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The Potential Economic Value of a *Staphylococcus aureus* Vaccine for Neonates

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Abstract

The continuing morbidity and mortality associated with *Staphylococcus aureus (S. aureus)* infections, especially *methicillin-resistent Staphylococcus aureus* (MRSA) infections, have motivated calls to make *S. aureus* vaccine development a research priority. We developed a decision analytic computer simulation model to determine the potential economic impact of a *S. aureus* vaccine for neonates. Our results suggest that a *S. aureus* vaccine for the neonatal population would be strongly cost-effective (and in many situations dominant) over a wide range of vaccine efficacies (down to 10%) for vaccine costs (≤$500), and *S. aureus* attack rates (≥1%).

Keywords

Staphylococcus aureus; Vaccine; Economics

1. Introduction

The continuing morbidity and mortality associated with *Staphylococcus aureus* infections, especially methicillin-resistent *Staphylococcus aureus* (MRSA) infections, have motivated calls to make *S. aureus* vaccine development a research priority. Indeed, over the past two decades, MRSA persists in many healthcare settings and has spread fairly rapidly throughout

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the community, despite control efforts and policies. In fact, an increasing number of *S. aureus* isolates are demonstrating antibiotic resistance.[1-5]

Quantifying the potential economic value of such a *S. aureus* vaccine can help us understand how much to emphasize and invest in its development. Such information can help policy makers determine their areas of emphasis, manufacturers plan their research and development portfolio, funding agencies allocate resources, and scientists establish goals. It can also help define and establish desired vaccine characteristics and establish price targets. Constructing economic models early in a vaccine's development can help all stakeholders anticipate potential obstacles and adjust research plans accordingly. Economic models also can aid in choosing initial target populations for the vaccine.

Neonates, who typically have naive immune systems that leave them more susceptible to infections, are a potential target population. For example, the cumulative incidence of *Staphylococcus aureus* bacteremia among premature infants is approximately 4% and overall nosocomial infections 15-20%.[6-9] Frequent handling by family members, friends, and healthcare providers can facilitate spread. Infection control interventions such as contact precautions, education, decolonization, cohort nursing, and hand hygiene may not be always be effective or easy and inexpensive to implement.[10-12] Neonatal intensive care unit (NICU)-associated nosocomial infections result in significant neonatal morbidity and mortality, prolonged hospitalization, and extensive hospital costs.[9,13-15] Since the first reported case of MRSA in a hospitalized neonate in 1981, numerous outbreaks have occurred in the NICU population.[12,16-20]. Even when control of MRSA outbreaks is achieved, enduring eradication is rarely achieved.[11-12] One other factor makes neonates a potential target for a *S. aureus* vaccine. Neonates do not remain in the higher at-risk state indefinitely, as their immune systems eventually mature. So a *S. aureus* vaccine does not need to confer immunity for an extensive period of time.

Immunization can be either active (i.e., stimulating the neonate's immune system) or passive (e.g., providing immunoglobulins) but a passive immunization strategy may be preferable in an immuno-naive population such as neonates. Neonates born before 32 weeks gestation have not acquired IgG across the placenta and will not have coverage afforded by endogenous synthesis until 4-6 months after birth. [8,21] Passive immunization could immediately (but transiently) protect patients who cannot mount a timely or rapid enough response to active vaccination. Several candidate immunoglobulin preparations to prevent *S. aureus* infections or facilitate treatment of *S. aureus* associated bacteremia are currently under development.[8, 22-26]

We developed computer simulation models to evaluate the potential economic value of a *S. aureus* vaccine administered to neonates. The models simulated the decision of whether to immunize a neonate against *S. aureus*. Sensitivity analyses were conducted to assess how varying MRSA prevalence, vaccine cost and vaccine efficacy impacts the cost-effectiveness of a vaccination strategy. The results of our model may help guide policy making, research initiatives and design of future clinical studies.

2. Methods

2.1. Model Structure

Using TreeAge Pro 2008 (TreeAge Software, Williamstown, MA), we developed two stochastic decision analytic computer simulation models depicting the decision of whether or not to administer a *S. aureus* vaccine to a neonate. The first model evaluated the effects of a *S. aureus* vaccine in preventing all types of *S. aureus* infections [including methicillin-sensitive *S. aureus* (MSSA) and MRSA] while the second focused specifically on MRSA, a subset of

S. aureus infections that tends to have disproportionately worse outcomes than MSSA. Each model assumed both the societal and third party payor perspectives and simulated the potential cost-effectiveness outcomes of each scenario. The third party payor perspective included only direct medical costs, while the societal perspective accounted for both direct medical costs and patient productivity losses but did not include parent and caretaker productivity losses.

