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Cost effectiveness of a targeted age-based West Nile virus vaccination program

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ABSTRACT

Background: West Nile virus (WNV) is the leading cause of domestically-acquired arboviral disease in the United States. Several WNV vaccines are in various stages of development. We estimate the cost-effectiveness of WNV vaccination programs targeting groups at increased risk for severe WNV disease.
Methods: We used a mathematical model to estimate costs and health outcomes of vaccination with WNV vaccine compared to no vaccination among seven cohorts, spaced at 10 year intervals from ages 10 to 70 years, each followed until 90-years-old. U.S. surveillance data were used to estimate WNV neuroinvasive disease incidence. Data for WNV seroprevalence, acute and long-term care costs of WNV disease patients, quality-adjusted life-years (QALYs), and vaccine characteristics were obtained from published reports. We assumed vaccine efficacy to either last lifelong or for 10 years with booster doses given every 10 years.
Results: There was a statistically significant difference in cost-effectiveness ratios across cohorts in both models and all outcomes assessed (Kruskal-Wallis test $p < 0.0001$). The 60-year-cohort had a mean cost per neuroinvasive disease case prevented of $664,000 and disability averted of $1,421,000 in lifelong model and $882,000 and $1,887,000, respectively in 10-year immunity model; these costs were statistically significantly lower than costs for other cohorts ($p < 0.0001$). Vaccinating 70-year-olds had the lowest cost per death averted in both models at around $4.7 million (95%CI $2–$8 million). Cost per disease case averted was lowest among 40- and 50-year-old cohorts and cost per QALY saved lowest among 60-year cohorts in lifelong immunity model. The models were most sensitive to disease incidence, vaccine cost, and proportion of persons developing disease among infected.
Conclusions: Age-based WNV vaccination program targeting those at higher risk for severe disease is more cost-effective than universal vaccination. Annual variation in WNV disease incidence, QALY weights, and vaccine costs impact the cost effectiveness ratios.

1. Introduction

West Nile virus (WNV), a mosquito-borne flavivirus, is responsible for seasonal outbreaks of WNV disease affecting all areas of the continental United States as well as areas of Canada, Europe, Asia, and Africa [1,2]. It is the leading cause of domestically-acquired arboviral disease in the United States with over 43,900 cases and 1900 deaths reported to the Centers for Disease Control and Prevention (CDC) from 1999–2015 [3,4]. Cases of hospitalized WNV disease are estimated to cost an average of $56 million per year in disease-associated morbidity and mortality [5].

An estimated 70–80% of WNV infections are asymptomatic [6–8]. Most symptomatic persons experience an acute systemic febrile illness, often referred to as West Nile fever or non-neuroinvasive disease [9]. Less than 1% develop neuroinvasive or severe disease, which typically manifests as encephalitis, meningitis, or acute flaccid paralysis (AFP) [10]. Among patients with neuroinvasive disease, the overall case-fatality ratio is approximately 10% [3]. Although persons of all ages can develop neuroinvasive disease, the incidence is higher in people >50 years [3,11].

There are no specific treatments or vaccines for WNV disease. Prevention relies on community and household prevention efforts to reduce mosquito densities, personal protective measures to

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decrease exposure to mosquitoes, and screening of blood donors [2,12]. Although these prevention measures have been shown to decrease the risk of WNV infection, cases can still occur because of variable use of these interventions and limitations in efficacy [2,4,13,14].

Several WNV vaccine candidates are under development, including two (ChimeriVax-WN02 and WNV-DENV) that have completed phase 2 clinical trials [15–18]. One study has evaluated the cost-effectiveness of a single dose of a theoretical WNV vaccine administered in a universal program to everyone in the United States [19]. We present a cost-effectiveness analysis of WNV vaccination program targeting groups at increased risk for severe WNV disease.

2. Materials and methods

We built a mathematical Markov model (using @Risk 6.3, Palisade Corporation, Ithaca, NY) to estimate the costs and health outcomes of vaccination with WNV vaccine compared to no vaccination among different age cohorts (Fig. 1). Our model tracks, from entry until age 90 years, the probability of a person becoming infected with WNV, and subsequently developing clinical disease and disability (Model available in Supplementary materials). We used the model to examine the cost-effectiveness of vaccinating different age-cohorts, spaced at 10 year intervals from ages 10–70 years (7 cohorts). We examined each cohort under two scenarios: (1) initial vaccination would give lifelong protective immunity (LPI model), similar to protection elicited from yellow fever vaccine [20]; and (2) initial vaccination that would provide only 10 years of protective immunity (TPI model), with a booster dose administered every 10 years, similar to chimeric Japanese encephalitis vaccine based on yellow fever 17D vaccine [21]. Comparing vaccinated to unvaccinated cohorts, we calculated cost-effectiveness ratios as follows: per WNV disease case averted, per WNV-related quality-adjusted life-year (QALYs) saved, per WNV-related disability averted, per WNV neuroinvasive disease case averted, and per WNV-related death averted. We used a societal perspective, which includes all costs and benefits regardless of who pays the cost or gets the benefit [22]. All costs are expressed in 2012 U.S. dollars. Both costs and health outcomes were discounted at 3% [22].

