

Modeling the Effect of Different Vaccine Effectiveness Estimates on the Number of Vaccine-Prevented Influenza-Associated Hospitalizations in Older Adults

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We compared influenza vaccine–prevented hospitalizations in adults aged ≥ 65 years for a range of hypothetical effectiveness estimates. During 2012–2013, a vaccine with 10% effectiveness (66% coverage) would have averted approximately 13 000 hospitalizations, and a vaccine with 40% effectiveness would have averted approximately 60 000 hospitalizations. Annual vaccination is merited in this vulnerable population.

Keywords. influenza; vaccine effectiveness; older adults; hospitalization.

Influenza is estimated to cause a substantial number of hospitalizations and deaths each year in the United States [1–3]. Most influenza-associated morbidity and mortality is concentrated in older adults aged ≥ 65 years, a population at increased risk for complications associated with influenza. During 2012–2013, the rate of laboratory-confirmed influenza-associated hospitalizations in older adults was 3- to 6-fold higher than during the 2 previous seasons [4]. Influenza vaccination is the main prevention strategy for influenza. During 2012–2013, interim estimates of influenza vaccine effectiveness against medically attended laboratory-confirmed influenza acute respiratory illness indicated moderate effectiveness; however, the lowest estimates were reported for older adults [5]. To explore the range of hospitalizations that could be prevented with different levels of vaccine

effectiveness in mild and moderate severity seasons in this vulnerable group, we used a previously published model to estimate the number of prevented or averted hospitalizations from influenza vaccination and applied a range of hypothetical vaccine effectiveness estimates [2]. We used rates of influenza-associated hospitalizations from 2 seasons: 2012–2013, representing a moderate to severe season, and 2011–2012, a mild season.

METHODS

Details of the model to estimate the number of influenza-associated hospitalizations averted by vaccination have been previously described [2]. In brief, we estimated the number of influenza-associated hospitalizations for older adults in the United States during 2011–2012 and 2012–2013 using rates of influenza-associated hospitalizations from FluSurv-Net, a collaboration of >14 geographically distributed sites that conduct population-based surveillance for laboratory-confirmed influenza-associated hospitalizations and provides real-time tracking of influenza hospitalizations (Supplementary Table 1) [6]. FluSurv-Net captures only laboratory-confirmed influenza results from testing initiated by clinicians providing clinical care; therefore, we corrected for clinician testing practices and test sensitivity using a multiplier and then extrapolated the adjusted rates to calculate national hospitalization estimates [2]. Influenza vaccination coverage rates from 2011–2012 and 2012–2013 were derived from vaccination status reported by self or proxy via the Behavioral Risk Factor Surveillance System and only cover the noninstitutionalized population [7]. Using the reported vaccination coverage estimates and a range of hypothetical vaccine effectiveness estimates varying from 10% to 70%, we estimated the number of influenza-associated hospitalizations that would have occurred in the absence of vaccination; the number of reported hospitalizations was subtracted from those occurring in the absence of vaccination to estimate the number of averted hospitalizations for each hypothetical vaccine effectiveness estimate. We estimated the number needed to vaccinate to prevent 1 hospitalization (NNTV) by number vaccinated (vaccine coverage \times population), divided by the number of prevented hospitalizations. The prevented fraction was the proportion of averted hospitalizations divided by the estimated number of hospitalizations without vaccination. This model does not account for indirect effects of vaccination.

