PNEUMOCOCCAL 7-VALENT CONJUGATE VACCINE: PROJECTED COSTS AND BENEFITS FOR THE ARMY MEDICAL COMMAND

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ABSTRACT

In February 2000, the FDA approved a new pneumococcal 7-valent conjugate vaccine (PCV7) which targets the 7 most common serotypes of *S. pneumoniae,* an important cause of morbidity and mortality that disproportionately affects infants and children. The Advisory Committee on Immunization Practices (ACIP) has recommended that the vaccine be administered to all children under two years of age, and to those ages 2 to 5 who are considered at high risk for the disease.

We have reviewed available databases for populations eligible to receive the vaccine through U.S. Army Medical Command (MEDCOM) treatment facilities and for the utilization of health care resources for diseases associated with *S. pneumoniae* on an inpatient and outpatient basis. This data includes FY95-99 inpatient cases of meningitis, bacteremia, bacterial pneumonia, and other conditions, and FY99 outpatient cases of otitis media.

A brief summary of the epidemiology, including temporal trends, of these diseases for infants and young children is presented along with MEDCOM's and society's projected costs and benefits from the vaccine. It will serve as a baseline for more in-depth yearly follow up analysis after initiation of vaccine program by MEDCOM.

INTRODUCTION

Streptococcus pneumoniae or pneumococcus is the leading cause of morbidity and mortality among infants and children. It causes invasive bacterial diseases, including bacteremia, sepsis, and meningitis as well as noninvasive infections, such as bacterial pneumonia, otitis media and sinusitis.

In the United States, more than 17,000 cases of pneumococcal bacteremia, 700 cases of pneumococcal meningitis, and 200 deaths due to pneumococcal meningitis are reported each year among children under five. Pneumococcal meningitis in childhood has been associated with 8% mortality and may result in neurological sequelae (25%) and hearing loss (32%) in survivors. There are also more than 5 million cases of otitis media in children under five every year, resulting in 27 million doctor visits. [1, 7, 10]

Pneumococcal disease costs the U.S. health care system an estimated $1.5 billion annually. The associated direct health care costs and indirect nonmedical costs are substantial. Compounding the problems associated with *S. pneumoniae* is the phenomenon of antibiotic resistance. [5]

On February 17, 2000, the FDA approved a new pneumococcal 7-valent conjugate vaccine known commercially as Prevnar™. The vaccine targets the 7 most common serotypes of *S. pneumoniae (4, 6B, 9V, 14, 18C, 19F, and 23F),* which account for approximately 80% of invasive pneumococcal disease, 85% of bacterial pneumonia, and roughly 60% of acute otitis media due to *S. pneumoniae*

(12-24% of all acute otitis media). These serotypes are also among the most resistant to antibiotics traditionally used to treat pneumococcal infections. [3, 10]

Initial tests have demonstrated its efficacy against the seven serotypes to approach 100%, and near 90% efficacious against all pneumococcal serotypes for invasive disease. It appears to be less effective in reducing non-invasive pneumonia, with efficacy rates at approximately 33%. Although the vaccine has not been approved for otitis media prevention a 7-9% reduction in otitis media and a 20% reduction in the consequential need for ear tubes has also been demonstrated. [2] These results are summarized in Table 1.

The ACIP recommends coverage of all children under 24 months and children 24-59 months at high risk for the disease due to sickle cell disease, HIV infection, chronic illness or weakened immune system. The final revision in ACIP recommendations should be published later this year, but includes consideration for immunization of all children 24-59 months of age with priority given to children who are of Alaska Native, American Indian and African American descent and children who attend group child care. Other children who may benefit from immunization include socially or economically disadvantaged and those who have had frequent or complicated acute otitis media within the previous year. [6, 7]

METHODS

We reviewed the military's Standard Ambulatory Data Records (SADR) and Standard Inpatient Data Records (SIDR) for potentially vaccine preventable conditions including FY 95-99 inpatient cases of meningitis, bacteremia, pneumococcal pneumonia, and tympanostomy procedures. International Classification of Diseases, Ninth Revision Clinical Modification (ICD-9CM) codes represented in the analysis were 320.1, 790.7, and 481, and Current Procedural Terminology (CPT) code 20.01, respectively (Charts 1 and 2). Outpatient data for otitis media (ICD-9CM code 382) was included; however, data was only available for FY99 (Chart 3). Inpatient otitis media cases were not included in the analysis to avoid double counting.

