Appendix 4.4
VALUES ASSIGNED TO SELECTED VARIABLES IN OTA'S COST-EFFECTIVENESS ANALYSIS OF VACCINATION AGAINST PNEUMOCOCCAL PNEUMONIA

The assumptions, rationales, and data sources used to develop values assigned to **8** of the 12 variables used in the cost-effectiveness analysis in chapter 4 are described in this appendix. Variables described below include: 1) QALY weighings, 2) discount rate, 3) cost of vaccination, 4) percent of pneumonia that is pneumococcal, **5)** percent of pneumococcal pneumonia caused by the 14 types of pneumococci represented in the licensed pneumococcal vaccine, 6) vaccine efficacy rate 7) side effects associated with use of the vaccine, and 8) duration of immunity. The remaining four variables, i.e., rate of pneumonia death, rate of decline for pneumonia deaths, rate of hospital cases of pneumonia, and rate of ambulatory visits for pneumonia, are not discussed in this appendix. Data sources for these four variables are cited in chapter 4.

QALY Weighings

In OTA's cost-effectiveness analysis in chapter 4, the measure quality-adjusted life years (QALYs) was used to quantify the effects of a pneumococcal vaccination program. QALYs are a measure recently developed to quantify, in common measurable units, changes in health status resulting from a reduction or an increase in years of illness or life expectancy. As noted in chapter 4, QALYs incorporate rankings of different disability states in terms of their relationship to complete health, on the one hand, and death, on the other. Thus, for example, on a scale where a year of complete health is ranked 1 and death is O, a year of minor illness might rank as .9, and a year of serious illness might rank as .2.

Weighings of different disability states used to calculate QALYs can be developed by asking people, "Taking into account your pain and suffering immobility, and lost earnings, what fraction of a year of life with a specific disability would you be willing to trade in order to spend the remaining fraction of the year disability-free?" (Weinstein, **1977).** If, for example, an individual would be willing to give up a quarter of a year of life with stomach ailments in order to have three-quarters of a year of life disability-free, then a year of life with stomach ailments would rank as .75.

Very little work has been done in the area of developing weighings of different disability states that reflect more than the subjective evaluations of one or two individuals. An exception, however, is the empirical work done by Bush, Chen, and Patrick (Bush, 1973; Patrick, 1973). By asking groups of students and medical professionals to rank various states of functional disability, these investigators have developed a number of social indexes of changes in health status and quality of life.

QALY weighings used in OTA's cost-effectiveness analysis of pneumococcal vaccination were based on the weighings of particular disability states that Bush, Chen, and Patrick derived from a survey of students in their analysis of a phenylketonuria (PKU) screening program (Bush, 1973). Selected rankings of the 30 levels of functional disability that were differentiated in this analysis are presented in table 4.4A.

In the base case analysis, weighings used to calculate QALYs were as follows: a year of total health was valued at 1; a year of nonbed disability, .6; **a** year of bed disability, .4; and death, O. The .6 value

Table 4.4A.—Selected Rankings of Functional Disability States Derived From a Survey of Students by Bush, Chen, and Patrick

Functional status			
1	2	3	Weight[a]
Traveled freely	Walked freely	Performed major and other activities	1.000
Confined to house	Walked freely	Performed self-care, but not major activity	.594
Confined to house	In bed or chair	Performed self-care, but not major activity	.534
In hospital	In bed or chair	Performed self-care, but not major activity	.428
In hospital	In bed or chair	Required assistance with self-care	.343
Death	Death	Death	0.000

[a]The weightings of functional disability states derived by Bush, Chen, and Patrick are probably the best quality scale currently available These weightings, however, are a value rather than a utility function They have not been subjected to the probabilistic tests, based on probabilities of different combinations of health states, required of a true utility function (Shepard, 1979)

for nonbed disability is the value Bush, Chen, and Patrick derived for disabilities that confine a person to home. The .4 value for bed disability is an intermediate value between the values they derived for hospital-bed disabilities and home-bed disabilities. With nonbed disability valued at .6 and total health valued at 1, eliminating nonbed disability would improve quality of life by .4 (l-.6); eliminating bed disability would improve quality of life by .6 (l-.4).

