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Original Investigation

Cost-Effectiveness of Adjuvanted Versus Nonadjuvanted Influenza Vaccine in Adult Hemodialysis Patients

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Background: Currently more than 340,000 individuals are receiving long-term hemodialysis (HD) therapy for end-stage renal disease and therefore are particularly vulnerable to influenza, prone to more severe influenza outcomes, and less likely to achieve seroprotection from standard influenza vaccines. Influenza vaccine adjuvants, chemical or biologic compounds added to a vaccine to boost the elicited immunologic response, may help overcome this problem.

Study Design: Economic stochastic decision analytic simulation model.

Setting & Participants: US adult HD population.

Model, Perspective, & Timeframe: The model simulated the decision to use either an adjuvanted or nonadjuvanted vaccine, assumed the societal perspective, and represented a single influenza season, or 1 year.

Intervention: Adjuvanted influenza vaccine at different adjuvant costs and efficacies. Sensitivity analyses explored the impact of varying influenza clinical attack rate, influenza hospitalization rate, and influenza-related mortality.

Outcomes: Incremental cost-effectiveness ratio of adjuvanted influenza vaccine (vs nonadjuvanted) with effectiveness measured in quality-adjusted life-years.

Results: Adjuvanted influenza vaccine would be cost-effective (incremental cost-effectiveness ratio $<$\$50,000/quality-adjusted life-year) at a \$1 adjuvant cost (on top of the standard vaccine cost) when adjuvant efficacy (in overcoming the difference between influenza vaccine response in HD patients and healthy adults) $\geq$60% and economically dominant (provides both cost savings and health benefits) when the \$1 adjuvant's efficacy is 100%. A \$2 adjuvant would be cost-effective if adjuvant efficacy was 100%.

Limitations: All models are simplifications of real life and cannot capture all possible factors and outcomes.

Conclusions: Adjuvanted influenza vaccine with adjuvant cost $\leq$\$2 could be a cost-effective strategy in a standard influenza season depending on the potency of the adjuvant.

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INDEX WORDS: Influenza vaccine; hemodialysis; vaccine adjuvant; seasonal influenza; computer simulation; computer model; cost-effectiveness; immunodeficiency; end-stage renal disease.

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Currently, more than 340,000 individuals are receiving long-term hemodialysis (HD) therapy for end-stage renal disease and therefore are particularly vulnerable to influenza, prone to more severe influenza outcomes, and less likely to achieve seroprotection from standard influenza vaccines.[1-10] Influenza vaccine adjuvants, chemical or biologic compounds added to a vaccine to boost the elicited immunologic response, may help overcome this problem. Adjuvanted influenza vaccines currently are on the market in Europe and in late clinical development in the United States for the general older adult population, who show decreased responses to nonadjuvanted vaccines due to immunosenescence.[11-18] The HD population also is a potential target for such adjuvants[17] and have been the participants in recent clinical trials.[18]

Although a prior study explored the potential economic value of an adjuvanted influenza vaccine in the older adult population, the economic value of an adjuvanted vaccine in the HD population is unclear.[19] Therefore, we developed a computer simulation model to estimate the potential economic value of a seasonal influenza vaccine adjuvant for adults receiving regular HD. Sensitivity analyses explored the effect of varying adjuvant cost and efficacy, influenza risk, and probabilities of various influenza outcomes.

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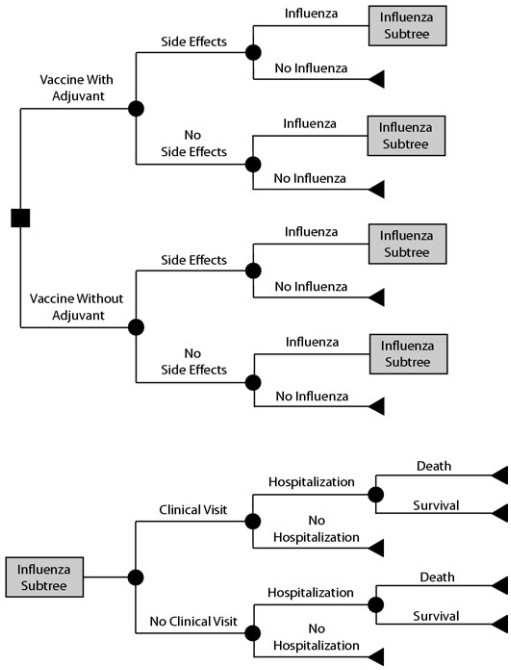

Figure 1. General model structure.

