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On Influenza and School Closings: Time for Prospective Studies

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Rodriguez and colleagues¹ are to be commended for seizing the opportunity of the natural experiment in Seattle and King County, Washington, to examine whether school closure reduced post-closure absenteeism. About half the schools closed and half stayed open during the week-long winter break in late February 2007. The authors made the best of a serendipitous situation. They did not observe any difference in absenteeism in the two weeks after the break period in the two groups of schools. The authors delineate potential explanations for this result. First, as Figures 1 and 3 show, the seasonal influenza epidemic was likely past its peak at the time of the school closing. Second, being absent from school is a very nonspecific outcome not well-calibrated against influenza – particularly when the epidemic peak has passed.

If the great epidemiology spirit in the sky had moved the 2007 winter break to the early part of the influenza season, would school absenteeism have been lower in the closed compared with the open schools? Even if it had, would that have told us what we really want to know? Namely, how does school closing during an epidemic affect the incidence of influenza illness, not only in school children, but in the population as a whole? Modeling efforts in addition to those cited by Rodriguez et al have found that closing schools is effective, both alone and in combination with other social distancing measures.² Due to the high social cost,³ the trade-offs between closing schools and leaving them open need to be considered. However, simulation studies are only as good as, or at least no better than, the data on which they are based.

The study by Rodriguez et al raises a fundamental question. Why are there not more well-designed, prospective studies of influenza and influenza interventions in the U.S.? Prospective household- and school-based studies are conducted in many other countries. The US Centers for Disease Control and Prevention (CDC) is funding prospective, group-randomized studies of influenza vaccination of school children with active surveillance in Senegal and India to evaluate the indirect effects of vaccination. If in other countries, then why not also in the U.S.?⁴ To prepare for introducing the multivalent pneumococcal vaccination, prospective, longitudinal household- and school-based studies of pneumococcal carriage were conducted in Finland, France, England, Bangladesh, and elsewhere. Prospective, longitudinal meningococcal carriage studies are being prepared in several countries in Africa by the MenAfriCar consortium in anticipation of the new meningococcal A vaccine. In the wake of the H1N1 influenza pandemic, prospective household-based influenza studies are already being planned or conducted in many countries in Europe and Asia.

The US has a history of prospective, population-based studies of influenza, but this history has been all but lost. Intensive surveillance of families with school-age children for influenza virus infections was conducted from 1975 to 1979 in Seattle, Washington, USA.⁵ Active community surveillance of acute respiratory illness took place in Tecumseh, Michigan, from 1976 to

1981.⁶ A large longitudinal 10-year study of illness of families in Cleveland, Ohio, USA was conducted from 1 January 1948 through 31 May 1957.⁷ In May 1957, the first reports of the new antigenic variant of influenza virus A occurred in Asia. In anticipation of the influenza pandemic, the Cleveland study was reactivated in September 1957. Sixty of the families agreed to participate again,⁸ providing important clinical and epidemiologic prospective data including age-specific influenza illness attack rates used today to calibrate influenza simulators.

The US should expand its capacity for more prospective, population-based field studies of infectious diseases in general. However, I focus here on influenza, particularly, the coming 2009–2010 season. We have an opportunity not just to plan interventions for this autumn when H1N1 returns, but also to plan to evaluate these interventions.

How should we evaluate the effect of closing schools on transmission during an outbreak? We are unlikely to have the opportunity to compare schools that are closed with those that stay open, (because most will close in a serious epidemic,) or even to contemplate randomizing them to such an intervention. However, imagine that school children in many schools and their families are followed prospectively, with influenza illness (or in the ideal situation, infection) confirmed biologically on a weekly basis or when symptoms are observed. Then when a school is closed, children and their families can continue to be followed actively for illness and be tested for influenza infection. With 100 or 1000 or more such schools, we should be able to observe whether the epidemic in a school is cut short once the school was closed. The influenza illness attack rates in the families before and after closing the schools could be compared to examine the indirect effect of school closing on family members.⁹ Such studies for evaluating indirect effects are called minicommunity studies because the household serves as a small community. The study design is not perfect. Family members, including school children, could be exposed from other sources, and temporal trends could play role. If every case of influenza-like illness cannot be biologically confirmed, then a random sample of such case can be tested to estimate the proportion that is actual influenza.¹⁰

School-based ascertainment of cases with subsequent follow-up in families was done to study H1N1 influenza transmissibility during the spring 2009. This is another approach to develop for the 2009–2010 season. However, influenza moves fast, so that first having to ascertain the cases in the school, and then following the family can lead to ascertainment bias, as well as making laboratory confirmation of influenza infection more difficult.

In preparation for the expected H1N1 outbreak, the National Institute for Allergy and Infectious Diseases (NIAID) should actively support implementation of more field studies of influenza in the U.S., in particular, prospective household- and school-based studies. Such studies are crucial to understand the natural history of influenza and to evaluate the effects of interventions such as vaccination and school closure, at the individual level as well as the community level. Household-based prospective studies with specific outcome measures are also an excellent platform for evaluating efficacy of vaccination – not only how it protects against influenza illness, but how it affects infection and person-to-person transmission. Such knowledge is essential for understanding the overall public health effects of vaccination and for constructing valid computer simulation models. Just before vaccination of school children was recommended in the US, there was a brief opportunity to plan to evaluate the intervention systematically by planning community randomized studies with phased implementation of the vaccination program.⁴ We are unlikely to have an orderly, phased implementation of H1N1 vaccination this fall. Hence, it will be important to implement prospective studies to evaluate indirect effects of vaccination on influenza illness attack rates as a function of vaccination coverage in the schools and in the communities.

Some say that such prospective studies with specific outcomes are too costly. But are we to be satisfied with uncertain null results as in the well-done study of Rodriguez et al? Given the cost of school closure and the cost of vaccinating school children, is it not worthwhile to know conclusively what will benefit public health?

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Biography

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