

Massachusetts Instítute of Technology Engíneeríng Systems Dívísíon

Working Paper Series

ESD-WP-2007-22

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Richard C. Larson

Center for Engineering Systems Fundamentals Massachusetts Institute of Technology Cambridge, Massachusetts 02139 rclarson@mit.edu

August 2007

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Richard C. Larson Center for Engineering Systems Fundamentals Massachusetts Institute of Technology Cambridge, Massachusetts 02139

ABSTRACT

The emergence of influenza with virulence comparable to the famous 1918-1919 "Spanish Flu" has the potential to kill hundreds of millions of people worldwide. Should we find ourselves being forced to 'live with the flu,' it is imperative that we recognize that there are things that we can do – many simple – that may decrease the chance of our loved ones, our co-workers and ourselves becoming infected with the flu. The key is to decrease the number of new infections created by each newly infected person. And this relates to mathematical modeling of the disease, a very simple example of which is shown here.

Pandemic influenza represents a credible threat to the lives of hundreds of millions of people worldwide. The trigger event will likely be the mutation of a flu virus presently in birds, pigs or other animals, to become human-to-human efficiently transmittable. From the moment of the trigger event, at least six months will be required to develop a safe and effective vaccine, and then only for a small fraction of the planet's inhabitants. For six months or longer, we will all be 'naked' against the flu.

Much 'flu research', including mathematical modeling, suggests that once the flu starts, it will simply run its course -- suggesting there is not much we can do. It's as if the flu imposes on us a Russian Roulette partially loaded gun, and when nature pulls the trigger there is a given chance that we will be hit, regardless of what else we do. But we do not believe that to be true. Evidence from the 2003 SARS epidemic, recent analyses of the 1918-1919 "Spanish Flu," and our own mathematical modeling suggest that there is much we can do to reduce the likelihood that we as individuals, our family members and our co-workers become sickened with the flu.

The results strongly suggest that reductions in the number and intensity of daily humanto-human contacts, using methods of 'social distancing,' may dramatically reduce the spread of infection, once the flu is among us. Special attention must be directed at that 20 to 40 percent of the population having the maximum frequency of daily human contacts. And delay kills. It is important for the social distancing controls, both voluntary and mandated, be implemented early and maintained until the threat is over.

Let's do some math. There is a fundamental input constant for most existing models, the 'basic reproductive ratio R_0 ,' defined to be *the mean number of new influenza infections* created by a newly infected person in a population full of susceptible people. Suppose that early in the epidemic I become infected with the flu and that I infect 3 other individuals before I am committed to bed and rest. Suppose you are also infected and that you infect 2 others before you are isolated in bed. Our 'average' ' R_0 ' in this simple case is (3 + 2)/2 = 2.5. With past pandemic flu's such as in 1918-1919, a typical R_0 across the entire population is found to be between 2.0 and 2.5. One can see that if R_0 is greater than one, the epidemic grows exponentially for a while, until the number of remaining susceptible people drops below some critical point. What is surprising here is that such a small R_0 is all that is needed to create a pandemic. Intuitively, seeing the havoc caused in 1918-1919, one might think that R_0 needs to be 10 or 20! No, averaged across the population, it is less than 3.0. That's the 'good news' as it is so much easier to reduce R_0 from 3.0 to one than from 10 to 1. If one can find a sequence of simple steps to reduce R_0 to be less than 1.0, rather than exponential growth, one then enjoys exponential decay as the disease dies away. Evidence suggests that this is what happened with the eradication of SARS in Hong Kong and elsewhere in 2003.

