Estimating Deaths Due to Influenza and Respiratory Syncytial Virus

To the Editor: Dr Thompson and colleagues[1] developed a statistical model to estimate deaths attributable to influenza and respiratory syncytial virus (RSV). We are concerned that their model was inappropriate. When designing a model to attribute causality to deaths, a reasonable initial approach would be to assume that the number of deaths due to a specific virus in any given week was proportional to the number of laboratory reports of that virus in that week. The total number of deaths would be the sum of the contributions from each virus, plus the seasonal background of deaths due to other causes. Similar models have been used successfully to estimate the proportion of gastrointestinal disease attributable to rotavirus[2] and the proportion of bronchiolitis and pneumonia attributable to RSV and other pathogens.[3] Additional terms and factors could be included to account, for example, for improving sensitivity of surveillance over time, but the core of the model would remain linear and additive.

An appropriate analysis could use linear regression, a generalized linear model (GLM) with a Poisson error distribution and an identity link, or maximum likelihood for a non-GLM. Instead, Thompson et al used a Poisson model in which the number of deaths increased exponentially with the number of laboratory reports and the effects of each virus (and the seasonal background) on the number of deaths were multiplicative rather than additive. We do not believe that there is plausible justification for fitting such a model to these data.

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To the Editor: Dr Thompson and colleagues[1] presented a model that uses influenza and RSV surveillance data to estimate virus-associated mortality. The authors propose that this model replace Serfling-type models, which have been used for 40 years to estimate deaths attributed to influenza by subtracting a model-generated baseline from observed winter deaths.[2,3]

The model of Thompson et al averages 34 470 (range, 7608-68 328) total seasonal influenza-related deaths for 1976-1999. This average, much higher than previous reports (approximately 20 000; range, 0-40 000 for 1972-1992),[3] suggests that the Serfling models underestimate the mortality burden and that the new model corrects this problem. In fact this is not the case. A Serfling-type model[4] estimated an average of 37 500 (range 0-74 500) all-cause excess deaths for 1976-1999. Both models report an increase in influenza-related deaths in the 1990s, which for Serfling models is fully explained by a rapidly increasing population of very elderly Americans (for whom influenza-related mortality risk increases exponentially),[5] together with increased circulation of the virulent subtype influenza A(H3N2).[4]

Although Thompson et al offer their model as superior, they do not provide graphical or statistical evidence of acceptable fit or model validation. Nor do they compare their influenza mortality estimates with those based on Serfling models. In fact, their individual season estimates of pneumonia and influenza deaths correlate poorly with Serfling estimates ($R^2<0.5$), and this comparison reveals an unexplained time dependency (FIGURE). The doubling in their surrogate measure of virus activity (from ≈8% to ≈16% influenza-positive specimens, Table 1[1]) over the study period leads to large underestimates (1970s) and overestimates (1990s) of influenza mortality relative to Serfling estimates. For perspective, the 1980-1981 season was considered very severe, yet the authors' model estimated only 4068 influenza-related pneumonia and influenza deaths compared with 9700 by a Serfling model.[1,4]

The Thompson model produces essentially constant estimates of RSV-related mortality for the 1990s, 80% of which are stated to be deaths in elderly individuals. If this is so, then the authors should be able to demonstrate a 40% increase in RSV deaths among those aged 85 years or older during the 1990s when this population increased by approximately 40%. Such straightforward validation would provide evidence that this model does indeed measure RSV deaths in the elderly population.

A model that requires the additional complexity of viral surveillance data for mortality estimates sharply limits historical comparison within the United States and eliminates comparison with most other countries. We propose that rigorous dem-

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