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The Potential Economic Value of a *Staphylococcus aureus* Vaccine among Hemodialysis Patients

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Abstract

Staphylococcus aureus infections are a substantial problem for hemodialysis patients. Several vaccine candidates are currently under development, with hemodialysis patients being one possible target population. To determine the potential economic value of a *Staphylococcus aureus* vaccine among hemodialysis patients, we developed a Markov decision analytic computer simulation model. When *Staphylococcus aureus* colonization prevalence was 1%, the incremental cost-effectiveness ratio (ICER) of vaccination was ≤$25,217/quality-adjusted life year (QALY). Vaccination became more cost-effective, as colonization prevalence, vaccine efficacy, or vaccine protection duration increased or vaccine cost decreased. Even at 10% colonization prevalence, a 25% efficacious vaccine costing $100 prevented 29 infections, 21 infection-related hospitalizations, and 9 inpatient deaths per 1,000 vaccinated HD patients. Our results suggest that a *Staphylococcus aureus* vaccine would be cost-effective (i.e., ICERs ≤$50,000/QALY) among hemodialysis patients over a wide range of *Staphylococcus aureus* prevalence, vaccine costs and efficacies, and vaccine protection durations and delineate potential target parameters for such a vaccine.

Keywords

Staphylococcus aureus; Vaccine; Economics; Hemodialysis; Cost-effectiveness

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Introduction

Patients with end-stage renal disease undergoing hemodialysis (HD) treatment have a heightened risk of bacterial infections, particularly from *Staphylococcus aureus* (*S. aureus*) [1–3]. This is due in part to the elevated rate of *S. aureus* nasal colonization among HD patients, an established risk factor for vascular access infections and resulting bacteremic complications that can be more than twice that in the general population [3–4]. Complications of invasive *S. aureus* infections, including endocarditis, septic arthritis, and osteomyelitis, occur in 5.6% to 16.5% of cases and add to patient mortality and treatment costs [5–7]. Hospitalization rates for infection among HD patients have increased over 40% since the mid-1990s, with the number of admissions for bacteremia/septicemia rising to 112 per 1,000 patient-years in 2008 [8]. Infection continues to be a leading cause of mortality in this patient population, particularly during the first three months of dialysis treatment [8–9].

If an *S. aureus* vaccine becomes available, vaccination may be a viable approach to preventing *S. aureus* infections among HD patients. Vaccine developers have already made progress toward advancing *S. aureus* vaccination. In the past decade, developers completed Phase II (January 2010) and III (July 2006) clinical trials assessing the safety of one *S. aureus* vaccine and the efficacy of another in the active immunization of adult HD patients [10–11]. Vaccine candidates induced significantly elevated antibody levels to *S. aureus* antigens in several studies [12–14]. In addition to favorable serological indicators, one study associated vaccination with a lowered incidence of bacteremia in HD vaccinees [15]. Though protective effects began to wane less than a year following vaccination, booster vaccination provided a way to extend vaccine protection duration without increasing serious adverse reactions [16].

Establishing goals and targets for vaccine cost, efficacy, and protection duration and setting thresholds for identifying target populations during the course of vaccine development are of great importance to maximizing vaccine dissemination and utilization [17]. We developed a Markov computer simulation model to evaluate the economic value of vaccinating HD patients with an *S. aureus* vaccine. Sensitivity analyses varied *S. aureus* colonization prevalence and vaccine cost, efficacy, and duration of vaccine protection. The results of our model can help funders, policy makers, and vaccine manufacturers establish risk thresholds for and anticipate the impacts of vaccine costs and efficacy levels on the introduction and continued administration of an *S. aureus* vaccine among HD patients.

Methods

Model Structure

We adapted our previously published Markov model constructed in TreeAge Pro Suite 2009 (TreeAge Software, Williamstown, MA) to determine the potential economic value of *S. aureus* vaccination among HD patients from the third-party payer perspective [18]. Figure 1 illustrates the model structure, which included five Markov states representing an HD patient's *S. aureus* colonization and infection status: (1) not *S. aureus* colonized, (2) *S. aureus* colonized without active infection, (3) active *S. aureus* infection with outpatient treatment, (4) active *S. aureus* infection with inpatient treatment, and (5) death (absorptive). For each trial, an HD patient went through the model twice—once vaccinated and once not vaccinated—starting off either colonized (*S. aureus* colonized without active infection Markov state) or not colonized (not *S. aureus* colonized Markov state) based on the local *S. aureus* prevalence. Patients regularly received booster vaccinations when undergoing the vaccination option.

National data from the United States Renal Data System (USRDS) determined the age of the HD patients entering our model (61 years) [8]. Each patient in the model had a specific dialysis vascular access type (i.e., tunneled dialysis catheter, arteriovenous fistula, or arteriovenous graft) and underwent dialysis treatment three times a week [8, 19]. Time steps, or cycles, in the model reflected the duration of the vaccine's protective effects and corresponded to the frequency of booster vaccination. Each trial used a set cycle length of 3, 6, 9, or 12 months, as based on schedules of HD patient evaluation for ongoing dialysis treatment and existing standards for vaccination [20–23]. The vaccine's efficacy attenuated the probability of *S. aureus* infection, but vaccinees could experience vaccine-related side effects.

