,516**	**(210.18)**	**(12.93)**	**(6.15)**	**(34)**

(N): Naval base
(A): Army base
Average populations (complements) of Army bases during the epidemic are derived from the best approximation of remaining historical records.

The pandemic seemed to have reached its peak among US civilians roughly two or more months after the virus started to infect the encampments along the coast. There only exist some incomplete records of

the spread of the disease in the civilian population. Military records are much more detailed and comprehensive.

The data used in this study come from two different sources. First, actual daily influenza case numbers and complement size information from two army bases, Upton and Fort Lewis, were gathered from the National Archives at College Park MD. Second, Chart 6 of the *Annual Report of the Navy Department* (1920) for the fiscal year 1919 presents a graph of the daily case incidence per 1000 station complement on 16 larger naval stations (p.2426).

Table 1 identifies the bases and provides summary statistics. The incidence data along with estimates of daily complements at the naval bases were used to determine the reported daily number of new cases. For most bases in the dataset, weekly average complement figures were reported in the *Annual Report of the Navy Department* (1920, Table No. 1, p.2430). The base populations and the number of susceptibles were adjusted to reflect inflows of additional susceptibles during the epidemic or outflows of troops using available information.

We used the daily number of cases to estimate the components of SEIAR model given in equation 1. Following Longini, et al. (2004, 2005), we assumed a mean incubation period of 1.2 days and an average infectious period of 4.1 days (30% for 3 days, 40% for 4 days, 20% for 5 days, and 10% for 6 days' infectious period). As in Longini, et al.(2004), we also assumed 67% of infected people developed symptoms, 33% remained asymptomatic, and that symptomatic people were half as infectious as those with influenza symptoms. Finally, equation 2 was used to estimate daily values of the infectivity parameter β.

RESULTS

Table 2 presents average values of the daily estimates of β. Four bases (e.g., Boston, Charleston, Gulfport, and Quantico) had substantial secondary peaks in the later stages of the epidemic.

Variation of β over Time and Across Bases

SEIAR model assumes that β is constant over time. Philipson argues that people may change their behavior during an epidemic (Philipson, 1996). They may reduce the rate at which they contact potential carriers of disease or engage in preventive measures to reduce transmissibility. However, it does not appear that preventive measures were particularly effective during the Spanish flu epidemic, since 78% of nurses at the San Francisco Hospital still became infected (Chowell, et al., 2006a).

Transmissibility given contact may vary with the duration of the epidemic. The effective infectious period is likely to be longer for the initial case than for cases arising after the announcement and recognition by public (health) officials about the presence of the serious disease (Becker, 1989). Infectivity may vary also with the duration of the epidemic due to the error-prone influenza virus (RNA virus) replication process (Domingo and Holland, 1997).