Figures 1 and 2 depict the general structure of both the general *S. aureus* and the MRSA specific vaccine decision models. Each neonate entering the *S. aureus* model receives or does not receive a *S. aureus* vaccine. The neonate then has a probability of developing a *S. aureus* infection (the attack rate in unvaccinated neonates not vaccinated; the attack rate multiplied by 1-vaccine efficacy in vaccinated neonates). A neonate with a *S. aureus* infection then has a probability of developing one or more of the following clinical syndromes: skin and soft tissue infection (SSTI), urinary tract infection (UTI), bacteremia, pneumonia, or endocarditis. For example, one newborn traveling through the model could develop a soft tissue infection whereas another could exhibit multiple clinical manifestations including SSTI, pneumonia, and endocarditis. Each clinical syndrome is accompanied by a probability of requiring essential diagnostic and therapeutic procedures. The MRSA-specific model is similar in structure, except that the attack rate and the probabilities of developing each clinical syndrome are specific to MRSA.

For each simulation run, the following equation determined the incremental cost-effectiveness ratio (ICER) of neonate vaccination:

$$\mathrm{ICER}=\frac{\mathrm{Cost}_{\text{Neonatal Vaccination}}-\mathrm{Cost}_{\text{No Neonatal Vaccination}}}{\mathrm{Effectiveness}_{\text{Neonatal Vaccination}}-\mathrm{Effectiveness}_{\text{No Neonatal Vaccination}}}$$

2.2. Data Inputs

Table 1 lists the input parameters for the *S. aureus* and MRSA vaccine models, respectively, including probabilities, costs, and utilities, as well as the distribution parameters and data sources used for each variable. Probabilities assume beta distributions, except the probability of developing an MRSA-attributable abscess and the probability of developing MRSA osteomyelitis, which assume triangular distributions. We use triangular distributions for all costs, except for the cost of death which is a fixed $5,000.[27] All costs are in 2008 U.S. dollars. A discount rate of 3% is used to convert past and future costs into 2008 dollars.

Our models measure effectiveness of vaccination in quality-adjusted life-years (QALYs). The probability distributions of projected life expectancy come from the Human Mortality Database.[22] Each clinical outcome results in an attendant QALY decrement that is assumed to persist for the duration of the condition. A urinary tract infection resulted in QALY decrement down to 0.73, an abscess down to 0.642, pneumonia down to 0.58, and bacteremia, endocarditis, or osteomyelitis down to 0.53.[23-24,28] Death results in a loss of QALYs equal to the projected QALY-adjusted life expectancy of a newborn.[29]

Our models assume that infective endocarditis and osteomyelitis are treated with a 42-day course of vancomycin and soft tissue infections with a 10-day course of vancomycin. All other MRSA infections are assumed to necessitate a 14-day course of antibiotic treatment. Vancomycin is dosed by weight with its cost being $0.014472 per milligram. The distribution of newborn birth weights is drawn from the Centers for Disease Control and Prevention VitalStats Birth information web database.[30]

2.3. Sensitivity Analyses

Sensitivity analyses look at varying the values of all parameters simultaneously across their distributions in Table 1 as well as focusing on certain key parameters. We systematically test a wide range of vaccine efficacies (10% to 99%) and a wide range of *S. aureus* and MRSA attack rates (from 0.1% to 10%). Varying the cost of vaccination from $100-$1,000 per neonate helps us understand how different price points would affect the vaccine's economic value. We also evaluate the potential impact of minor and major vaccine side effects. Minor side effects include both local and self-limited systemic side effects that only require home treatment with over the counter medications. Since, currently, the potential major side effects of a *S. aureus* vaccine are unknown, we use cost data from a major potentially debilitating vaccine side effect, Guillain-Barré Syndrome (GBS). (Note that this does not imply that GBS will be a side effect of a *S. aureus* vaccine). Probabilistic (Monte Carlo) sensitivity analyses examine the effects of varying all parameters simultaneously using all the distributions on Table 1.

3. Results

3.1 Overall Results

Each simulation run consisted of 1,000 trials of 1,000 neonates (or 1,000,000 total newborns traveling through the model). The top half of Table 2 compiles select key simulation scenarios results from the all *S. aureus* model, and how they trend with the *S. aureus* infection attack rate, vaccine efficacy, and vaccine cost. The lower half of Table 2 lists analogous results from the MRSA-specific model. (Not displayed are numerous other simulation runs utilizing intermediate vaccine cost and efficacy values.)