At the end of every cycle, HD patients could remain in the same Markov state or transition to another. If colonized, patients could stay colonized or develop a clinically apparent *S. aureus* infection and be treated and medically decolonized. Each patient continued through the model until he or she reached the death state due to death from infection (i.e., inpatient infection-related mortality), from other causes (i.e., general HD patient mortality), or from reaching the end of his or her life expectancy (median: 4.8 years) [24].

All patients with an active *S. aureus* infection received intravenous antibiotic treatment (with costs uniformly distributed between the costs of cefazolin and vancomycin) and underwent medical decolonization (combination of mupirocin, rifampin, and chlorhexidine), which could also cause side effects. Decolonized patients could become recolonized in subsequent cycles. Patients with active infection as determined by the results of agar-based clinical isolates had probabilities of being treated either as outpatients (active *S. aureus* infection with outpatient treatment Markov state) or as inpatients (active *S. aureus* infection with inpatient treatment Markov state). Those treated as inpatients could have an invasive infection with or without any combination of the following clinical conditions: abscess, endocarditis, line infection, osteomyelitis, pneumonia, septic arthritis, and septic embolism. Hospitalization costs were condition-specific, age-stratified, and based on data from the Healthcare Cost and Utilization Project (HCUP) [25]. Using the American Medical Association's CPT Code/Relative Value Search, clinical procedure costs were derived from Medicare's relative value payment amount for each CPT code [26]. Total costs of invasive infection included costs of access site removal and insertion procedures specific to the patient's access type.

Each model simulation run involved 1,000 trials of 1,000 HD patients (i.e., 1,000,000 unique outcomes). For each simulation, we evaluated the incremental cost-effectiveness ratio (ICER) of *S. aureus* vaccination according to the following equation:

$$\mathrm{ICER}=\frac{\mathrm{Cost}_{S.\ aureus\ \mathrm{vaccination}}-\mathrm{Cost}_{\mathrm{No}\ S.\ aureus\ \mathrm{vaccination}}}{\mathrm{Health\ Effects}_{S.\ aureus\ \mathrm{vaccination}}-\mathrm{Health\ Effects}_{\mathrm{No}\ S.\ aureus\ \mathrm{vaccination}}}$$

where health effects are measured in quality-adjusted life years (QALYs). A $50,000/QALY threshold determined whether the vaccination strategy was cost-effective in a given scenario [27].

Data Inputs

Our model included probability, cost, time, and QALY parameters as shown in Table 1. Input values came from published literature or expert consultation (Dr. Robert R. Muder, Chief, Division of Infectious Diseases, VA Pittsburgh Healthcare System and Dr. Kenneth J. Smith, Section of Decision Sciences and Clinical Systems Modeling, University of Pittsburgh) and assumed distributions or point values based on the available data. An annual

discount rate of 3% converted all past and future costs to 2011 US$. Number of antibiotic treatments represented the full course of antibiotics associated with a patient's clinical condition (derived from MICROMEDX online[28], refined by expert opinion), receiving treatment three times a week according to his or her dialysis schedule (e.g., a condition associated with a 4-week course of antibiotics received 12 antibiotic treatments).

Patients had baseline QALYs based on their ongoing dialysis treatment and age for the duration of their lifetime. If a patient experienced infectious complications or side effects from vaccination or treatment, net QALYs were the product of the patient's baseline QALY and the utility weight associated with those additional conditions [29]. Patients with multiple clinical conditions received the utility weight resulting in the greatest QALY decrement. These utility weights applied to patients' net QALYs for the duration of each condition, based on the duration of hospitalization for that condition (Table 1). The annual 3% discount rate also applied to future QALYs. Patients accrued the maximum costs of antibiotic treatment and hospitalization from among those associated with their conditions.

Sensitivity Analyses

Sensitivity analyses examined variations in key model parameters by systematically changing their values to determine their effects on the cost-effectiveness of *S. aureus* vaccination. As studies have shown widely ranging *S. aureus* nasal colonization prevalence in HD patients (e.g., affected by location-specific or temporal factors) [4, 30], we performed simulations ranging the probability of colonization from 1% to 40%. We also varied the vaccine's cost ($100 to $300) to represent a wide range based on the Centers of Disease Control and Prevention (CDC) vaccine price list [31], as well as its efficacy (25% to 75%) and protection duration (3 to 12 months). Booster vaccination frequencies of 3, 6, 9, and 12 months corresponded to vaccine protection duration. Probabilistic sensitivity analyses sampled values from all input parameter distributions over the ranges indicated in Table 1.