The Managed Care Forecasting and Analysis System (MCFAS) was utilized to obtain denominator data for the military beneficiary populations eligible to receive the vaccine through the army's military treatment facilities (MTFs). We assumed that this population and its utilization of MTF services would remain in a steady state over the observation period.

Incident cases were defined as patients with no prior visit within 21 days. All return visits under 21 days were considered follow up. For the outpatient otitis media group, patients with less than 3 follow up visits per incident were defined as simple cases while patients with 3 or more follow up visits per incident were considered a more costly complex case. [4]

Vaccination coverage was based on the ACIP recommended schedule of 4 doses for newborns given at 2, 4, and 6 months of age with a booster dose at

12-15 months. Schedules for “catch-up” vaccination were as follows. Children 7-11 months of age should receive 3 doses, 2 of which must be at least 4 weeks apart, with the third dose administered after the one-year birthday and separated from the second dose given at least 2 months apart; children 12-23 months of age should receive 2 doses given at least 2 months apart; and, if indicated for children 24-59 months, they should receive 1 dose. [6, 7, 10]

The current military cost of the vaccine ($42.22) was used to calculate vaccine cost (Table 2). “Catch-up” vaccination costs for children born prior to the vaccination period were applied for the initial year of vaccination only. Inflation and administration costs were not taken into account.

U.S. Army policy for use of PCV7 is pending the final revision of ACIP recommendations. Our findings are based on vaccination of all children under 2 years of age vs all children under 5 years of age given the recommended immunization schedule. The distribution of PCV7 preventable diseases among these groups is displayed in charts 1-3.

Vaccine efficacy rates, direct health care costs, and indirect (work-loss) costs were obtained from published or reported clinical trials and papers (table 1). [1, 2, 3, 4, 10] A conservative approach that would underestimate cost savings was used when variable rates were found.

Because indirect cost savings were mostly of benefit to society as a whole rather than MEDCOM, savings were categorized accordingly. Cost due to complications (i.e. death, hearing loss, disability) and other miscellaneous costs, such as medication were not taken into account.

Expected preventable cases (table 3) during this follow up period were based on the average of reported cases in the preceding 5 years when data was available. For outpatient cases, we were limited to cases reported in the previous year. And because tympanostomy procedures were phased out of inpatient care and added to outpatient care during our observation period we were limited to the average of the first 2 years of observation.

Vaccine efficacy rates and expected preventable cases were used to calculate initial year (FY2001) cost savings (tables 4 and 5). The duration of efficacy or protective life of the vaccine was assumed to the fifth birthday for infants under 2, and 3 years for children 2-5, with protection waning from 100% to 93% in years 2-5. Based on this assumption expected benefits and cost savings were extrapolated for the vaccine cohort over a 3 to 5 year window (table 6).[4]

The vaccine's projected cost benefit was based on differences between total extrapolated cost savings and initial/subsequent year vaccine costs (table 7).

PCV7 PREVENTABLE DISEASES AND ASSOCIATED COSTS*

Disease	% Prevented by Vaccine	Medical Cost per case	Work-Loss Cost per case
Pneumococcal Meningitis	90%	$9208	$1492
Pneumococcal Bacteremia	90%	$1922	$312
Pneumococcal Pneumonia	33% **	$1167	$263
Tympanostomy	20%	$1869	$443
Otitis Media – Simple case Complex case	7% 19%	$134 $389	$141 $589

* Lieu et. al., 2000; **Black et al., 2000

TABLE 1

Projected Vaccine Costs: Initial and subsequent years

FY 2001				
Fiscal Year Avg User Population				Costs
Age 0-6 months**	14280		Age 0-6 months (4 doses)	$2,411,606
Age 7-11 months**	14280		Age 7-11 months (3 doses)	$1,808,705
Age 1	28864		Age 1 (2 doses)	$2,437,276
Vaccine costs: Infants < 2 years			Total	**$6,657,587**
			With catch-up immunizations	
Age 2	28381		Age 2 (1 dose)	$1,198,246
Age 3	28344		Age 3 (1 dose)	$1,196,684
Age 4	28392		Age 4 (1 dose)	$1,198,710
Age 5	27587		Age 5 (1 dose)	$1,164,723
			Total	**$4,758,363**
Vaccine costs: Children < 5 years			Grand Total	**$11,415,950**