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RESULTS

The estimated number of averted influenza-associated hospitalizations in the United States among adults aged ≥ 65 years ranged from 2383 to 21 987 for vaccine effectiveness ranging from 10% to 70% during the mild season (2011–2012), and from 13 238 to 119 532 during the moderate to severe season (2012–2013) (Figure 1A; Supplementary Table 2). The number of averted hospitalizations was higher during 2012–2013, compared with the milder season (2011–2012) for all vaccine effectiveness estimates. However, during both 2011–2012 and 2012–2013, the prevented fraction of averted hospitalizations for each hypothetical vaccine effectiveness estimate was similar and ranged from 6.3% for a vaccine effectiveness of 10%, to 38% for a vaccine effectiveness of 70%. Compared with a vaccine with 10% effectiveness, a vaccine with effectiveness of 20% prevented almost twice as many hospitalizations, and a vaccine with effectiveness of 60% prevented approximately 7-fold more hospitalizations. The NNTV also varied by season; for a vaccine effectiveness of 40%, the NNTV was 476 during 2012–2013 and 2456 during 2011–2012 (Figure 1B; Supplementary Table 2). NNTV was highest with low vaccine effectiveness and varied substantially when vaccine effectiveness increased during 2011–2012; this was less so in 2012–2013. When stratified by age group, for each season and vaccine effectiveness estimate, approximately 25% of averted hospitalizations among persons ≥ 65 years of age were in the 65- to 74-year age group, 38% were in the 75- to 84-year age group, and 36% were in the ≥ 85 -year age group; these proportions reflect the distribution of influenza-associated hospitalizations in these age groups (Supplementary Tables 1 and 2). The prevented fraction of averted hospitalizations was similar for all age groups among those aged ≥ 65 years.

DISCUSSION

We show that influenza vaccination would be expected to prevent a substantial number of hospitalizations in older adults in the United States for all hypothetical vaccine effectiveness estimates, during both mild and moderate to severe seasons, and that even modest improvements in vaccine effectiveness could result in substantial reductions in the number of hospitalizations. Older adults are particularly vulnerable to complications related to influenza infection and have high rates of influenza-associated hospitalizations [6]. In a moderately severe influenza season, even a vaccine with low effectiveness (eg, 10%) averted approximately 13 000 hospitalizations, whereas a vaccine with modest vaccine effectiveness (eg, 40%) averted approximately 60 000 hospitalizations in our model; the NNTV varied from 2151 to 476 for the same scenarios. This demonstrates that annual influenza vaccination may reduce morbidity associated with influenza in older adults even when vaccine effectiveness is low.

Our data suggest that strategies that improve vaccine effectiveness in older adults could have a significant impact on morbidity, with even modest improvements in vaccine effectiveness producing substantial benefits in adults aged ≥ 65 years. Although immunogenicity may not correspond directly to increased protection against illness, higher postvaccination antibody levels have been demonstrated in older adults for both adjuvanted and high-dose inactivated influenza vaccines compared with standard-dose inactivated vaccines [8–10]. Phase 3 clinical trials with older adults evaluating protection against laboratory-confirmed influenza suggest that an adjuvanted compared with a nonadjuvanted vaccine offered 22% relative efficacy against influenza A(H3N2) infection (although no protection against all circulating viruses) [11], and high-dose