While some debate exists over the exact ICER threshold at which an intervention becomes cost-effective, traditionally ICERs under $50,000/QALY suggest that an intervention may be relatively cost-effective.[31] In general, interventions costing less than $20,000 per QALY have very good evidence for adoption while those costing greater than $100,000 per QALY have fairly poor evidence for adoption.[32] When vaccination is both less costly and more effective than no vaccination, vaccination is the dominant strategy (i.e., choosing to vaccinate is clearly beneficial).

3.2 S. aureus Vaccine Cost of $100 per Patient

When vaccine cost is $100 per patient and vaccine efficacy is as low as 10%, vaccination is cost-effective as long as *S. aureus* attack rate is at least 1%. Increasing vaccine efficacy to 25% means that the vaccine is cost-effectiveness down to a lower *S. aureus* attack rate: 0.1%. At this vaccine cost, vaccination becomes the dominant strategy at the following combinations: efficacy is 25% and the *S. aureus* attack rate is at least 10%; efficacy is 50%-75% and the *S. aureus* attack rate is equal to or greater than 5%; efficacy reaches 90% and the *S. aureus* attack is at least 2%.

3.3 S. aureus Vaccine Cost of $200 per Patient

Although increasing per patient vaccine cost to $200 does change some of cost-effectiveness thresholds, vaccination remains cost-effective at a wide range of efficacy and prevalence levels. Even at a vaccine efficacy as low as 10%, vaccination is cost-effective when the *S. aureus* attack rate is 1%. Raising vaccine efficacy levels to the range of 25%-50% lowers the *S. aureus* attack rate threshold for cost-effectiveness to 0.1%. Vaccination remains dominant for a wide range of vaccine efficacy and *S. aureus* attack rates. Even when vaccine efficacy is 50%, vaccination is dominant when the *S. aureus* attack rate is greater than or equal to 10%. When vaccine efficacy crosses 75%, vaccination dominates when the *S. aureus* attack rate is at least 5%.

3.4 S. aureus Vaccine Cost of $1000 per Patient

Even when vaccine cost is raised to $1000 per patient, vaccination remains relatively cost-effective for a vast majority of the scenarios. At an efficacy of 10%, vaccination is cost-effective when the *S. aureus* attack rate is at least 2%. For vaccine efficacy anywhere between 25% and 25%, vaccination is cost-effective as long as the *S. aureus* attack rate is at least 1%. Vaccination is never economically dominant when vaccine cost $1,000 per patient.

3.5 MRSA-specific Results

As the bottom half of Table 2 shows, a *S. aureus* vaccine is cost-effective under a wide variety of circumstances even when considering prevention of only MRSA (and not MSSA). A fairly low efficacy vaccine is still fairly cost-effective at a cost as high as $1000 vaccine as long as the MRSA attack rate is at least 1%.

3.6 Minor and Major Vaccine Side Effects

Adding vaccine minor side effects to the model has little effect, even when minor side effects are very common. Adding major side effects has little impact as long as the probability of major side effects does not exceed 0.5%. For example, when vaccine costs $1000 per patient, ICER values do not change significantly even with a minor side effect probability of 90%. At the same vaccine cost, vaccination remains cost-effective when the probability of major vaccine side effects <0.5%, even when the *S. aureus* infection attack rate is as low as 1% and vaccine efficacy is as low as 50%.

4. Discussion

4.1 Study Implications

Our results suggest that a *S. aureus* vaccine would be strongly cost-effective (and in many situations economically dominant) over a wide range of vaccine efficacies, vaccine costs, and *S. aureus* attack rates. It is fairly compelling that vaccination is still cost-effective at fairly low vaccine efficacies (as low as 25%) and *S. aureus* attack rates (as low as 0.1%), well below those seen in many neonatal units. It is also noteworthy that even when the vaccine is fairly costly ($1000 per patient), it is still cost-effective. Our analyses may be more consistent with a passive immunization approach (or an unusually rapidly acting active immunization) since they did not account for a potential delay before the neonate can mount an adequate response to active immunization. In fact, passive immunization may be a more favorable or practical approach since neonates' immune systems may not be adequately developed to respond to a vaccine.

The target population for a *S. aureus* vaccine could be either the overall neonatal population or more specifically low birth weight (≤1,000 g), who appear to have the highest rates of MRSA infection, potentially because of their immature immune systems, prolonged hospital stays, and exposure to invasive devices and procedures. In our model, attack rates of 2-10% are more consistent with low birth weight (≤1,000 g), while lower attack rates of 0.1-1% are consistent with higher birth weight neonates (>1,000 g).[6-9] If a *S. aureus* vaccine targeted low birth weight neonates (≤1,000 g) with a median 5% *S. aureus* attack rate, with a vaccine that costs $200 and has a 50% efficacy, then our model suggests that the ICER value would be approximately $158 per QALY, well below suggested thresholds for cost-effectiveness. Lowering the cost of the vaccine to $100 would make the immunizing all low birth weight neonates economically dominant, i.e., both saving costs and providing health benefits, strong evidence for its adoption.