**Assumed even distribution

Subsequent Years							
Fiscal Year Avg User Population					Costs		
	FY 2002	FY 2003	FY 2004		FY 2002	FY 2003	FY 2004
Age 0	28475	28422	28452	Age 0 (4 doses)	**$4,808,858**	**$4,799,907**	**$4,804,974**

TABLE 2

COST OF VACCINE

- Projected Vaccine Cost - Average User Patient Catchment Area (Includes all services using Army MTFs with residence in a 40 mile radius of an Army hospital's catchment area):
  - Vaccination of children under 2 years:

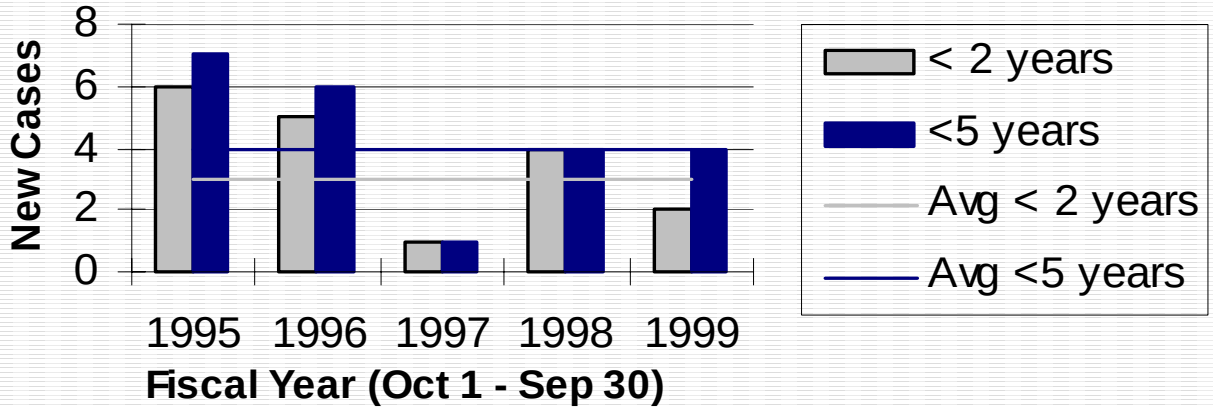
    $6.7 M initial year costs, $4.8 M subsequent year costs
  - Vaccination of children under 5 years:

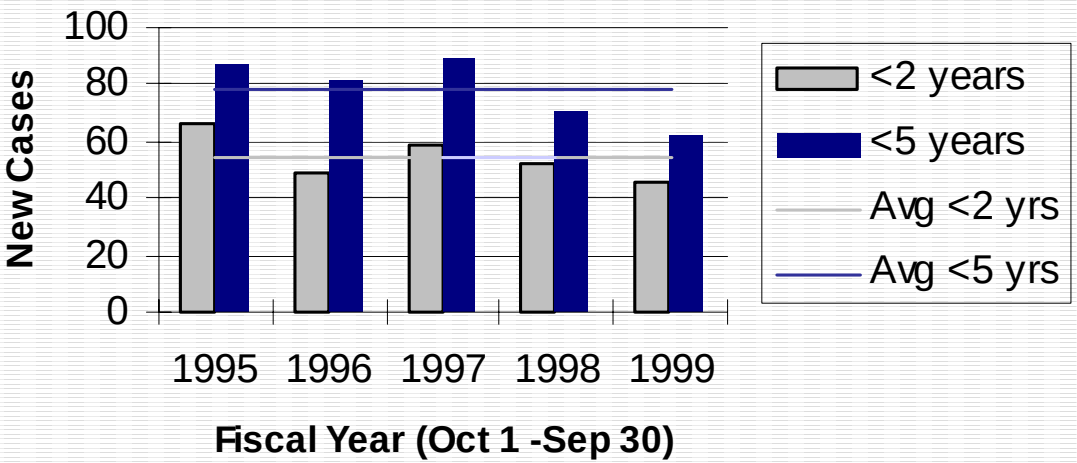
    $11.4 M initial year costs, $4.8 M subsequent year costs