Results

Table 2 shows the ICERs for vaccination in scenarios with varying *S. aureus* prevalence and vaccine cost and efficacy when the vaccine's protective effects lasted 3 to 12 months. ICERs for vaccination were well below $50,000/QALY in all scenarios tested. Systematically varying *S. aureus* colonization prevalence and vaccine cost, efficacy, and protection duration in sensitivity analyses showed the degree to which each of these parameters affected the ICERs for *S. aureus* vaccination. In Table 2, "Vaccinate" corresponds to scenarios where vaccination was less costly and more effective than no vaccination, and therefore economically dominant (i.e., negative ICERs). Vaccination became more cost-effective as *S. aureus* colonization prevalence, vaccine efficacy, and duration of vaccine protection increased. Vaccination quickly became the dominant strategy when the probability of colonization was ≥20% at most vaccine costs, efficacies, and protection durations tested. At a 1% colonization rate, vaccination was not the dominant strategy but still remained cost-effective; ICERs ranged from $1,248/214 48/QALY to $25,217/QALY. At a 5% colonization rate, vaccination became dominant when the vaccine's cost was ≤$100, efficacy was ≥75%, and protection duration was ≥6 months. For an *S. aureus* colonization prevalence ≥30%, vaccination generally dominated no vaccination (Table 2).

S. aureus vaccination saved costs when economically dominant. Vaccines protecting for 3 months saved between $77 (40% colonization, $100 cost, 25% efficacy) and $3,796 (40% colonization, $100 cost, 75% efficacy) per person vaccinated. Savings ranged from $44 (20% colonization, $100 cost, 25% efficacy) to $4,399 (40% colonization, $100 cost, 75% efficacy), $108 (30% colonization, $200 cost, 25% efficacy) to $4,539 (40% colonization, $100 cost, 75% efficacy), and $5 (10% colonization, $100 cost, 25% efficacy) to $4,635

(40% colonization, $100 cost, 75% efficacy) for vaccines protecting for 6, 9, and 12 months, respectively. Savings increased with colonization prevalence, vaccine efficacy, and protection duration, but decreased with increasing vaccine cost. At a given prevalence, the scenarios with the lowest vaccine cost ($100), highest efficacy (75%), and longest protection duration (12 months) yielded the greatest savings: at 5% colonization prevalence, savings ranged from $76 ($200 cost, efficacy 75%,12 month duration) to $424; at 10% prevalence, savings ranged from $139 ($300 cost, efficacy 75%, 9 month duration) to $1,166; at 20% prevalence, vaccination saved between $44 ($100 cost, efficacy 25%, 6 month duration) and $2,452; at 30% prevalence, savings ranged from $108 ($200 cost, efficacy 25%, 9 month duration) to $3,615; and at 40% prevalence, it ranged from $77 ($100 cost, efficacy 25%, 3 month duration) to $4,635 per vaccinated individual.

Figure 2 illustrates the cost per infection averted for different colonization rates and durations of protection with a $100, 50% efficacious vaccine. Negative costs imply cost savings per infection averted with vaccination. A vaccine protecting for 12 months provided cost savings per averted infection for all colonization rates ≥5%. Even a 3-month protective vaccine saved costs per averted infection when the colonization rate was ≥20%.

Population Level Infection-related Outcomes

Over the course of a vaccinated HD patient's lifetime in the scenario with a 10% *S. aureus* colonization prevalence , vaccination prevented 29, 69, and 128 *S. aureus* infections per 1,000 HD patients vaccinated for vaccine efficacies of 25%, 50%, and 75%, respectively. Additionally, a 25% efficacious vaccine averted 21 hospitalizations and 4 inpatient deaths; a 50% efficacious vaccine averted 52 hospitalizations and 9 inpatient deaths; and a 75% efficacious vaccine prevented 96 hospitalizations and 17 inpatient deaths over the course of 1,000 vaccinated patient lifetimes. At a 30% colonization prevalence, vaccination averted to 340 infections, 61 to 254 hospitalizations, and 11 to 44 inpatient deaths per 1,000 vaccinated HD patients over their lifetime, varying by efficacy (25% to 75%). *S. aureus* infections, hospitalizations, and inpatient deaths averted increased with increasing vaccine efficacy (i.e., greater vaccine efficacy averted more *S. aureus* clinical outcomes) and probability of colonization.

DISCUSSION

Forecasting the impact of a vaccine early in its course of development may help increase its adoption and continued utilization [17]. Modeling can help guide investments prior to vaccine licensure, provide benchmarks for vaccine pricing and efficacy, and establish target populations. Our group has previously reported the economic impact of vaccines for various infectious diseases, including *S. aureus* for other patient populations [32–33] as well as *Clostridium difficile* [34] and influenza [35]. Results from these studies suggested that an *S. aureus* vaccine would be cost-effective in high-risk patient populations, such as neonates and orthopedic patients.