FIGURE 2
THE PEAK AND AVERAGE VALUES OF β FOR EACH OF THE 18 BASES
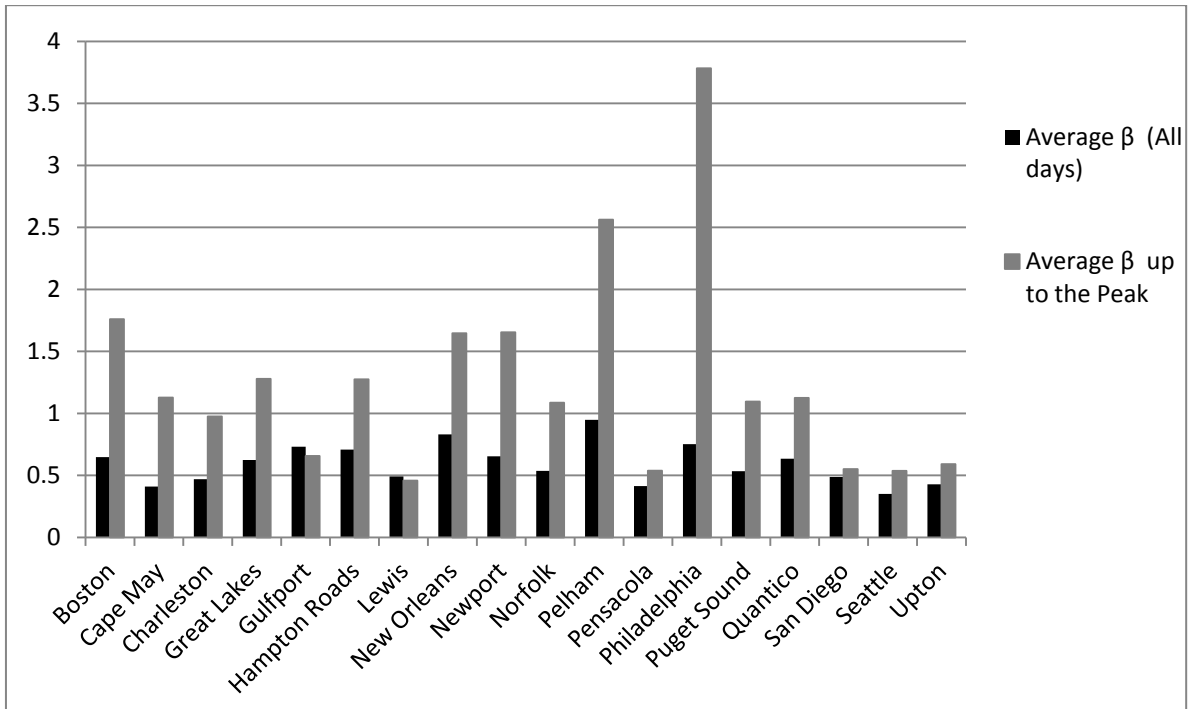
The data presented in Figure 2 and Table 2 indicate that β declines during the course of the epidemic. Table 3 reports a regression of the natural logarithm of β on the day of the epidemic at each base and a set of base dummy variables. The logarithmic specification is based on Becker's suggestion that β declines exponentially with time:

$$\beta(t) = \beta_0 \exp\{\theta + u_t\}, \tag{9}$$

where $\theta < 0$ and u_t is a normally distributed error term with mean 0 (Becker, 1989).

TABLE 2
AVERAGE VALUE OF INFECTIVITY PARAMETER (β)

Station	Average β (All days)	Average β (Week 1)	Average β (Week 2)	Average β (Week 3)	Median β (All days)	Number of Days to the Peak	Average β up to the Peak
Boston	0.6472	1.7598	0.1467	0.5899	0.3164	7	1.7598
Cape May	0.4102	0.8446	0.1094	†	0.1821	5	1.1273
Charleston	0.4697	1.0142	0.2645	0.3722	0.3578	8	0.9749
Great Lakes	0.6235	1.7359	0.3513	0.1898	0.3352	11	1.2784
Gulfport	0.7318	0.6683	0.4848	0.4421	0.5218	10	0.6559
Hampton Roads	0.7083	1.7042	0.4490	0.3050	0.3746	11	1.2749
Lewis	0.4915	0.3649	0.3010	0.5047	0.4260	29	0.4570
New Orleans	0.8307	2.2668	0.4232	0.3878	0.3791	11	1.6457
Newport, RI	0.6535	1.4354	0.2105	0.2444	0.2961	6	1.6541
Norfolk	0.5359	1.1831	0.3744	0.2094	0.3247	9	1.0861
Pelham	0.9479	3.6237	0.5429	0.2383	0.3385	11	2.5621
Pensacola	0.4133	0.5729	0.5479	0.4615	0.4016	20	0.5380
Philadelphia	0.7521	2.7904	0.2666	0.3472	0.3236	5	3.7824
Puget Sound	0.5334	1.2392	0.5594	0.2717	0.2599	11	1.0957
Quantico	0.6345	1.7458	0.5981	0.3171	0.4208	15	1.1252
San Diego	0.4869	0.6342	0.4810	0.4436	0.3749	25	0.5505
Seattle	0.3503	0.4343	0.2404	0.3230	0.2453	5	0.5363
Upton	0.4276	0.9818	0.4241	0.4176	0.3183	22	0.5905
Average	**0 5916**	**1.3889**	**0.3764**	**0.3568**	**0.3442**	**12.3**	**1.2608**
Median	**0.5797**	**1.2111**	**0.3988**	**0.3472**	**0.3369**	**11.0**	**1.1105**