An effective *S. aureus* vaccine could have a substantial market. The models' results highlight the substantial burden of MRSA infections in the neonatal population. Neonates are at

increased-risk for Staphylococcal infections. Currently, MRSA exposure is very possible in the healthcare setting. For instance, data from the National Healthcare Safety Network at the Centers for Disease Control and Prevention (CDC) show that 78% of healthcare-associated infections in patients under the age of 3 are central line-associated bloodstream infections (CLABSI) and 20.6% of all CLABSIs occur in NICU patients. *S. aureus* was the pathogenic isolate in 9.9% of all CLABSIs, and 56.8% of those isolates exhibited methicillin resistance.[5] According to a study by Lessa et al. that analyzed data from the National Nosocomial Infections Surveillance System (NNIS), 1995–2004, there were 4831 *S. aureus* hospital-acquired infections among 578,521 neonates. Of the 4302 of the *S. aureus* isolated had susceptibility tests performed 975 (23%) were MRSA. Additionally, there has been a significant increase in both *S. aureus* and MRSA since 1995.[33] Additionally MRSA exposure in the community is becoming a growing problem. A single death of a neonate from MRSA can be devastating. Add the variety of other possible infection outcomes and it is clear that MRSA may be a significant threat for neonates. Preventing even only a fraction of these infections can pay significant dividends.

The considerable potential benefits of a *S. aureus* vaccine supports further investment into its development. Realizing that the market may support relatively high vaccine price points could encourage more vaccine developers to pursue this area. Higher price points with reasonable adoption could translate into ample revenues, justifying upfront investment into research and development. Additionally, the target efficacy window is fairly wide. Scientists and developers do not necessarily have to design the “perfect” vaccine that provides close to 100% protection. Even vaccines that offer low protection may be valuable. Moreover, our study suggests that third party payors would benefit from covering the *S. aureus* vaccine, even when the cost of the vaccine is fairly high. Anticipating insurance coverage for a vaccine can be additional motivation for a manufacturer to develop the vaccine.

While several *S. aureus* vaccine candidates have emerged, none have reached the market. StaphVAX®, a promising capsular bivalent polysaccharide-protein conjugate vaccine, passed an initial phase III trial evaluating safety and efficacy for the prevention of *S. aureus* associated bacteremia in end-stage renal disease patients undergoing chronic hemodialysis. However, when the vaccine failed to meet its primary efficacy endpoint in a second, larger phase III trial, development halted.[34] The manufacturer is currently developing a vaccine intended to confer protection against an additional capsular polysaccharide type and two toxins. Several immunoglobulin preparations are in various stages of pre-clinical and early clinical development for the prevention of staphylococcal infection and as adjunctive treatment of *S. aureus* bacteremia.[13,25,35-36]

Intercell (Vienna, Austria) in cooperation with Merck and Company (Whitehouse Station, NJ, USA) are developing V710, which is in Phase II testing in end stage renal disease patients. Nabi also is currently in the process of developing PentaStaph™, a multi-target *S. aureus* polysaccharide conjugate and toxoid vaccine. In addition to coverage for capsular polysaccharide types 5 and 8 that were included in the original StaphVAX® vaccine, TriStaph™ also targets type 336. These three polysaccharide conjugates have been implicated in a majority of *S. aureus* infections. Nabi also plans to add coverage for two toxins, one of which is associated with the severe SSTIs common to CA-MRSA infections, to the product in order to produce the PentaStaph™ vaccine.[27] The hemodialysis population is a challenging population for vaccine efficacy testing since they exhibit a suboptimal response to immunoprophylaxis and are unlikely to exhibit or maintain a substantial increase in antibody levels. Selection of a different population for a proof-of-principle study may be an important consideration for the production and efficacy testing of future vaccine candidates.[36] The neonate population shares the characteristic of compromised immunity with the dialysis study population and may pose the same challenge to vaccine development.