Due in part to their reduced immunoresponsiveness associated with chronic renal failure and frequent exposures to invasive devices and healthcare environments, HD patients comprise another group at elevated risk for infections, including *S. aureus* infections [1–3]. For this reason, higher doses of hepatitis B vaccine are recommended for HD patients in comparison to the general population [21]. According to the CDC, HD patient immunization practices are based on both age and high-risk conditions and include vaccinations for hepatitis B, pneumococcal polysaccharide, and annual inactivated influenza [20, 36]. Additionally, the duration of immunity following an HD patient's vaccination is shorter than that of a healthy patient. Consequently, the CDC recommends that HD patients have their hepatitis B antibody titers checked annually and that booster vaccination be performed when titers are

low [21]. This shorter duration results from both impairments in the immune system and declining antibody levels due to protein loss, as is the case with nephrotic syndrome.

HD patients routinely receive medical care at dialysis centers. Vaccination in these centers is ideal, given the frequency of patient visits. Vaccination programs that use approaches involving system changes, such as standing orders, raise immunization rates more than programs that use other approaches [37]. For vaccines targeted to persons with high-risk conditions, the CDC Task Force on Community Preventive Services recommends multiple interventions in combination [38]. With these considerations in mind, it is not surprising that vaccine developers have already proceeded to pursue an *S. aureus* vaccine for HD patients. Clinical trials have contributed to advancements in the development of a functioning *S. aureus* vaccine [10–16]. In addition to the active immunization options being explored, several passive immunization candidates are currently underway, with several having already completed Phase II and/or III clinical trials [39].

Our results suggest that an *S. aureus* vaccine would be cost-effective among HD patients over a wide range of *S. aureus* colonization prevalence, vaccine costs and efficacies, and durations of vaccine protection. Alexander et al. reported a 15.9% persistent *S. aureus* nasal colonization rate among HD outpatients[4], while Kirmani et al. reported a 40% colonization prevalence[30], our results show that vaccination of HD patients at both of these rates can be cost-effective, dominating for many vaccine characteristics. The population-level impact of an *S. aureus* vaccine among HD patients can be sizable, with vaccination preventing up to 317 hospitalizations and 55 inpatient deaths associated with 425 *S. aureus* infections per 1,000 vaccinated HD patients at 40% colonization prevalence (75% vaccine efficacy). Though ICERs for *S. aureus* vaccination remained ≤$50,000/QALY in all scenarios tested, they decreased further with higher *S. aureus* prevalence, lower vaccine cost, greater vaccine efficacy, or longer duration of vaccine protection. Even for vaccines with the lowest efficacy (25%) and shortest protection duration (3 months), the ICERs for vaccination versus no vaccination were ≤$25,217/QALY. Vaccination quickly became the dominant strategy for vaccines with ≥50% efficacy and ≥6 months of protection when *S. aureus* prevalence was ≥20% and vaccine cost was ≤$200. These results emphasize the important roles of local prevalence and vaccine cost in the implementation of an *S. aureus* vaccine. As the distribution of access types represented in our model reflected usage by a heterogeneous cohort of HD patients[8], the effects of 305 vaccination on each type were not compared individually, however access type could have an effect on the probability of infection given colonization and the cost of treatment. When planning an *S. aureus* vaccination program in HD patients, vaccine developers, insurance payers, and other decision makers involved in the distribution and administration of the vaccine may want to focus particularly on the risk of *S. aureus* colonization and the cost of the vaccine to the local HD patient community.

Our model tended to be conservative about the potential benefits of an *S. aureus* vaccine, as it used lower estimates of infection-related procedural costs and excluded rarer *S. aureus* complications (e.g., meningitis, atrial thrombus, and stroke). Our model required patients to have *S. aureus* nasal colonization prior to becoming infected, underestimating the rate of overall colonization (e.g. including oropharynx, axilla, and groin colonization) as well as cases of infection without preceding colonization. The model did not consider the additional benefits of reducing transmission, indirectly protecting those not vaccinated.

Limitations

All computer simulation models are simplified portrayals of the environments and situations they simulate. Our model did not account for all possible outcomes of *S. aureus* infection in HD patients. Available data restricted the array of clinical conditions included in the model,

and parameterization involved derivation from a range of studies and databases of varying quality. Though sensitivity analyses attempted to address a wide range of scenarios, individual case variability may extend beyond the included parameter values. Also, our results may not be applicable to younger patients, as individuals in our HD patient population were ≥61 years of age. Our analysis was limited to HD patients; the cost-effectiveness of vaccination may be different for peritoneal dialysis patients, as their rates of *S. aureus* colonization and infection are not well defined and varies in the reported literature.

Conclusions

Our results suggest that an *S. aureus* vaccine for HD patients would be cost-effective over a wide range of estimated *S. aureus* prevalence, vaccine costs and efficacies, and durations of vaccine protection. Vaccination could reduce the incidence of *S. aureus* infections in this at-risk population, yielding projected benefits for both individual patients and patient populations that would outweigh the costs of the vaccine and the impact of possible side effects.