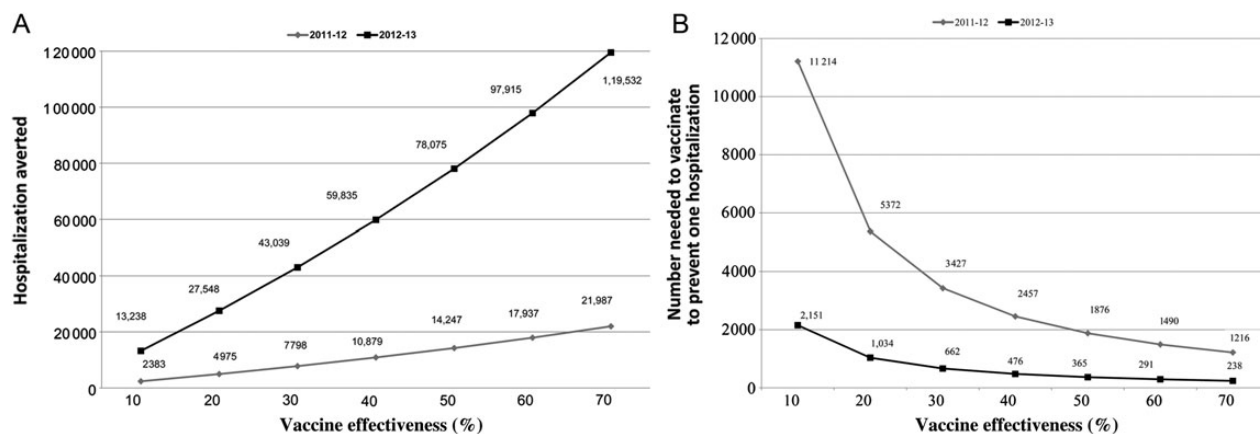


Figure 1. A, Estimated number of averted influenza-associated hospitalizations in adults aged ≥ 65 years in the United States. B, Estimated number of US adults aged ≥ 65 years needed to vaccinate to prevent 1 hospitalization, for a range of hypothetical influenza vaccine effectiveness estimates during 2 influenza seasons.

compared with a standard-dose inactivated vaccine offered 24% relative efficacy against influenza A and B illnesses [12]. If confirmed, these incremental improvements in relative efficacy could mean a significant number of outcomes averted in this vulnerable age group by new vaccines. Cost-effectiveness analyses could give additional insights into additional material benefits from these vaccines.

There are inherent challenges in evaluating vaccine effectiveness in older adults. During 2012–2013, observational studies reported moderate vaccine effectiveness; low, nonstatistically significant estimates were reported for older adults [5]. Studies that enroll participants of all ages may have difficulty enrolling an adequate number of older adults due to care-seeking patterns for acute respiratory infection, and after stratification by age group, the ≥ 65 -year age group often lacks the sample size to adequately assess vaccine effectiveness. This problem is compounded by the fact that a larger sample size is necessary for the evaluation of vaccine effectiveness when the estimate is lower. Vaccine effectiveness may also be less in older adults for a number of reasons, including changes in innate immunity, antigen presentation, and adaptive immunity associated with advancing age [8]. In addition, many factors can affect influenza vaccine effectiveness estimates, such as prior influenza infections and vaccination, frailty, and comorbidities—all of which are more common with increasing age. Finally, influenza viruses undergo continuous genetic changes, and effectiveness of the influenza vaccine may vary depending on the similarities between vaccine strains and circulating viruses. There are limited reports of vaccine effectiveness or efficacy among adults aged ≥ 65 years with good design and adequate sample size in the literature. Thus, by applying a range of potential vaccine effectiveness estimates and using different rates of hospitalizations, our model may reflect a real-world range of benefits from vaccines in older adults.

The model we present here has several limitations. We might have underestimated the number of averted hospitalizations since we did not account for influenza-associated hospitalizations due to circulatory causes or exacerbations of chronic pulmonary or cardiac conditions. However, the hospitalization rates in our model were similar to other published estimates from models using pneumonia and influenza *International Classification of Diseases, Ninth Revision* discharge diagnoses [2]. Influenza vaccine coverage estimates were derived from self-reported vaccination status and thus are subject to recall bias. They were based on telephone surveys with relatively low response rates, and selection bias may remain after weighting adjustments. The relevance of these estimates is limited to the United States and other countries with high vaccine coverage among the elderly, as high vaccine coverage was an important contributor to the number of averted hospitalizations in our model. Nevertheless, even higher coverage closer to the 2020

Healthy People goal of 70% could further increase the number of prevented hospitalizations (data not shown). Finally, we did not account for possible indirect effects of vaccination on community illness.

Despite these limitations, we estimated a substantial number of prevented hospitalizations from influenza vaccination in older adults even with a vaccine with low vaccine effectiveness and during seasons with different degrees of severity. Thus, annual influenza vaccination should be encouraged by clinicians caring for elderly adults. Vaccines with improved vaccine effectiveness, compared with current trivalent standard-dose influenza inactivated vaccines, could result in more averted hospitalizations in this vulnerable population; however, supporting data are pending or lacking. Ongoing efforts to improve vaccines for this vulnerable group are warranted.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (<http://cid.oxfordjournals.org>). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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