†Epidemic ended before week 3

In Table 3, the coefficient of the day of the epidemic is negative and statistically different from zero at the 0.01 level, providing evidence that the value of β declines during the course of the epidemic. We also estimated the Becker specification separately for each base. The estimated value of β was negative for 16 of 18 bases and statistically significant at the 0.10 level or better (two-tail test) for 10 of these bases. The estimated value of β was positive for two bases but only statistically significantly different from zero at conventional levels for one base, Lewis. In some of the bases, there are secondary peaks (e.g., Gulfport and Charleston) which lead to a rejection of the hypothesis of a decline in β.

TABLE 3
VARIATION IN β OVER TIME AND ACROSS BASES

Column:	(1)	(2)
Dependent Variable:	Log(β)	
Independent Variable	Coefficient*	Standard Error
Constant	-0.8766[c]	0.1412
Day of Epidemic	-0.0070[a]	0.0026
Dummy Variables for Bases**		
Boston	-0.2510	0.1822
Cape May	-0.4932	0.2500
Charleston	-0.0229	0.1556
Great Lakes	0.0247	0.1988
Gulfport	0.2826	0.2124
Hampton Roads	0.2014	0.2156
Lewis	0.2426	0.1578
New Orleans	0.1555	0.1941
Newport, RI	-0.0841	0.2497
Norfolk	-0.0980	0.2124
Pelham	0.0476	0.1844
Pensacola	-0.2979	0.2305
Philadelphia	-0.4467[b]	0.2260
Puget Sound	-0.8314[c]	0.2503
Quantico	0.0284	0.1543
San Diego	0.0566	0.2038
Seattle	-0.3888	0.2705
R^2	**0.0684**	
Number of Observations	**610**	

*Levels of statistical significance: a = 0.01, b = 0.05, c = 0.10.
** Upton is the excluded base.

Table 3 examines variations in the daily value of log(β) across bases, holding day of the epidemic constant. The set of coefficients of the dummy variables for bases are statistically significant at the 0.01 level, leading to the conclusion that the level of β differed across bases.

Finally, we examined whether the average value of β varied with base size or whether bases that experienced their epidemics at later dates might have reduced the transmission of influenza through the adoption of public health or quarantine measures (Merkel, et al., 2006). The first reported case was at a receiving ship in Boston on August 28, 1918, which we designated as Day 1. We found a positive relation of β with complement size and starting date for the whole of the epidemic, although neither coefficient was statistically significant at conventional levels.

Sensitivity Analysis

In their analysis of influenza type A, Longini, et al. (2005) assume that there are both asymptomatic and symptomatic cases. Chowell, et al. (2006a, b) also assume there are asymptomatic cases during the1918-19 flu. Mills, et al. (2004) do not consider asymptomatic influenza cases in their estimation.

TABLE 4
COMPARISON OF β ESTIMATES FOR ASYMPTOMATIC AND SYMPTONATIC CASES

Station	Asymptomatic Cases	Symptomatic Cases
Boston	0.6472	0.5194
Cape May	0.4102	0.3586
Charleston	0.4697	0.3731
Great Lakes	0.6235	0.5064
Gulfport	0.7318	0.4666
Hampton Roads	0.7083	0.5874
Lewis	0.4915	0.3497
New Orleans	0.8307	0.6421
Newport, RI	0.6535	0.4541
Norfolk	0.5359	0.4450
Pelham	0.9479	0.7913
Pensacola	0.4133	0.3200
Philadelphia	0.7521	0.6114
Puget Sound	0.5334	0.4434
Quantico	0.6345	0.4533
San Diego	0.4869	0.4013
Seattle	0.3503	0.2648
Upton	0.4276	0.3371
Average	**0 5916**	**0.4625**
Median	**0.5797**	**0.4492**