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Highlights

- We model the potential economic value of a *Staphylococcus aureus* vaccine in hemodialysis patients
- Sensitivity analysis varied colonization prevalence and vaccine characteristics
- Vaccination was cost-effective for all tested scenarios and quickly became economically dominant
- Vaccination would be cost-effective over a wide range of prevalence rates and vaccine costs, efficacies, and protection durations

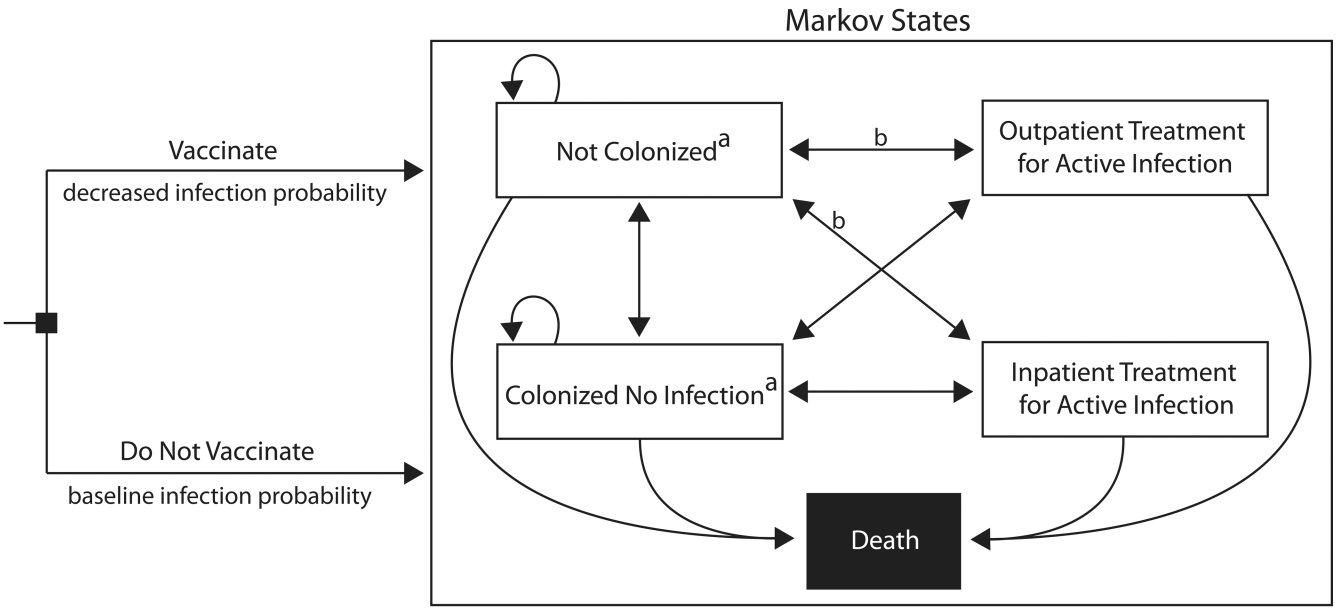

FIGURE 1.
Markov model structure

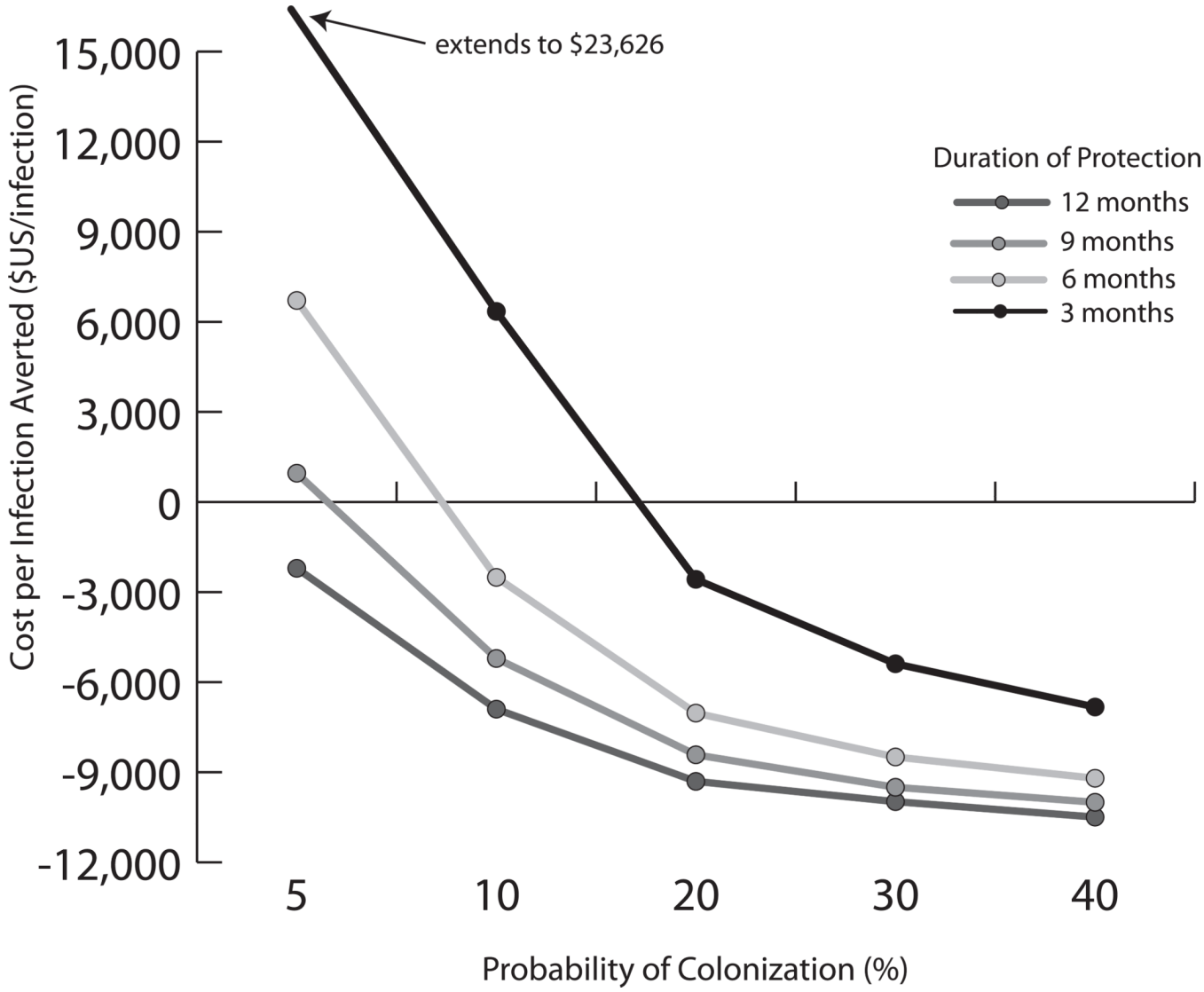

FIGURE 2.
Cost per infection averted for a $100 vaccine with 50% efficacy at varying colonization rates.

Table 1

Table of Inputs.

Description (Units)	Distribution Type[a]	Mean	Standard deviation, Standard Error[c], or Range	Source
Costs (US$)				
Cefazolin, 20mg/kg IV after dialysis (initial)	Gamma	3.90	2.91	[40–41]
Cefazolin 1g Dose (subsequent)	Gamma	2.93	2.19	[40–41]
Vancomycin, 1 g/dose (initial)	Gamma	10.80	7.51[b]	[41]
Vancomycin, 500 mg/dose (subsequent)	Gamma	5.40	3.76[b]	[41]
Decolonization Regimens:				
Mupirocin, 300 mg Dose	-	15.91	-	[42]
Rifampin, 2x Day/10 Days	-	66.77	32.35[b]	[41]
Chlorhexidine, 4% Cholorhexidine Gluconate	-	29.56	-	[41]