Of course, bringing a *S. aureus* vaccine to market would involve surmounting a variety of scientific hurdles. More than a decade of vaccine research and development has resulted in notable scientific advances, including the increasing availability of genomic sequences of *S. aureus* strains, but there is still a great deal unknown about the complex interaction between *Staphylococcus aureus* and the human host.[25] MRSA possesses a variety of virulence factors that complicate vaccine development, including factors influencing bacterial attachment, penetration of bacteria into tissue, and evasion of host defenses.[37-38] *S. aureus* has exhibited capsular variations, multiple toxins, and the ability to persist in biofilms and as small-colony variants.[39] Moreover, MRSA colonization and disease manifestation may not be the result of a single protein product.[36] The complex nature of MRSA virulence and the pathogen-host interaction makes it unlikely that a single immunologic target will be sufficient to confer protection against antibiotic resistant strains of *S. aureus*. In addition, many candidate vaccines have failed to eliminate MRSA and instead only been able to reduce infection severity.

While researchers have successfully conferred protection against *Staphylococcus aureus* in murine subjects, they have struggled to do so in humans. One possible explanation for this discrepancy is the inherent difference between human and murine immune response to *S. aureus*. Another observation is that some murine infection models rely on such high levels of bacteria that overwhelm the innate immune response of the host. Human infection may be due to much smaller amounts of bacteria, frequently introduced through broken skin or a medical device, that are not effectively recognized and eliminated by the immune system.[15]

In developing our model, we endeavored to remain very conservative about the benefits of a vaccine. It did not consider how the vaccine may reduce the transmission of *S. aureus* (e.g., herd immunity effects). Furthermore, by decreasing the incidence of *S. aureus* infections, a vaccine could reduce antibiotic use, which in turn could curb the development of antibiotic resistance among various pathogens. This includes curtailing the use of and resistance to MRSA decolonization regimens, such as mupirocin.[1,13,40]

4.2. Limitations

All mathematical and computational models are simplifications of real life and cannot account for every possible scenario that may arise from *S. aureus* vaccination or infection. Our model assumed that a vaccine will be safe and that administration will result in few side effects or adverse events. Safety is paramount for neonates, and regulatory bodies such as the Food and Drug Administration are unlikely to license a risky vaccine for neonates. As a result, neonates may not be the initial target population for a *S. aureus* vaccine. A requirement for successful completion of safety trials en route to FDA licensure is preserving neonatal safety, but it bears repeating. The data inputs (Table 1) used for this model were compiled from reports and studies of varying quality, but represent the best available approximations of these values. QALY values may not capture all the potential benefits of vaccination and illness prevention, such as obviating parental emotional pain and suffering from having an infected child, caretaker productivity costs, or *S. aureus* transmission to family members. Our goal was to remain conservative about the benefits of a vaccine. So, our model did not include the impact that an ill neonate would have on family members and other caretakers, which underestimates the potential value of a *S. aureus* vaccine.

4.3 Conclusions and Future Directions

Our results suggest that a *S. aureus* vaccine for the neonatal population would be strongly cost-effective (and in many situations dominant) over a wide range of vaccine efficacies, vaccine costs, and MRSA prevalence levels. The considerable potential benefits of a *S. aureus* vaccine supports further investment into its development. Realizing that the market may support relatively high vaccine price points could encourage more vaccine developers to pursue this

area. Additionally, scientists and developers do not necessarily have to design the "perfect" vaccine that provides close to 100% protection, since even vaccines that offer low protection may be valuable. Moreover, third party payors may benefit from covering the *S. aureus* vaccine, even when the cost of the vaccine is fairly high. As vaccine research and development continue to evolve, emerging data from clinical trials could be used to further refine our model predictions.

