Dual Pneumococcal and Influenza Vaccination: Severe Concerns About the Composition of the Control Groups

To the Editor—We have read with interest the article by Hung et al [1] on the effects of dual vaccination with a 23-valent pneumococcal vaccine and a trivalent influenza vaccine. The authors observed a difference in the occurrence of pneumonia and cardiovascular incidents between the patients who received both vaccines, the patients who received 1 of the 2 vaccines, and the patients who were not vaccinated. A significant difference in cerebrovascular incidents and in mortality was observed only between the dual vaccinees and the unvaccinated patients.

The observational nature of this study, in which patients were free to choose which vaccinations they would receive, makes it prone to selection bias. In previous studies on influenza vaccination, it has been observed that a large and significant part of the difference in the occurrence of medical complications between vaccinated and unvaccinated patients—if not the entire observed effect—is attributable to the difference in health status between the 2 groups: vaccination is associated with a more active lifestyle and a better health status [2]. Although few of the presented baseline characteristics differed significantly between the groups in this study, selection bias cannot be excluded.

In this light, it is important to describe the different groups. Hung et al [1] state, in the first paragraph of the Results, that “25,393 [patients] were unvaccinated. Fifty-five percent of the unvaccinated declined vaccination by choice, whereas the remaining 45% were excluded for other reasons stated in the exclusion criteria.” This last sentence is unclear; it suggests that the control group (no vaccination) consisted of ~14,000 patients who declined vaccination plus the ~11,400 patients who did...
not receive vaccination because of exclusion criteria, namely, “known allergy to components of the study vaccine, those with immunosuppression as a result of underlying illness or treatment, those who had received anticancer chemotherapy or radiation therapy during the preceding 12 months, and HIV-infected patients.” Inclusion of these 11,400 patients in the nonvaccinated group could have major effects on the results.

We hope the authors can clarify this issue.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

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References