Hospitalization:				
Non-invasive Infection (ages 45–64)	Triangular	19,010	6,819 – 23,694	[25]
Non-invasive Infection (ages 65–84)	Triangular	14,678.5	6,519 – 21,457	[25]
Abscess (ages 45–64)	Gamma	7,593	774[c]	[25]
Abscess (ages 65–84)	Gamma	8,489	1,970[c]	[25]
Bacteremia (ages 45–64)	Gamma	14,391	787[c]	[25]
Bacteremia (ages 65–84)	Gamma	13,691	551[c]	[25]
Endocarditis (ages 45–64)	Gamma	23,844	4,409[c]	[25]
Endocarditis (ages 65–84)	Gamma	24,379	3,648[c]	[25]
Line Infection (ages 45–64)	Gamma	19,715	437[c]	[25]
Line Infection (ages 65–84)	Gamma	20,562	504[c]	[25]
Osteomyelitis (ages 45–64)	Gamma	26,024	6,609[c]	[25]
Osteomyelitis (ages 65–84)	Gamma	14,767	4,309[c]	[25]
Pneumonia (ages 45–64)	Gamma	22,834	860[c]	[25]
Pneumonia (ages 65–84)	Gamma	20,868	589[c]	[25]
Septic Arthritis/Septic Embolism (ages 45–64)	Gamma	24,693	440[c]	[25]
Septic Arthritis/Septic Embolism (ages 65–84)	Gamma	19,626	326[c]	[25]
Clinical Procedures:				
Transthoracic Echocardiogram	Gamma	161.66	47.02	[26]
Arteriovenous Graft Insertion	-	722.00	-	[26]
Arteriovenous Graft Removal	-	606.82	-	[26]
Tunneled Dialysis Catheter Insertion	-	288.80	-	[26]
Tunneled Dialysis Catheter Removal	-	143.38	-	[26]
Temporary Catheter	-	122.65	-	[26]

