Correspondence

Pneumococcal Polysaccharide Vaccine May Not Prevent Hospitalization for Pneumonia in Elderly Individuals

To the Editor—The recently published cohort study by Vila-Córcoles et al. [1] adds valuable data that inform the ongoing controversy regarding the effectiveness of 23-valent pneumococcal polysaccharide vaccine (23vPPV) against hospitalization for pneumonia among the elderly population. However, confounding may have biased the estimate of effect in favor of protection from vaccination.

This study presents unadjusted estimates for vaccine effectiveness that indicate no benefit against hospitalization for pneumonia (vaccine effectiveness, −12%; 95% CI, −39% to 19%). With adjustment for age and sex, the estimate increased (vaccine effectiveness, 4%; 95% CI, −19% to 22%). When additionally adjusted for factors suggesting sickness (i.e., outpatient visits, hospitalization for pneumonia, chronic lung disease, chronic cardiomyopathy, and immunoincompetence), the point estimate became much larger, statistically significant, and in favor of vaccination (vaccine effectiveness, 26%; 95% CI, 8%–41%). This model instability suggests possible confounding by indication associated with a “healthy vaccinee” effect, in which healthier subjects were more likely to have received vaccination. Residual confounding is possible, given that only a small number of factors were adjusted for in the model. It would be useful to know the stability of coefficients for other variables in the model when each factor was added or removed.

In addition, the authors discuss influenza vaccination as a confounder in some models. Yet this is not adjusted for in the model for hospitalization with pneumo-

nia. Persons who were vaccinated with 23vPPV were more likely to be vaccinated with influenza vaccine. In the discussion section, the authors refer to supplementary analyses restricted to the influenza season. These did not adjust for influenza vaccination status and revealed an even greater effect for 23vPPV, with 95% CIs that almost included no effect (vaccine effectiveness, 31%; 95% CI, 2%–80%).

Vila-Córcoles et al. [1] describe considerable uncertainty around their point estimates for vaccine effectiveness. Given the potential for confounding, their conclusions that “23-valent PPV should be recommended for all subjects aged ≥65 years” [1, p. 867] on the basis of its ability to prevent pneumonia may be overstated.

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Reply to Skull et al.

To the Editor—We thank Skull et al. [1] for their questions. When trying to identify patterns of associations between exposures and outcomes in epidemiology, the goal of the modeling process is usually to find the most parsimonious statistical model—that is, the simplest model that satisfactorily describe the data [2].

In our study, the method to select a subset of covariates to include in a proportional hazards regression model was the purposeful selection method of Hosmer and Lemeshow [3]. One of the steps is to assess whether removal of the covariate has produced an important change in the coefficients of the variables remaining in the model. We used a value of ≥20% as an indicator of an important change in a coefficient. All of the initial models included age, sex, number of outpatient visits in the previous 2 years, history of hospitalization for pneumonia, diabetes, chronic cardiopathy, chronic lung disease, smoking, immunocompromised status (cancer, severe nephropathy or liver disease, or receipt of immunosuppressive medication), and influenza vaccination status. We proved the stability of coefficients for all variables in all of the models when each factor was added or removed to confirm that the factor was neither statistically significant nor an important confounder [3]. In addition, the models were compared using the partial likelihood ratio test and the Akaike Information Criterion, and we assessed the adequacy of the models.

In our study, no “healthier” subjects were more likely to have received pneumococcal polysaccharide vaccine (see table 1 in our study [4]), so an unadjusted analysis underestimated vaccine effectiveness. The possible confounding by indication was taken into account like any other con-

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