Table 4 compares our estimates of β with and without including asymptomatic cases. For each base, the estimated value of β when asymptomatic cases are included exceeds the estimated value for the procedures including only symptomatic cases. Across bases, the average value of β dropped from 0.59 to

0.46 and the median from 0.58 to 0.45 when only symptomatic (observed) cases were included for the parameter estimation.

DISCUSSION

Some investigators report the contact number (σ) or the "reproductive number R", as in Mills, et al. (2004). More commonly, investigators report the basic reproductive ratio (R_0). R_0 shows the average number of secondary cases arising from the introduction of a single infective if all individuals are susceptible to the disease. The magnitude of this parameter is particularly important. In a simple deterministic epidemic model, if all individuals are susceptible, then R_0 equals the contact number, but if not all individuals are susceptible, R_0 is the fraction of the population initially susceptible multiplied by the contact number. Values of the case fatality rate and of β are specific to each base and are taken from Tables 1 and 3, respectively.

Table 5 compares our findings with those reported in seven other studies. Since we found that β over the course of the epidemic, estimates of R_0 based on the early stages of an epidemic are larger than those that include all days of the epidemic. For example, in our data set using asymptomatic cases, the average value of R_0 for days up to the peak is 3.92 while the average is only 1.84 when all epidemic days are included.

Two studies by Chowell, et al. for San Francisco and Geneva, Switzerland include asymptomatic cases and use daily data (2006a, b) and all other estimates are based on weekly data. For San Francisco, the Chowell, et al. (2006a) estimated value of R_0 for the first five days of the epidemic is 3.72 (with a very large standard error) and 2.38 for the first 17 days. In San Francisco, the peak number of daily influenza cases was around 30 days after the onset of the epidemic, so that their 17 day does not include all of the period prior to the peak. Our estimate of the pre-peak period for all bases taken together (3.92) is slightly above the Chowell, et al. 5 day estimate and considerably in excess of their pre-peak (17-day estimate). We conclude that the epidemic was much more infectious on military bases (on average) than in San Francisco.

The Second Wave of the Geneva epidemic (October-November, 1918) appears to be more infectious than the epidemic on our military bases. The Chowell, et al. (2006b) estimate of R_0 for the whole of the epidemic for Geneva (3.75) is higher than our estimate (1.84).

The only other estimates for the U.S. are those by Mills, et al. (2004) for 45 cities. Their basic model and method of estimation are similar to ours, but they include only symptomatic cases. They first construct a daily simulation model of the influenza epidemic, which is changed to a tenth of day increments of when more than 10% of the population is infectious. Their SEIR model assumes the same relative level of infectiousness by day of infection as we. These relative values are presented in a histogram (Mills et al., Supplementary Figure 1) and are attributed to Longini, et al. (2004). They further assume that 2% of those infected die with a mean survival time of two weeks (Supplementary Figure 2). This case fatality rate is far smaller than the 6.2% figure reported for our military bases. This difference may illustrate the extremely high mortality rate of the 1918-1919 flu for young adults, characteristic of the population of military bases. Higher fatality rates among the infected raise R_0 since the rate of infection among survivors must be higher to generate the same number of subsequent cases.

Because they do not have daily cases, Mills, et al. (2004) match deaths from the simulation models with weekly data on excess deaths from influenza and pneumonia reported by the Bureau of the Census (1919). Mills, et al. report estimates of the "reproductive number R" for each city. The 45 city data set yields "initial" values of the contact number ranging from less than 1.0 to more than 6.0 (Figure 2, p. 905) with a median of 2.0 (interquartile range 1.7 to 2.3). Mills, et al. also report what they refer to as "extreme" estimates of the contact number obtained by matching the excess deaths in the two epidemic weeks with the greatest exponential growth rate. The extreme values range from above 1.0 to 6.5 with a median of 2.7 (interquartile range 2.3 to 3.4).