Two sets of values for weighings used to calculate QALYs in the sensitivity analysis were derived: 1) by using the square root of each of the weights used in the base case (i. e.,= and=); and then 2) by using the square of each weight (i. e., $(.4)^2$ and **(.6)2). Use** of the square root of each weighting made the vaccine slightly less cost-effective, and use of the square of each weighting made vaccination slightly more cost-effective. [1]

To quantify the effects (i.e., changes in morbidity and mortality) of pneumococcal vaccination in terms of QALYs, an initial assumption was made that a single day was worth 1 /365 the value of a year. Thus, for example, a day of perfect health was assumed to be worth 1/365 the value of a year of perfect health. Similarly, the value of a day of serious illness was assumed to be worth 1/365 that of a year of serious illness.

Projections were made of the reduction in days of pneumococcal pneumonia morbidity that would result among the vaccinated population. Then excess days of pneumococcal pneumonia morbidity among the unvaccinated population were multiplied by the weighings discussed above. In the base case, excess nonbed-disability days among the unvaccinated were multipled by .4, and excess bed-disability days were multipled by .6. In the sensitivity analysis, one time, excess nonbed-disability days were multiplied by $\sqrt{.4}$ and excess bed-disability days by $\sqrt{.6}$; another time, they were multiplied by $(.4)^2$ and $(.6)^2$, respectively. To produce QALY equivalents, weighted days of excess pneumonia morbidity were then divided by 365.

To convert into QALYs both the effect of vaccine side effects and the effect of illnesses not prevented by pneumococcal vaccination among vaccinees in extended years of life, the same general approach, weighings, and assumptions described above were used. To estimate the latter effect, individuals whose lives were extended by vaccination were assumed to have the same average number of disability days per extended year of life as other individuals in their age group,

[1]See table 4.4 in ch. 4.

Discount Rate Applied to Costs and Effects Occurring After 1978

Cost-effectiveness ratios for pneumococcal vaccination that OTA calculated in chapter 4 were based on a one-time, hypothetical pneumococcal vaccination program conducted in June **1978.** Many of the costs and effects of the hypothetical program would not be realized in **1978,** but would occur in subsequent years. In the base case analysis, these costs and effects were discounted at the rate of 5 percent. In the sensitivity analysis: 1) a 10-percent discount rate was used; and then 2) no discount rate was used.

Discounting (i.e., valuing future costs and effects at less than their present worth) is a standard economic procedure. The practice of discounting the costs of public programs usually is based upon two related rationales. First, discounting takes into account social time preference, reflecting the fact that individuals generally would prefer to receive benefits now rather than in the future. Second, discounting takes into account the social opportunity costs of capital, reflecting the fact that money invested in a public program could have been invested in a private enterprise and received a real rate of return (e. g., interest).

Much has been written on discounting procedures, but there is still no consensus on the most appropriate method for selecting a discount rate. In the base case analysis of pneumococcal vaccination in chapter **4,** costs and effects occurring after 1978 were discounted at a 5 percent rate, because this rate was believed to be a fairly accurate reflection of the societal discount rate. The 10-percent rate used in the sensitivity analysis is the rate that the Office of Management and Budget (OMB) recommends for discounting the costs of Government projects (U. S., Exec. Off. Pres., OMB, 1971). The effects of using no discount rate were calculated in the sensitivity analysis for purposes of comparison.

One of the conflicts in economics literature concerns the appropriate discount rate to use for costs and effects when the social opportunity cost of capital and the social time preference rate diverge, due to taxes and market imperfections. In OTA's analysis in chapter 4, effects of pneumococcal vaccination were discounted at the same rate as costs. [2]

[2]It may be quite rational for the discount rates applied to costs and QALYs to be different, and for some programs to be delayed as a result. Many existing Federal programs technically could have been implemented long ago, but were not thought by the Congress to be sufficiently worthwhile in relation to their costs. As a society becomes more affluent, its members are probably willing to spend more to save (or "buy") one QALY; therefore, a program that is not sufficiently cost-effective to be implemented now may be worthwhile in the future.

This approach was used to maintain a constant trade-off between dollars and life years (Weinstein, 1977). Theoretically, if a program's effects are not discounted at the same rate as its costs, the program's cost-effectiveness can be improved simply by delaying the program's starting date.[3]

The assumption of constant costs was made throughout OTA's analysis. Discount rates used in both the base case and the sensitivity analysis were net of inflation.