Description (Units)	**Distribution Type[a]**	**Mean**	**Standard deviation, Standard Error[c], or Range**	**Source**
Physician Consultation	-	75.77	-	[26]
Agar-based Clinical Culture	-	12.12	-	[43]
Utility Weights				
Healthy Year (ages 45–64)	-	0.92	-	[44]
Healthy Year (ages 65–84)	-	0.84	-	[44]
Dialysis	-	0.6528	0.095	[45–50]
Non-invasive Infection (Outpatient)	Beta	0.725	0.035	[51–52]
Non-invasive Infection (Inpatient)	Beta	0.71	0.084	[51, 53–54]
Bacteremia	Beta	0.57	0.0566	[55–56]
Abscess	Beta	0.648	0.094	[51–52, 57]
Endocarditis	Beta	0.587	0.0603	[55, 58–59]
Line Infection	Beta	0.648	0.094	[51–52, 57]
Osteomyelitis	Uniform		0.53 – 0.59	[60–61]
Pneumonia	Beta	0.625	0.0636	[62–63]
Septic Arthritis	-	0.600	-	Expert Opinion
Septic Embolism	Triangular	0.76	0.60 – 0.89	[64]
Antibiotic Side Effects	Uniform	-	0.980 – 0.999	[65]
Vaccine Side Effects	Triangular	0.950	0.710 – 1.00	[50]
Probilities				
Access Site Type:				
Arteriovenous Fistula	-	0.550	-	[8]
Arteriovenous Graft	-	0.272	-	[8]
Tunneled Dialysis Catheter	-	0.178	-	[8]
S. aureus Outcomes:				
Infection given Colonization [d]	Uniform	-	0.111 – 0.200	[66–67]
Hospitalization given Infection	-	0.746	-	[5]
Invasive Infection (Bacteremia) given Hospitalization	-	0.428	-	[5]
Secondary Clinical Outcomes given Invasive Infection[e]:				
Abscess	Triangular	0.078	0.032 – 0.191	[5, 9, 68–69]
Endocarditis	Triangular	0.107	0.011 – 0.171	[5, 9, 68–70]
Line Infection	Triangular	0.0773	0.076 – 0.0786	[71]
Osteomyelitis	Triangular	0.045	0.022 – 0.113	[5, 9, 68–70]
Pneumonia	-	0.160	-	[72]
Septic Arthritis	Triangular	0.04	0.032 – 0.048	[9, 68–70]
Septic Embolism	Triangular	0.056	0.048 – 0.072	[9, 68]
Mortality:				

Description (Units)	Distribution Type[a]	Mean	Standard deviation, Standard Error[c], or Range	Source
All Causes (ages 60–64)[e]	-	0.168	-	[8]
All Causes (ages 65–69)[e]	-	0.200	-	[8]
All Causes (ages 70–79)[e]	-	0.257	-	[8]
Non-invasive Infection (Inpatient)	-	0.118	-	[73]
Bacteremia	-	0.202	-	[5]
Endocarditis	-	0.545	-	[7]
Pneumonia	Beta	0.368	0.174	[72, 74–76]
Septic Arthritis/Septic Embolism	-	0.222	-	[77]
Side Effects from Vaccination	-	0.050	-	Expert Opinion
Side Effects from Antibiotic Treatment	-	0.570	-	[65]
Number of Antibiotic Courses				
Outpatient Treatment	Uniform		4 – 6	Expert Opinion, [28]
Abscess	-	12	-	Expert Opinion, [28]
Bacteremia	-	12	-	Expert Opinion, [28]
Endocarditis	Uniform	-	12 – 18	Expert Opinion, [28]
Line Infection	Uniform	-	6 – 12	Expert Opinion, [28]
Osteomyelitis	-	18	-	Expert Opinion, [28]
Pneumonia	-	6	-	Expert Opinion, [28]
Septic Arthritis/Septic Embolism	-	12	-	Expert Opinion, [28]
Duration of Hospitalization (Days)[f]				
Drug Treatment Side Effects	-	7		[65]
Vaccine Side Effects	Triangular	0.75	0.5 – 1.0	[78]
Non-invasive Infection (Outpatient) (ages 45–64)	Gamma	4.8	−0.5[c]-	[79]
Non-invasive Infection (Outpatient) (ages 65–84)	Gamma	6.2	−1.5[c]-	[79]
Non-invasive Infection (Inpatient) (ages 45–64)	Gamma	6.75	2.276	[79]
Non-invasive Infection (Inpatient) (ages 65–85)	Gamma	7.6	1.98	[79]
Abscess (ages 45–64)	Gamma	4.8	−0.5[c]	[79]
Abscess (ages 65–84)	Gamma	6.2	−1.5[c]	[79]
Bacteremia (ages 45–64)	Gamma	7.1	0.2[c]	[79]
Bacteremia (ages 65–84)	Gamma	7.4	0.2[c]	[79]
Endocarditis (ages 45–64)	Gamma	105.	1.5[c]	[79]
Endocarditis (ages 65–84)	Gamma	10.6	1.1[c]	[79]