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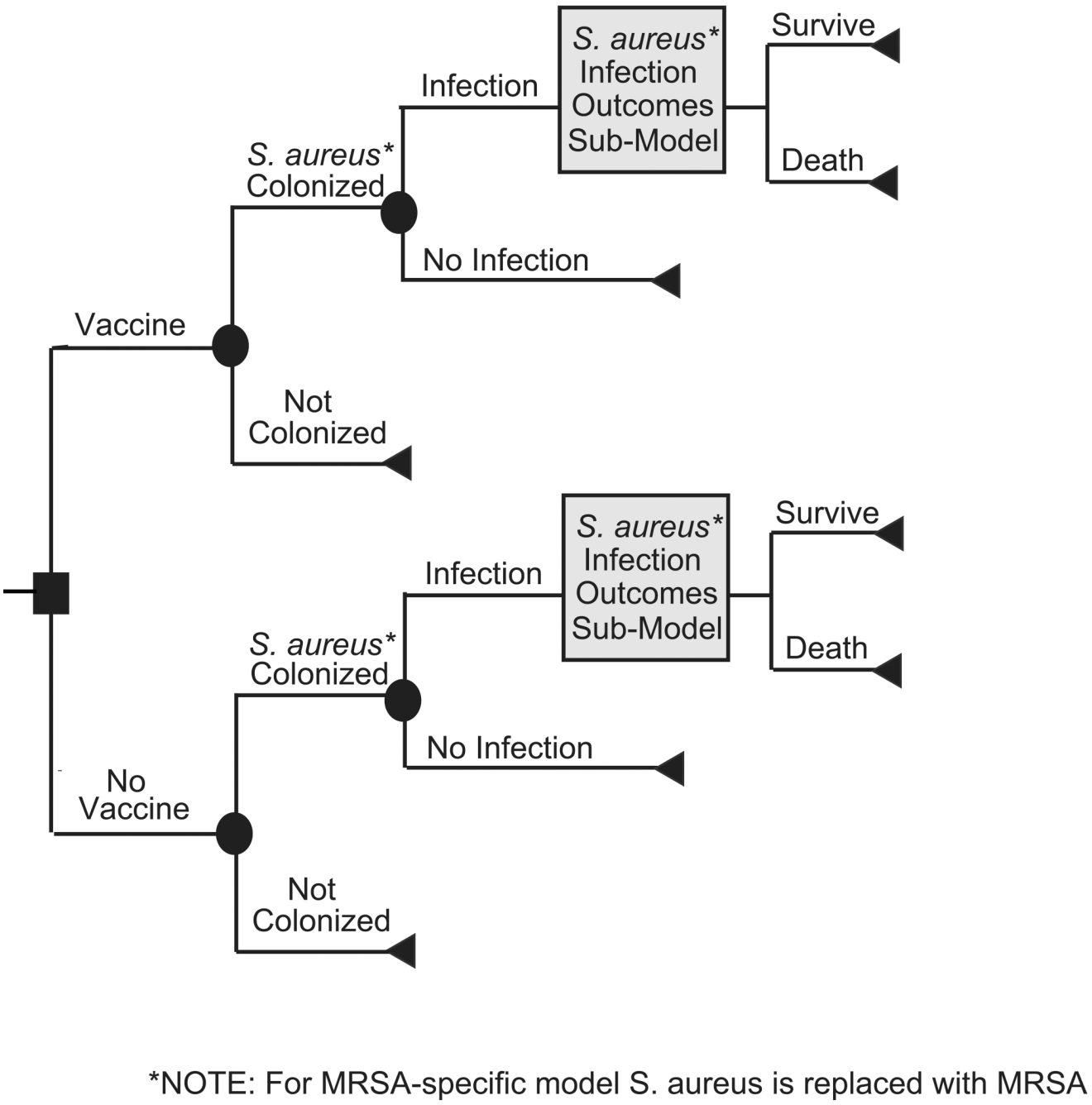