    - Not adjusted for inflation or administration costs

Pneumococcal Meningitis and Bacteremia (New Cases by Fiscal Year)

Meningitis



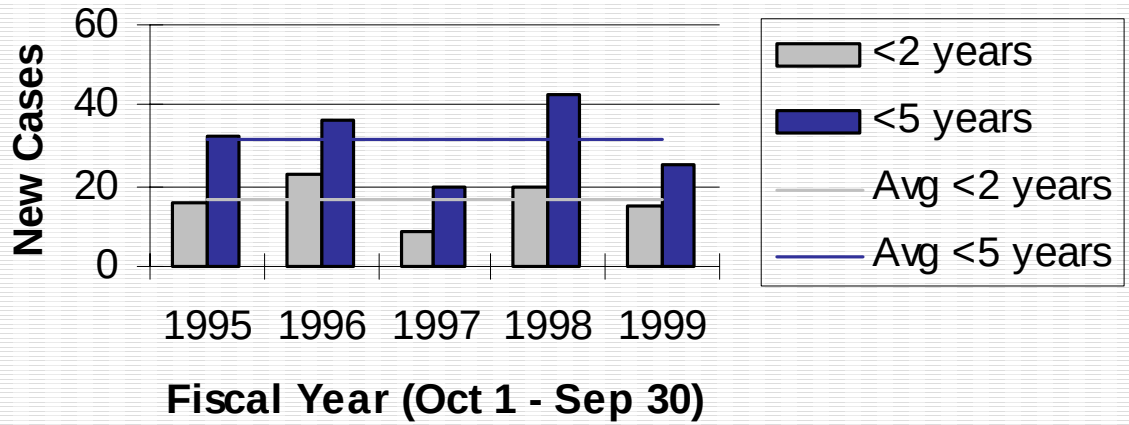


Bacteremia

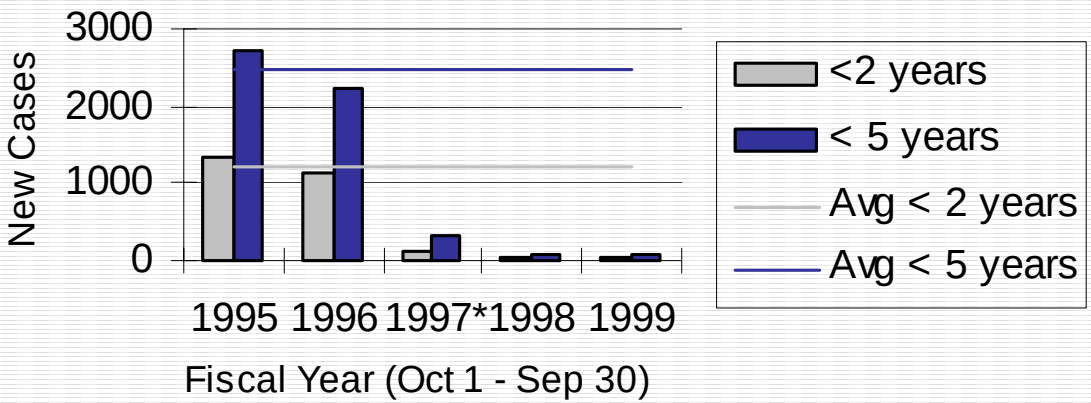
CHART 1

Pneumococcal Pneumonia and Tympanostomy (New Cases by Fiscal Year)