METHODS

Decision Model

Figure 1 shows the general structure of the computational decision analytic model, developed using TreeAge Pro 2009 (TreeAge Software, www.treeage.com), which simulated the decision of using an adjuvanted versus nonadjuvanted influenza vaccine in an adult patient (median age, 64 years) requiring long-term HD therapy.[10] The model assessed the cost-effectiveness of this decision from the societal perspective. Each vaccinated patient had a risk of vaccine side effects (ie, local pain or inflammation), which would require over-the-counter anti-inflammatory medications. Each individual receiving the nonadjuvanted vaccine had a risk of contracting influenza, determined using the seasonal influenza attack rate mitigated by the efficacies of the vaccine. The adjuvant bridged the gap between influenza vaccine efficacy in an HD patient and a healthy adult by a proportion (ie, adjuvant efficacy).

Vaccine efficacy decreases an individual's risk of influenza by 1 – vaccine efficacy and, if the individual contracts influenza, the risk of hospitalization and mortality by 1 – vaccine efficacy (ie, a 100% efficacious vaccine would decrease a patient's probability of getting influenza to zero; a 75% efficacious vaccine would decrease a patient's probabilities of developing influenza, being hospitalized if he or she develops influenza, and not surviving influenza by 75%). Adjuvant efficacy is the degree to which the adjuvant increases influenza vaccine efficacy from observed levels in HD patients to those of healthy adults. Therefore, a 100% efficacious adjuvant brings influenza vaccine efficacy in an HD patient (eg, 63%) to levels seen in healthy adults (eg, 80%). A 75% efficacious adjuvant covers the gap between influenza vaccine efficacy in an HD patient (eg, 63%) and that in a healthy adult by 75% (eg, 63% to 72%). Adjuvant efficacy of 100% means that an HD patient has influenza vaccine efficacy equal to that of a healthy adult. In other words, each individual receiving the adjuvanted vaccine has a risk of developing influenza corresponding to $P_{NAV\text{-}HD} + [\text{Adjuvant Efficacy} \times (P_{NAV} - P_{NAV\text{-}HD})]$, where $P_{NAV\text{-}HD}$ is the probability of an HD patient developing influenza after receiving a nonadjuvanted vaccine and P_{NAV} is the probability of a healthy adult developing influenza after receiving a nonadjuvanted vaccine.

Contracting influenza could result in asymptomatic infection or symptomatic infection followed by a clinical visit, hospitalization, or death.

Data Inputs

Table 1 lists data inputs for our model with distributions and sources. When possible, data came from published meta-analyses. Probability and utility variables drew from β distributions, whereas cost and duration variables drew from γ distributions. Variables that had limited data drew from triangular distributions. A 3% discount rate adjusted all costs to 2010 US dollars.[41]

Limited available data for influenza clinical attack rates in the HD population required us to use serologic data from clinical studies that reported seroprotection rates. The definition of seroprotection is a hemagglutination inhibition antibody titer $\geq$40.[40] When hospitalization and mortality data for HD patients were not available, data from diabetic populations, who have similar influenza outcomes, served as a proxy.[42-44] Sensitivity analyses were used to analyze the robustness of this assumption.

Each simulation run consisted of sending 1,000 hypothetical adult HD patients (median age, 64 years) through the model 1,000 times for a total of 1,000,000 trials. For each run, the incremental cost-effectiveness ratio (ICER) of the adjuvanted vaccine versus the standard vaccine was calculated as the ratio of cost difference between the adjuvanted and nonadjuvanted vaccines to the difference in effectiveness of the adjuvanted and nonadjuvanted vaccines.

The measure of effectiveness was quality-adjusted life-years (QALYs). Adjuvanted vaccine was considered cost-effective if the ICER decreased to <$50,000/QALY, an often-cited threshold.[45]

Sensitivity Analyses

Sensitivity analyses explored the impact of varying key variables, including adjuvant efficacy (range, 0%-100%); adjuvant cost, that is, the added cost of an adjuvant to the influenza vaccination cost (range, $0-$5); probability of a clinic visit when sick with influenza (range, 0%-80%); probability of hospitalization from influenza (range, 0.25-10 times the baseline of 1.2%); and death (range, 0.25-10 times the baseline of 0.2%) from influenza. Additional analyses also explored the impact of requiring a second administration of adjuvanted vaccine. Each dose had a given efficacy and cost. An individual had a treatment adherence value reflecting whether the second dose was received (eg, 100% adherence meant that each individual received the second dose; 75% meant that only three-quarters of individuals received the second dose). Each dose had a risk of side effects. Additionally, probabilistic sensitivity analyses determined the effects of simultaneously varying all variables across the distributions listed in Table 2.

RESULTS

Overall Results

Table 3 lists how the ICER of using an adjuvanted versus nonadjuvanted vaccine varies with adjuvant cost and efficacy and clinical influenza attack rate. The ICER was fairly sensitive to adjuvant cost. In general, adjuvanted vaccine was no longer cost-effective (ie, ICER >$50,000/QALY) when adjuvant cost was >$2. Adjuvant efficacy also drives the ICER. Adjuvant efficacy should be at least 60% for