Description (Units)	Distribution Type[a]	Mean	Standard deviation, Standard Error[c], or Range	Source
Line Infection (ages 45–64)	Gamma	9.2	0.2[c]	[79]
Line Infection (ages 65–84)	Gamma	9.8	0.4[c]	[79]
Osteomyelitis (ages 45–64)	Gamma	8.0	0.3[c]	[79]
Osteomyelitis (ages 65–84)	Gamma	9.5	0.4[c]	[79]
Pneumonia (ages 45–64)	Gamma	8.7	0.4[c]	[79]
Pneumonia (ages 65–84)	Gamma	9.0	0.3[c]	[79]
Septic Arthritis/Septic Embolism (ages 45–64)	Gamma	9.8	0.1[c]	[79]
Septic Arthritis/Septic Embolism (ages 65–84)	Gamma	8.7	0.1[c]	[79]

[a] Based on available data

[b] Standard deviation represents variations in the average wholesale price (AWP) across manufactures

[c] Value is a standard error

[d] Yearly value, modeled as a time dependent parameter

[e] Clinical conditions of HD patient hospitalized for invasive *S. aureus* infection

[f] Durations used for QALY decrements

Table 2

Incremental cost-effectiveness ratio (ICER: US$/QALY) of vaccination compared to no vaccination at different *Staphylococcus aureus* colonization prevalence, vaccine costs and efficacies, and durations of vaccine protection.

Vaccine Cost	Vaccine Efficacy	Prevalence of SA Colonization (%)					
		1	5	10	20	30	40
Vaccine Protection for 3 Months							
$100	**25%**	8,371	7,265	5,944	3,521	1,482	Vaccinate
	50%	7,972	5,571	2,801	Vaccinate	Vaccinate	Vaccinate
	75%	7,508	3,198	Vaccinate	Vaccinate	Vaccinate	Vaccinate
$200	**25%**	16,880	16,759	14,221	11,499	8,987	6,971
	50%	16,382	15,920	10,854	5,495	1,038	Vaccinate
	75%	11,226	15,938	6,415	Vaccinate	Vaccinate	Vaccinate
$300	**25%**	25,217	24,256	22,128	19,441	16,845	14,380
	50%	24,889	21,860	19,059	12,957	8,356	4,322
	75%	24,361	19,257	14,182	5,441	Vaccinate	Vaccinate
Vaccine Protection for 6 Months							
$100	**25%**	4,171	3,119	1,929	Vaccinate	Vaccinate	Vaccinate
	50%	3,826	1,532	Vaccinate	Vaccinate	Vaccinate	Vaccinate
	75%	3,310	Vaccinate	Vaccinate	Vaccinate	Vaccinate	Vaccinate
$200	**25%**	8,581	7,499	6,186	3,746	1,682	Vaccinate
	50%	8,162	5,698	2,995	Vaccinate	Vaccinate	Vaccinate
	75%	7,784	3,336	Vaccinate	Vaccinate	Vaccinate	Vaccinate
$300	**25%**	12,928	11,793	10,355	7,919	5,646	3,705
	50%	12,411	10,003	7,202	2,064	Vaccinate	Vaccinate
	75%	12,221	7,702	2,836	Vaccinate	Vaccinate	Vaccinate
Vaccine Protection for 9 Months							
$100	**25%**	2,856	1,865	753	Vaccinate	Vaccinate	Vaccinate
	50%	2,545	226	Vaccinate	Vaccinate	Vaccinate	Vaccinate
	75%	2,007	Vaccinate	Vaccinate	Vaccinate	Vaccinate	Vaccinate

Vaccine Cost	Vaccine Efficacy	Prevalence of SA Colonization (%)					
		1	5	10	20	30	40
	25%	5,848	4,893	4,978	3,693	Vaccinate	Vaccinate
$200	50%	5,563	3,264	595	Vaccinate	Vaccinate	Vaccinate
	75%	2,112	865	Vaccinate	Vaccinate	Vaccinate	Vaccinate
	25%	8,912	7,935	6,638	4,245	2,166	259
$300	50%	8,518	6,239	3,508	Vaccinate	Vaccinate	Vaccinate
	75%	8,077	3,920	Vaccinate	Vaccinate	Vaccinate	Vaccinate
Vaccine Protection for 12 Months							
	25%	2,082	1,063	Vaccinate	Vaccinate	Vaccinate	Vaccinate
$100	50%	1,733	Vaccinate	Vaccinate	Vaccinate	Vaccinate	Vaccinate
	75%	1,248	Vaccinate	Vaccinate	Vaccinate	Vaccinate	Vaccinate
	25%	4,384	3,371	2,168	Vaccinate	Vaccinate	Vaccinate
$200	50%	4,056	3,430	Vaccinate	Vaccinate	Vaccinate	Vaccinate
	75%	3,540	Vaccinate	Vaccinate	Vaccinate	Vaccinate	Vaccinate
	25%	6,704	5,573	4,440	2,072	147	Vaccinate
$300	50%	6,390	3,959	1,272	Vaccinate	Vaccinate	Vaccinate
	75%	5,855	1,593	Vaccinate	Vaccinate	Vaccinate	Vaccinate

Vaccinate: vaccination is less costly and more effective than no vaccination (i.e., dominant)