Pneumococcal Pneumonia



Tympanostomy

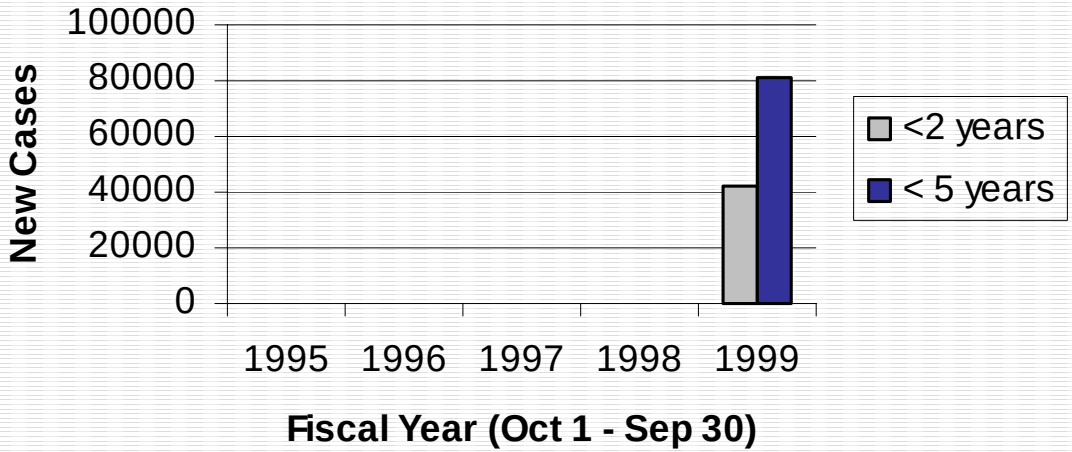


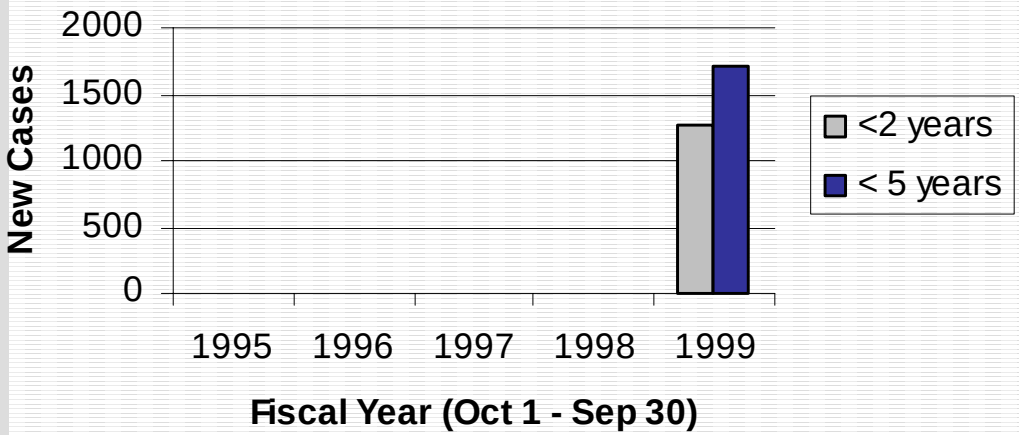
*Beginning of transition to same day outpatient surgery

CHART 2

Outpatient Otitis Media - New Cases FY1999

Simple Cases





Complex Cases

CHART 3

Expected Decrease in New Cases* Due to Vaccine – FY2001

Meningitis			
Under 2 years:	3.6 cases *	90% efficacy =	3 cases
Under 5 years:	4.4 cases *	90% efficacy =	4 cases
Bacteremia			
Under 2 years:	54.4 cases *	90% efficacy =	49 cases
Under 5 years:	78 cases *	90% efficacy =	70 cases
Pneumonia			
Under 2 years:	16.6 cases *	33% efficacy =	5 cases
Under 5 years:	31.2 cases *	33% efficacy =	10 cases
Tympanostomy			
Under 2 years:	1,236 cases *	20% efficacy =	247 cases
Under 5 years:	2,474 cases *	20% efficacy =	495 cases
Otitis Media – Simple Cases			
Under 2 years:	42,637 cases *	7% efficacy =	2,985 cases
Under 5 years:	81,659 cases *	7% efficacy =	5,716 cases
Otitis Media – Complex Cases			
Under 2 years:	1277 cases *	19% efficacy =	243 cases
Under 5 years:	1702 cases *	19% efficacy =	323 cases

* Meningitis, Bacteremia, and Pneumonia cases based on average reported cases from FY95 to FY99; tympanostomy procedure based on average reported from available data (FY1995, FY1996), and outpatient otitis media cases based on reported cases from FY99. Cases per fiscal year shown on Charts 1, 2, and 3. Efficacy rates listed on Table 2.