Now, we revert to an equation! Suppose I come face to face with N people on a day that I am infectious but asymptomatic. Many people who become infected with the flu have one such day before they feel and appear sick, and not being able to identify these people is what makes eradication of the flu so difficult. Define an 'indicator variable' as follows:

 $X_i = \begin{cases} 1 \text{ if person } i \text{ becomes sick as a result of exposure to me} \\ 0 \text{ if person } i \text{ does not become sick as a result of exposure to me} \end{cases}$

Now, we let *NI* be defined to be the number of people I will infect on this day. *NI* can be written as simply counting the indicator variables,

$$NI = X_1 + X_2 + X_3 + \dots = \sum_{i=1}^{N} X_i$$

Suppose for example N = 50 and that all X_i 's are 0 except for X_9 , X_{18} and X_{45} , each being equal to one. In that case, I have infected 3 of the 50 individuals I have came face to face with on this day.

Now, at any given level of intensity of face-to-face contact, there is a probability *p* that I will pass the infection on to the person I am facing. Using this fact, we can write an expression for the mean number of people I will infect on this day. It is simply the mean of $NI = X_1 + X_2 + X_3 + ... = \sum_{i=1}^{N} X_i$, which equals *Np*. We thus have a simple expression for R_0 , and that is

$$R_0 = Np.$$

Why do we do this? Because for pandemic flu, R_0 appears to many as some constant of nature, such as the gravitational constant = 6.67300 (10⁻¹¹)m³ kg⁻¹ s⁻². In fact many epidemiologists seem to treat it this way: "Consider a disease with R_0 equal to 3.635....Blah, blah, blah..." But flu is an infectious respiratory disease, spread by human contacts. Reduce human contacts, reduce prevalence of the flu. By writing $R_0 = Np$, we have expressed R_0 in terms of two other parameters, each of which we can control to some extent. We have a fighting chance of reducing R_0 , perhaps a little, perhaps even to below 1.0, the critical value to assure that the disease dies away rather than grows exponentially.

OK, how do we control N and p? One reduces N simply by reducing the number of faceto-face contacts we have each day. If a parent is shopping for groceries, rather than following the European tradition of daily shopping, perhaps one switches to weekly shopping, or, better yet, to groceries delivered to your door. If you manage a team of employees, rather than have face-to-face meetings during a flu emergency, have conference calls instead, with many workers telecommuting. Many companies have already created comprehensive pandemic flu plans that include telecommuting, reduced face-to-face encounters and even minimum desk spacing between workers. The desk spacing idea relates more to the parameter p, the probability that any given face-to-face contact will result in a new infection. How else can we reduce p? Wash hands with hot water and soap several times daily. Do not shake hands during greetings with colleagues. Cough or sneeze into your elbow, not into the open air. Be careful not to touch surfaces that might have recently been contaminated with flu virus. Encourage your city's large employers to stagger work hours so that public transportation subways and busses are less crowded during now-stretched-out rush hours. Even run the subways and busses with windows opened.

There are many common sense non-medical steps one can take, as an individual, a family, and a workplace, to reduce but not eliminate the chance of becoming infected with the flu. The key is to realize that you have some control. The arrival of the flu does not have to mean uncontrolled Russian Roulette. True, there is more we do not know about the flu than we do know. When a 1918-1919 type pandemic hits again, we do not know how severe it will be, we do not know the detailed physics of its progression, we do not know how it will mutate over the course of months, etc. But lack of some scientific knowledge does not mean we have to wait for a sequence of expensive scientific research projects to identify some common sense steps we can take that are almost guaranteed to reduce the likelihood that any one of us becomes infected. There is no current way known to stop the flu once it starts. But individually and collectively, we can impede its progress and reduce, perhaps significantly, the numbers who become infected. Key is to have a plan – individually, by family, by workplace and by community.

<u>Acknowledgement.</u> The Sloan Foundation of New York supported research leading to this article. We gratefully acknowledge that support.

References.

The central ideas of this paper are drawn from the recently published, "Simple Models of Influenza Progression Within a Heterogeneous Population," R. C. Larson, *OPERATIONS RESEARCH*, Vol. 55, No. 3, May–June 2007, pp. 399–412. Readers are invited to comment on this paper and on the general topic of influenza modeling at an on-line blog, <u>http://orforum.blog.informs.org</u>.

Additional recommended reading:

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