Cost of Vaccination

The cost of each pneumococcal vaccination was calculated by adding the retail cost of a dose of pneumococcal vaccine to a medical fee for administering a single dose. In the base case, it was assumed that pneumococcal vaccinations would be administered through the private sector at a total cost per vaccination of $11.37. The cost of each dose of pneumococcal vaccine was assumed to be $4.90, the price charged in the private sector by Merck Sharp and Dohme (Beck, 1978). The medical fee for administering each dose through the private sector was assumed to be $6.47. OTA derived this cost from the California relative value scale for injections, in which the charge for an injection is half the charge for a limited-examination followup visit (CMA, 1969). The charge for a limited-examination followup visit was estimated to be $12.97, an amount that is a 1978 update (reflecting changes in the consumer price index (CPI)) of the prevailing Medicare charge for such a visit in 1975 (Schieber, 1976).

In the sensitivity analysis, it was assumed that pneumococcal vaccinations would be administered through a public immunization program at a total cost per vaccination of $3.45. Under a mass public immunization program, with State or local governments buying pneumococcal vaccine in large quantities, the cost per vaccine dose very likely would be less than the cost in private sector. Fewer middlemen such as wholesale drug houses and pharmacists would be involved, manufacturers' packaging and distribution costs would be lowered, and manufacturers would be better able to time production with sales. For the sensitivity analysis, the cost of each vaccine dose was estimated to be about half the cost in the private sector, $2.45. This estimate was based on the average difference in prices charged to private physicians and to public programs for other vaccines, including influenza, measles, mumps, and rubella (Chin, 1978; Beck, 1978).[4] The medical fee for administering each vaccine dose would be less under a public immunization program, because pneumococcal vaccinations could be performed in large numbers; special clinics could even be used to administer the injections. In the sensitivity analysis, the cost of administering each dose of pneumococcal vaccine through a public immunization program was assumed to be $1,00, the estimated per dose cost of administering vaccines in other public vaccination programs (Hinman, 1978).

Percent of Pneumonia That Is Pneumococcal

A number of researchers have attempted in various hospital and ambulatory settings to determine the percentage of pneumonia cases that are caused by pneumococcal organisms (Roden, 1978). In many studies, percentage estimates have been derived directly from the isolation rates of pneumococci, i.e., from the percent of pneumonia cases in which pneumococci are isolated. Because of the problems discussed below, however, estimates based solely on pneumococcal isolation rates maybe unreliable.

Pneumococci can be isolated and identified by any one of three procedures: 1) blood tests, [5]2) transtracheal aspiration (lung puncture), or 3) sputum culture (throat culture). Each method has drawbacks. When pneumococci are found in the blood of patients with pneumonia, a diagnosis of pneumococcal pneumonia can accurately be made. Pneumococci enter the bloodstream, however, in only about 25 percent of persons with pneumococcal pneumonia, in those with severe cases of pneumococcal bacterenua. Blood tests, therefore, cannot be used to diagnose pneumococcal pneumonia in the approximately 75 percent of pneumonia patients whose pneumococcal infections are not bacteremic. Transtracheal aspiration can be used to diagnose pneumococcal pneumonia more accurately, but lung puncture is a potentially risky, unpleasant, and costly procedure. Sputum culture is an easier and more commonly used method of isolating pneumococci, but a number of authorities have questioned the reliability of this method—especially when used alone— in diagnosing pneumococcal pneumonia. On the one hand, healthy persons often carry pneumococci in their throats (Lund, 1971). The presence of pneumococci in a sputum culture, therefore, is not necessarily diagnostic of pneumococcal pneumonia

[3]For example: A program begun in 1978 might result in the immediate saving of one life at an immediate cost of $1,000. Its cost-effectiveness ratio for 1978 thus would be $1,000 per life. If the same program were delayed until 1979, and a 5-percent discount rate were applied only to costs, then the present value cost-effectiveness ratio for the 1979 program would be $950 per life.

[4]The prices of vaccines for public programs and private physicians are discussed in app. 4.5

[5]Blood tests include bacteriological tests, hemagglutination, and radioimmunoassay. (See Schiffman, 1971.)

(Barrett-connor, 1971; Austrian, 1975). On the other hand, patients with pneumococcal pneumonia sometimes do not show pneumococci in their sputum (Barrett-Connor, 1971).