TABLE 3

Expected Inpatient Pneumococcal Cost Savings Due to Vaccine – FY2001

INPATIENTS	Expected Cases Prevented	Expected Medical cost per case (MEDCOM)	Total Expected Medical Cost Savings	Expected Work-Loss cost per case (Indirect Costs)	Total Expected Cost Savings (MEDCOM + Indirect Costs)
Meningitis				$1492	
Under 2 years	3	$9208	$27,624		$32,100
Under 5 years	4		$36,832		$42,800
Bacteremia				$312	
Under 2 years	49	$1922	$94,178		$109,466
Under 5 years	70		$134,540		$156,380
Pneumonia				$263	
Under 2 years	5	$1167	$5,835		$7,150
Under 5 years	10		$11,670		$14,300
Tympanostomy*				$443	
Under 2 years	247	$1869	$461,643		$571,064
Under 5 years	495		$925,155		$1,144,440

*Tympanostomy procedures now phased out of inpatient care and placed into outpatient care. Therefore, costs of care may be over-estimated dur to the expected cost savings of having the procedure done on an outpatient basis.

TABLE 4

Expected Outpatient Otitis Media Cost Savings Due to Vaccine – FY2001

OTITIS MEDIA Outpatients	Expected Cases Prevented	Expected Medical cost per case (MEDCOM)	Total Expected Medical Cost Savings	Expected Work-Loss cost per case (Indirect Costs)	Total Expected Cost Savings (MEDCOM + Indirect Costs)
Children Under 2 Years:					
Simple cases	2985	$134	$399,990	$141	$820,875
Complex cases	243	$389	$94,527	$589	$237,654
Children Under 5 Years:					
Simple cases	5716	$134	$765,944	$141	$1,571,900
Complex cases	323	$389	$125,647	$589	$315,894

TABLE 5

Extrapolated Cost Savings: Protective Life of Vaccine*

TOTAL COST SAVINGS	Children under 2 years Initial Year Medical Cost Savings - MEDCOM (Total with indirect Costs) Initial Year Cost Savings	Children under 2 years Initial Year Medical Cost Savings - MEDCOM (Total with indirect Costs) Extrapolated Cost Savings Protective Life of Vaccine	Children under 5 years Initial Year Medical Cost Savings - MEDCOM (Total with indirect Costs) Initial Year Cost Savings	Children under 5 years Initial Year Medical Cost Savings - MEDCOM (Total with indirect Costs) Extrapolated Cost Savings Protective Life of Vaccine
Meningitis	$27,624 ($32,100)	$119,704 ($139,100)	$36,832 ($42,800)	$147,328 ($171,200)
Bacteremia	$94,178 ($109,466)	$405,542 ($471,374)	$134,540 ($156,380)	$520,862 ($605,414)
Pneumococcal Pneumonia	$5,835 ($7,150)	$25,674 ($31,460)	$11,670 ($14,300)	$43,179 ($52,910)
Tympanostomy	$461,643 ($571,064)	$1,981,140 ($2,450,720)	$925,155 ($1,144,440)	$3,308,130 ($4,092,240)
Otitis Media	$494,517 ($1,058,529)	$2,121,208 ($4,540,451)	$891,591 ($1,887,794)	$3,256,574 ($6,911,460)
Totals	$1,083,797 ($4,064,877)	$4,653,268 ($7,633,105)	$1,998,621 ($7,819,732)	$7,276,073 ($11,833,224)

* Extrapolation and protective life of vaccine, is based on a vaccine efficacy through year 5 for infants under 2 and a 3 year efficacy for children aged 2-5 with protection waning from 100% to 93% in years 2 to 5. (Lieu et al. 2000)

TABLE 6

Projected Cost Benefit

Pediatric Population	Vaccine Cost for Initial Year Vaccine Cohort (Table 1)	Average Vaccine Cost for Subsequent Year Vaccine Cohorts (Table 1)	Extrapolated Cost Savings: Protective Life of Vaccine (Table 7)	Total Savings: Initial Year Vaccine Cohort	Total Savings: Subsequent Year Vaccine Cohorts
Under 2					
MEDCOM	$6,657,587	$4,804,569	$4,653,268	-$2,004,319	-$151,301
TOTAL**			$7,633,105	+$975,518	+$2,828,536
Under 5					
MEDCOM	$11,415,950	Not Applicable	$7,276,073	-$4,139,877	
TOTAL**			$11,833,224	+$417,274	

**Includes Indirect Costs.

TABLE 7

Discussion

Our study reveals a degree of monetary cost-effectiveness for Pneumococcal vaccine, albeit more of the monetary benefits are not realized by MEDCOM, but rather by the Army and society as a whole (through decrease in lost work days for parents). This study attempted to quantify monetary benefits, however other greater benefits exist for the vaccine and should be considered when determining policy.