FIGURE 1.
Main Model Structure

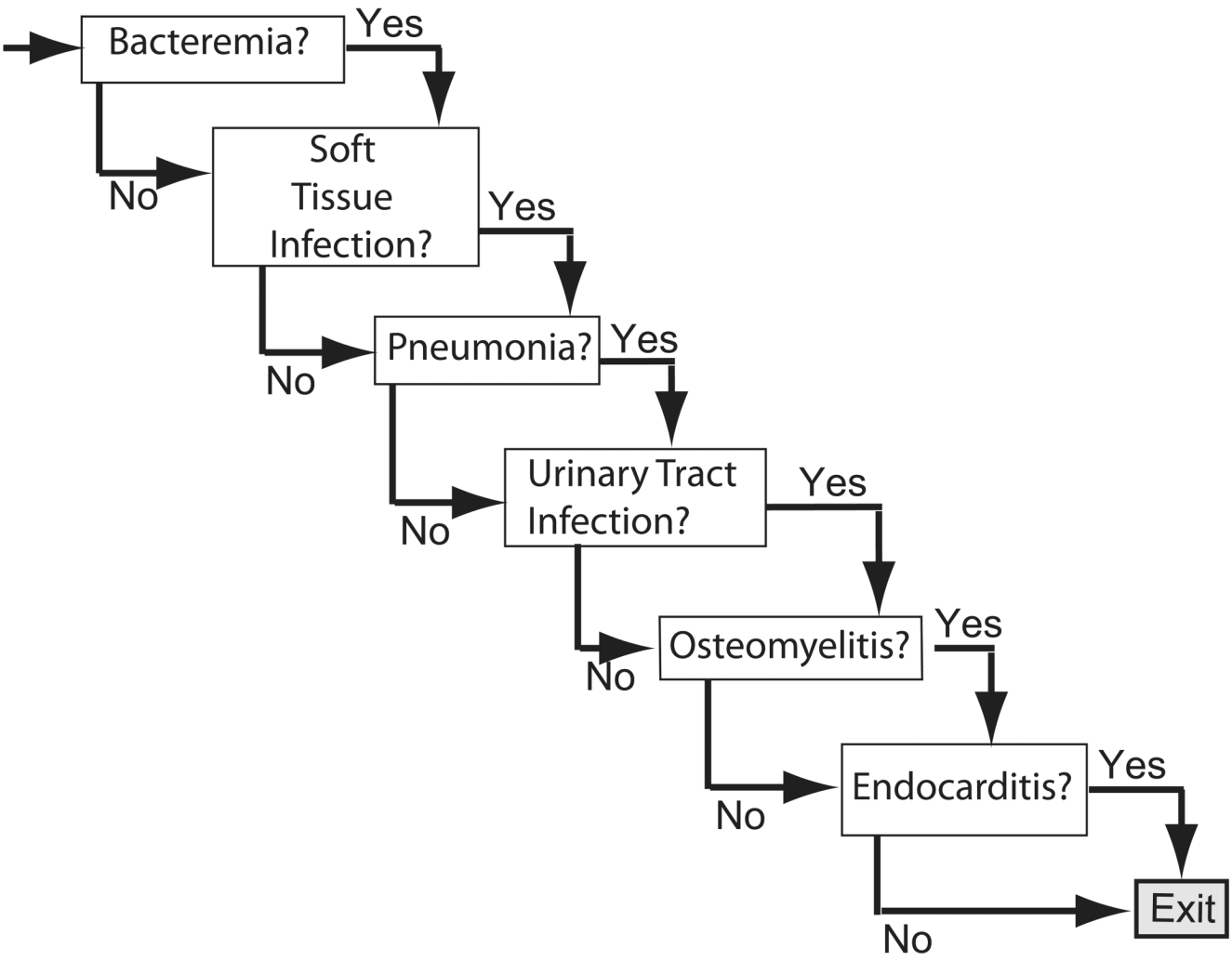

FIGURE 2.
S. aureus or MRSA Infection Outcomes Sub-Model

TABLE 1

Data Inputs for Model Variables

Description (units)	Mean	Range		Source
		Lower Limit	Upper Limit	
COSTS ($US)				
Procedures:				
Blood Culture	14.41	9.51	19.31	Hospitals
Complete Blood Count	12.24	8.08	16.40	Hospitals
Chest Radiograph	42.36	27.96	56.76	[41]
C-Reactive Protein	74.00	48.84	99.16	Hospitals
Computed Tomography	362.98	239.57	486.39	[41]
Echocardiogram	295.28	194.88	395.68	[41]
Erythrocyte Sedimentation Rate	4.93	3.25	6.61	Hospitals
Incision and Drainage	451.29	297.85	604.73	[41]
Lumbar Puncture	142.59	94.11	191.07	[41]
Lumbar Puncture Tests	50.06	33.04	67.08	Hospitals
Magnetic Resonance Imaging	359.06	236.98	481.14	[41]
Nuclear Scan	298.14	196.77	399.51	[41]
Triple Scan	269.86	178.11	361.61	[41]
Urinalysis	14.41	9.51	19.31	Hospitals
Urine Culture	14.47	9.55	19.39	Hospitals
Vancomycin Level	47.71	31.49	63.93	Hospitals
Voiding Cystourogram	275.87	182.07	369.67	[41]
Plain Radiograph for Osteomyelitis	28.04	18.51	37.57	[41]
Side Effects from Vaccination				
Major Side Effects, Societal Perspective	667363	578778	755947	[42]
Minor Side Effects	0.76	0.68	3.62	[43]
Hospitalization for:				
Bacteremia	7258.06	5302.62	9213.49	[44]
Endocarditis	46521.69	33988.00	59055.38	[44]
Osteomyelitis	15572.98	11377.37	19768.59	[44]
Pneumonia	3617.27	2642.72	4591.83	[44]
Soft Tissue Infection	4070.58	2973.90	5167.26	[44]
Urinary Tract Infection	6292.67	4597.32	7988.01	[44]
PROBABILITIES (%)				
Given S. aureus Infection				
Bacteremia	24.00	19.72*		[45-50]
Endocarditis	4.48	2.71*		[7,47]
Pneumonia	33.33	14.06*		[7,45,48-50]
Urinary Tract Infection	2.40	2.27*		[46,50]
Soft Tissue Infection	42.39	22.65*		[7,45-47]
Mortality	23.26	9.87*		[47,51]