A rate of attributable risk can be derived by comparing the sputum culture pneumococcal isolation rate (i. e., the percent of cases in which pneumococci are isolated from sputum samples) in a group of pneumonia patients to the comparable isolation rate in a group of non-pneumonia patients. [b] An estimate of the proportion of pneumonia cases caused by pneumococci can be based on the differences in pneumococcal carriage rates among patients with pneumonia and those without pneumonia. Basing estimates of attributable risk on differences in pneumococcal carriage rates, although arithmetically neat, involves making a considerable leap of faith. In fact, estimates of attributable risk that are based on differences in pneumococcal carriage rates may not be valid. As explained by David Fraser, M. D., of the Center for Disease Control (CDC) (Fraser, 1979)

> The bacterial flora of the throat are in a delicate balance which can be tipped by the use of antibiotics or the occurrence of various infections. It may be that viral infections increase the chance of colonization of the throat with pneumococci (or the chance of recovering pneumococci that are present) without necessarily leading to pneumococcal pneumonia. Alternatively, estimates could be based on data generated from examinations of Gram-stained sputum from patients with pneumonia. The diagnosis of pneumococcal disease could be based on the characteristic appearance of polymorphonuc]ear leukocytes, alveolar macrophages, and Gram-postive diplococci with a positive Quellung test or on demonstration of pneurnococcal organism or capsular antigens in blood or other body fluids. Few such studies have been done, however, and those that are available are based on small numbers and highly selected populations.

Most of the isolation rates and attributable risks reported in studies conducted in the United States suggest that the percent of pneumonia that is caused by pneumococcal organisms is between 12 and 62 percent:

1. A study of pneumonia cases among members of Group Health Cooperative, a prepaid group practice in Seattle, yielded an estimate of about 13 percent (Fey, 1975). In this study, 24 percent of the 100 pneumonia patients carried pneumococcal isolates, in comparison with 12.2 percent of the controls.
2. In a study of 100 adult pneumonia patients admitted to a large general hospital in Baltimore, 62 percent were diagnosed as having pneumococcal pneumonia, based on clinical diagnostic criteria (Fekety, 1971). Pneumococci were isolated from nasal or sputum samples in 68 percent of the 96 pneumonia patients and in 15 percent of the 78 control subjects.
3. In a study of 148 pneumonia patients at Milwaukee County General Hospital, pneumococci were isolated from the blood or sputum of 53 percent of the patients (Dorff, 1973).
4. In a study of pneumococcal vaccine at a San Francisco prepaid medical group, it was shown that 15.6 percent of all cases of clinical pneumonia among an unvaccinated group of patients were accompanied by pneumococcal isolates (Austrian, May 1, 1976).
5. In an Atlanta study at Grady Memorial Hospital, the isolation rate for pneumococci among pneumonia patients was reported to be 35 percent (Sullivan, 1972).
6. A study of children developing pneumonia in the Chapel Hill area of North Carolina showed pneumococcal isolates among 65,3 percent of hospitalized children with pneumonia and among 39.6 percent of the control group of hospitalized children without respiratory illness, demonstrating an attributable risk of 25.7 percent (Loda, 1968). In the same study, among children treated for pneumonia at private pediatric offices, 39.6 percent had pneumococcal isolates.
7. Finally, in a study of pneumonia at a chronic care hospital in New York, the percentage of pneumonia that was pneumococcal was found to range from 10.1 percent to 23 percent during four separate study periods (Bentley, n.d.).

In OTA's cost-effectiveness analysis of pneumococcal vaccination in chapter 4, in the base case, it was estimated that 15 percent of all cases of pneumonia are caused by pneumococci. This estimate, which may be conservative, was based on—in addition to consideration of the data discussed in the preceding paragraph—discussions with three infectious diseases researchers (Austrian, 1979; Filice, 1979; Fraser, 1979), and the results of two unpublished studies (Filice, n.d.; Bentley, 1979). In one of the unpublished studies, conducted under the auspices of the Center for Disease Control (CDC), Gregory Filice, M. D., conservatively estimated the incidence of pneurnococcal pneumonia to range from 12 to 37 cases per 100,000 persons per year (Filice, n.d.). Filice's estimate was based on the incidence of documented pneumococcal bacteremia in Charleston County, S.C. To the extent that pneumococcal bacteremia in this county had not been diagnosed, this estimate is likely to be unrealistically low, In the other unpublished study, David W. Bentley, M. D., of the Monroe Community Hospital, in Rochester, N. Y.,