We made conservative assumptions for the study that likely biased against a vaccination program, however in addition to these assumptions, there are other limitations to this study.

When extracting specific data from large databases, often the weakest link in the progression of data is the initial coding of the data. We do not know of any reports/papers that give an objective measure of the quality of the ICD-9 coding for the SIDR or SADR. Additionally, there may have been administrative changes such that cases are handled or coded differently, for example, there may be a tendency for some formally inpatient scenarios to be handled now as outpatient, thus making it more complicated to capture in a data search. We found this to be the situation for tympanostomy cases.

When we noticed the dramatic change in tympanostomy cases after 1996, we made inquires and found there was an administrative change from inpatient to outpatient procedures. Therefore, we used the average reported cases from 1995 and 1996 data as our anticipated future cases.

Much of our data on cost of the disease was from ‘Projected Cost-effectiveness of Pneumococcal conjugate Vaccination of Healthily Infants and Young Children” by Lieu et. al.. This study’s main considerations were the costs and benefits to society. Our study was more focused on the medical cost in the U.S. Army military health care system. The use of their data may inappropriately estimate costs especially if the government receives medical supplies at lower costs. Following assumptions from their paper, we also projected benefits beyond vaccination period. The vaccine is believed to be 100% effective for children under 2 and 93% effective in the 2-5 year range. Length of protection was estimated at 3-5 years.

For extrapolated cost savings, we assumed a steady-state population (the population that leaves the systems is equal to the population that enters the system). In future surveillance, if after implementation of the vaccine, a decrease in cases is not observed, it may be that our assumption was wrong (those who are vaccinated leave the system).

We were conservative in our assumptions regarding complication. Our study does not include costs for complications such as deafness, disability, death; does not include other miscellaneous costs such as prescriptions. Given the low number of meningitis cases expected annually, the probability of such complications is low; however, if the protective effect of the vaccine is extrapolated over the course of the vaccine’s assumed efficacious period, the cost savings from preventing these complications become more significant. To limit numerical and computation complications for the study, we did not factor in administrative costs nor adjust for inflation.

An additional benefit of the vaccine that is difficult to quantify is the impact on antibiotic resistance. The overuse of antibiotics has led to increased antibiotic resistance. The use of PCV7 may slow the progression of antibiotic resistance. Finally, a benefit of the vaccine that we did not quantify is the decrease in pain and suffering borne by parents and children with these infections and diseases.

CONCLUSION

In addition to the inherent benefits of the new pneumococcal 7-valent conjugate vaccine, our findings indicate that it has the potential to be a cost effective intervention for MEDCOM and society as a whole. It is estimated that the vaccination program will initially incur a loss if “catch-up” vaccinations will be required in the first year of vaccination. However, with protection lasting 3-5 years beyond the period of vaccination, subsequent savings can be expected.

Initial vaccination programs targeting children under 2 were more cost effective than universal vaccination programs for all children under 5. This was due to the higher incidence of disease in the under 2 age group (See Appendix 1). The high risk children in the 2-5 year age group would receive similar protective benefits and cost savings due to vaccination, and should therefore be included as recommended by the ACIP.

These findings were based on preliminary data and assumptions. They are intended to serve as a baseline for more in-depth surveillance and cost effectiveness analysis in the upcoming years as these populations are immunized and better population health and cost data becomes available.

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Rates of Pneumococcal Associated Disease & Tympanostomy by Age Group

Condition	Rate per 100,000 (<2)	Rate per 100,000 (2-5)	OR (95% CI)
Meningitis	6.1	0.6	8.6 (1.0-77.3)
Bacteremia	92.9	18.6	2.5 (1.2-4.9)
Pneumococcal Pneumonia	28.3	11.5	4.9 (3.0-7.9)
Otitis Media	75265	32741	6.97 (6.8-7.1)
Tympanostomy	2050	900	2.3 (2.1-2.5)

APPENDIX 1

Acknowledgements

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