Description (units)	Mean	Range		Source
		Lower Limit	Upper Limit	
Given MRSA Infection:				
Bacteremia	27.64	25.88*		[20,52-56]
Endocarditis	1.54	0.52*		[57]
Osteomyelitis	3.33	1.13*		[20]
Pneumonia	16.67	12.82*		[20,52,57]
Urinary Tract Infection	18.50	9.19*		[55,58]
Soft Tissue Infection	24.37	26.14*		[52,54,57,59-61]
Mortality	0.1935	0.12*		[20,51,54,57]

*Standard Deviation

Table 2

Incremental Cost-Effectiveness Ratios (ICERs) for Neonatal *Staphylococcus aureus (S. aureus)* Vaccination

All Staphylococcus. aureus Model						
Cost of Vaccine	***S. aureus* Attack Rate (AR)**	**Vaccine Efficacy**				
		0.1	**0.25**	**0.5**	**0.75**	**0.9**
$100						
	0.1%	71,609	33,293	15,406	8,405	78,99
	1%	6,252	2,450	996	566	364
	2%	3,182	1,031	299	47	***
	5%	956	138	***	***	***
	10%	292	***	***	***	***
$200						
	0.1%	128,392	48,743	25,668	21,873	16,753
	1%	13,321	5,522	2,625	1,514	1,187
	2%	6,715	2,542	1,064	542	376
	5%	2,520	716	150	***	***
	10%	1,041	137	***	***	***
$300						
	0.1%	175,146	84,725	38,733	29,151	23,423
	1%	23,178	7,756	4,025	2,545	1,959
	2%	10,214	3,959	1,819	987	785
	5%	4,056	1,382	434	149	47
	10%	1,782	420	***	***	***
$500						
	0.1%	320,971	176,788	63,407	50,172	47,581
	1%	39,368	14,358	6,892	4,384	3,636
	2%	17,842	6,879	3,053	1,882	1,672
	5%	6,878	2,388	1,030	522	377

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All Staphylococcus. aureus Model						
Cost of Vaccine	***S. aureus* Attack Rate (AR)**	**Vaccine Efficacy**				
		0.1	**0.25**	**0.5**	**0.75**	**0.9**
$1,000	**10%**	3,284	1,034	285	58	***
	0.1%	813,431	28,3074	143,605	96,925	81,078
	1	65,770	27,265	13,885	9,117	7,611
	2%	37,497	14,347	6,673	4,678	3,601
	5%	13,064	5,539	2,448	1,514	1,197
	10%	6,668	2,492	1,015	544	359
Methicillin Resistant *Staphylococcus aureus (MRSA) –specific Model*						
Cost of Vaccine	**MRSA Attack Rate (AR)**	**Vaccine Efficacy**				
		0.1	**0.25**	**0.5**	**0.75**	**0.9**
$100	**0.1%**	113,220	33,489	13,317	9,110	6,745
	1%	5,564	2,213	861	470	334
	2%	3,122	889	308	72	5
	5%	912	173	***	***	***
	10%	252	***	***	***	***
$200	**0.1%**	622,854	33,580	25,443	16,698	14,459
	1%	10,251	5,166	2,014	1,287	1,062
	2%	6,397	1,926	973	497	324
	5%	4,230	711	158	***	***
	10%	851	138	***	***	***
$300	**0.1%**	152,563	207,014	54,506	23,525	20,621
	1%	26,561	7,974	3,478	2,187	1,783

All Staphylococcus. aureus Model						
Cost of Vaccine	***S. aureus* Attack Rate (AR)**	**Vaccine Efficacy**				
		0.1	**0.25**	**0.5**	**0.75**	**0.9**
	2%	8,232	4,414	1,454	931	703
	5%	3,210	1,296	379	153	69
	10%	1,617	431	22	***	***
$500						
	0.1%	492,442	97,543	56,458	48,635	32,205
	1%	25,355	12,792	6,244	3,813	3,273
	2%	16,960	5,924	2,764	1,689	1,475
	5%	5,404	2,151	944	478	349
	10%	2,578	910	268	62	2
$1,000						
	0.1%	503,609	273,739	195,166	87,632	73,933
	1%	88,168	24,679	12,854	8,391	6,628
	2%	31,983	11,657	6,264	3,741	3,115
	5%	12,949	4,826	2,059	1,383	1,029
	10%	5,521	2359	975	482	346

Values shaded in light grey are cost-effective (≤$50,000/QALY)

Values shaded in dark grey with *** indicate that vaccination is the dominant strategy

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