Our estimate of the average value of R_0 for the whole of the epidemic using only symptomatic cases is 1.46 is below the median of 2.0 reported in Mills, et al.. However, it is probably more reasonable to

compare our estimate using data up to the peak of the epidemic with their initial estimate. In this case, our median estimate (2.94) is slightly higher than their median estimate of 2.7.

TABLE 5
ESTIMATED VALUES OF BASIC REPRODUCTIVE RATIO (R_0) FOR 1918-19 INFLUENZA

Military Bases	Time Period	Mean	Median	Minimum	Maximum	Inter-quartile range
Asymptomatic cases included	Up to peak	3.92	3.16	1.42	10.86	1.77– 5.02
	All days	1.84	1.64	1.05	2.74	1.36 – 2.16
Symptomatic cases only	Up to peak	3.99	2.94	1.34	10.86	1.97 – 4.01
	All days	1.84	1.46	0.92	7.10	1.24 – 1.94
45 U.S. Cities						
Mills, et al. (2004)	All Days		2.0	Less than 1.0	6.3	1.7 – 2.3
	Period of Highest Growth Rate		2.7	1.0	6.5	2.3 – 3.4
San Francisco						
Chowell, et al., (2006a), Asymptomatic cases included		Method:	Initial Growth Rate	Simple SEIR	Complex SEIR	Stochastic SIR
	First 5 Days (95% CI)		5.78 (3.80-8.15)	3.72 (2.01-5.44)	n.a.	1.96 (0.83-3.09)
	First 17 Days (95% CI)		2.98 (2.73-3.25)	2.38 (2.16-2.60)	2.20 (1.55-2.84)	2.10 (1.21-2.95)
Geneva, Switzerland			**First Wave***	**Second Wave***		
Chowell, et al. (2006b), asymptomatic cases included	(95% CI)		1.49 (1.45-1.53)	3.75 (3.57-3.93)		
England and Wales			**First Wave***	**Second Wave***	**Third Wave***	
Gani, et al. (2005)	All Days			1.55	1.70	
Ferguson, et al. (2006)	Period of highest growth rate		1.5-1.7			
Viboud, et al. (2006)	First Three Weeks		2.1			
		Assumed				
Chowell, et al. (2008), England and Wales	Period of Exponential Growth (95% CI)	3-day generation interval		1.39 (1.36-1.43)	1.39 (1.29-1.49)	
	Period of Exponential Growth (95% CI)	6-day generation interval		1.84 (1.75-1.92)	1.82 (1.61-2.05)	

*Geneva: First Wave (July 1918) and Second Wave (Oct.-Nov., 1918); England and Wales: First Wave (6/29/18-8/3/18), Second Wave (10/12/18-12/28/18), and Third Wave (2/18/19-4/5/19)

All estimates for England and Wales are based on weekly data and include only symptomatic cases. Gani, et al. (2005) provide estimates of R_0 using all days of the epidemic for the second wave (1.55) and third wave (1.70). These estimates are below our mean of 1.84 for all bases combined. However, the Gani estimates are inconsistent with Chowell, et al. (2008), who report much lower estimates of R_0 (1.39) based

on the very early days of the epidemic for these two waves. Since we assume an incubation period of 1.2 days and a mean infectious period of 4.1 days in calculating R_0, our estimates are based on a generation interval that is probably closer to the estimates by Chowell, et al. assuming a 3-day interval. Our estimate of R_0 using symptomatic cases up to the peak is 3.99. It would seem that the 1918-1919 flu epidemic on military bases in the U.S. was much more infectious than the second and third wave epidemics in England and Wales.

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