Each cohort was assumed to start with individuals being vaccinated or not at the beginning of the first year (Fig. 1). All cohorts were followed until 90-years-old (analytic horizon of 20–80 years depending on the cohort). A proportion of each cohort was assumed to be immune upon entry into the model based on background seroprevalence rates of WNV [7,23]. In addition, people experiencing a vaccine-related serious adverse event (SAE) were removed in the first year after accounting for vaccine and SAE costs [24]. They would not receive further doses of the vaccine and were assumed to be not at risk of WNV infection [25]. We applied age-specific all-cause mortality rates from the 2007 U.S. life tables to determine the number of survivors in the cohort over time [26]. Survivors both in vaccinated and non-vaccinated cohorts were at continued risk for WNV infection and developing clinical disease and disability according to their age and vaccination status. We assumed that those who do become infected with WNV will acquire natural immunity and will not be at risk of WNV infections in subsequent years.

The model utilized three types of inputs: age-specific probabilities; applied probability distributions; and constant probabilities (Table 1).

2.1. Data and assumptions

2.1.1. WNV disease incidence and complications

To determine WNV infection and death rates for the cohorts, we used age-specific WNV neuroinvasive disease incidence data reported to ArboNET from 2004–2012 [3]. Based on previously published studies, we calculated the incidence of WNV infection by multiplying the annual incidence of WNV neuroinvasive disease reported from 2004–2012 by 300 for persons aged 10–64 years and by 50 for persons aged ⩾65 years (Table 1) [27,28]. We then used the lowest incidence year (2011) and highest incidence year (2012) as the range to construct a uniform probability distribution of incidence of WNV infection for each age group in the model. We assumed that 20–30% (uniform distribution) of WNV-infected people would develop clinical disease (Table 1) [28,29]. Among those

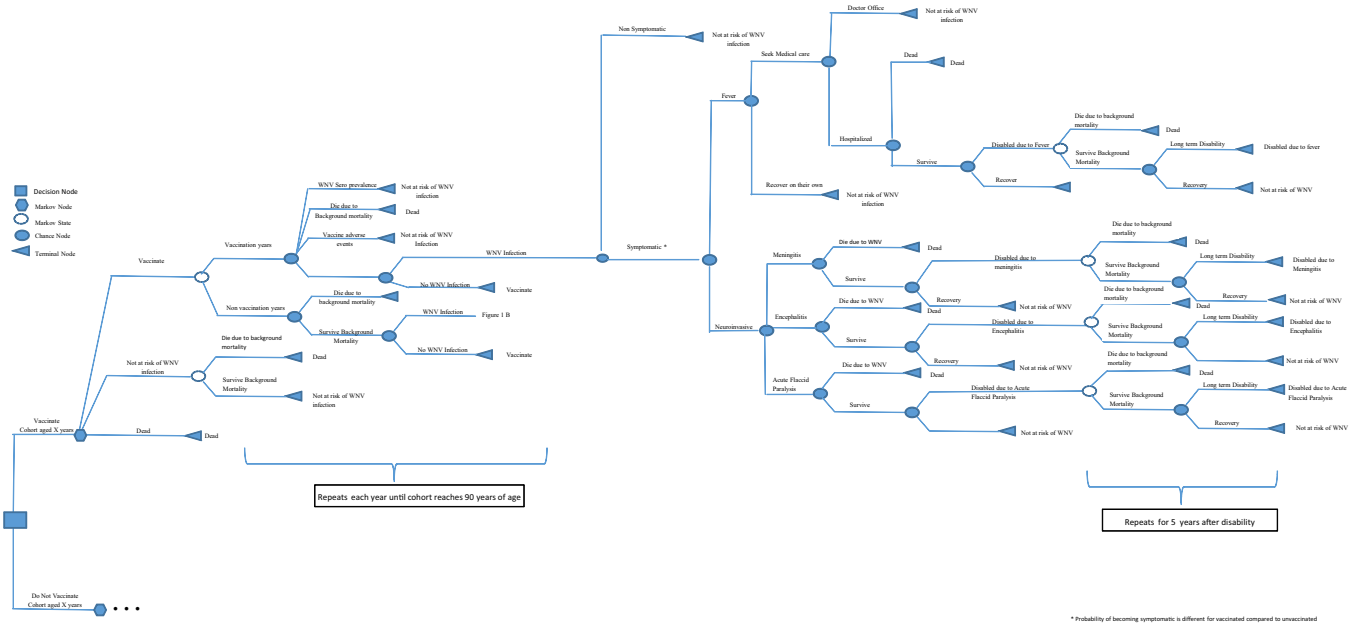

Fig. 1. Schematic diagram of the Markov Model.