[b] For a description of one manner in which attributable risk can be calculated, see app. 4.6.

attempted to quantify the incidence of pneumococcal pneumonia in institutionalized populations, mostly comprised of elderly patients (Bentley, 1979). From data collected in a 1974 study, he found that out of 157 patients with pneumonia, 27 (17 percent) had pneumococcal pneumconia. From data collected in a 1975 study, he found that out of 160 patients with pneumonia, 20 (13 percent) had pneumoctlccal pneumonia. More recently, he studied 95 patients with pneumonia and found that 20 (2 I percent) had pneumococcal pneumonia as diagnosed by transtracheal aspiration.

In the sensitivity analysis in chapter 4, the low estimate of 10 percent was selected to represent the low incidence of pneumococcal pneumonia reported in the studies cited earlier. The high estimate of 35 percent was based on the results of a survey of 45 medical practitioners and scientists that was conducted by Pracon, Inc. (Roden, 1978).

Percent of Pneumococcal Pneumonia Caused by Types of Pneumococci Represented in the Vaccine

The currently licensed pneumococcal vaccine contains antigenic polysaccharides from-and produces various levels of protection against pneumonia caused by—14 serotypes of pneumococci. Currently, however, there are at least 83 known pneumococcal types. In the base case analysis, it was assumed that 75 percent of all cases of pneumococcal pneumonia among all age groups are caused by the 14 types of pneumococci represented in the vaccine. In the sensitivity analysis, however, it was assumed: 1) that 50 percent of such cases among all age groups are caused by these 14 types; and 2) that 100 percent are. The potential effects of varying percentages among different age groups were not ascertained in OTA's analysis.

The 75 percent estimate for the base case analysis was based on data derived from several recent U.S. studies in which pneumococci were isolated from patients with pneumococcal pneumonia and typed.

1. In one study, conducted at a prepaid health plan in Seattle in 1971 and 1972, 73 percent of the 40 pneumococcal isolates recovered from ill patients were types found in the 14-valent vaccine (Fey, 1975).
2. A separate study conducted at a San Francisco prepaid health plan between 1974 and 1976 yielded similar results: 72 percent of the pneumococcal isolates extracted from unvaccinated patients with X-ray positive pneumonia contained types of pneumococci represented in the vaccine (Austrian, May 1, 1976).
3. In a third study, carried out between 1974 and 1976 at a chronic care hospital in New York, it was found that 72 percent of pneumococcal isolates recovered from 50 pneumonia patients were represented in the vaccine (Valenti, 1978).[7]
4. In addition, data from a multi-institutional study of bacteremic pneumococcal infection conducted in several American cities from 1967 to 1975 showed 78.6 percent of 3,644 isolates were types represented in the 14-valent pneumococcal vaccine (Austrian, et al, 1976).

The percentage of pneumonia caused by different types of pneumococci also was investigated in a number of earlier U.S. studies (Austrian, 1964; Finland, 1937). Because of evidence that incidence of pneumococcal infections caused by different types of pneumococci have been changing over the years, however, the results of these studies may not be directly relevant. In a study conducted between 1929 and 1935 at Boston City Hospital, for example, it was found that pneumococcal Types 1, 2, and 3 accounted for about 70 percent of the cases of bacteremia (Finland, 1973.) Several more recent studies, though, have found that the distribution among pneumococcal types is more disperse (Mufson, 1974).

The future impact of pneumococcal vaccine may be significantly influenced by variations over time in the relative incidence of diseases produced by various types of pneumococci. At some point in the future, a shift might occur in the percent of pneumococcal pneumonia cases among unvaccinated populations that are caused by the 14 types represented in the licensed pneumococcal vaccine. In the absence of any method for predicting the direction or extent of shifts in the incidence of pneumonia caused by specific types of pneumococci, however, for purposes of OTA's analysis in chapter 4 (in both the base case and sensitivity analysis), it was assumed that the percentage of pneumococcal pneumonia cases caused by the 14 types of pneumococci represented in the current vaccine would remain constant. If the duration of immunity conferred by the vaccine is only a few years, then this assumption is probably valid. If the vaccine confers lifetime immunity (an assumption used in the sensitivity analysis), however, then the assumption may not be valid.

Another assumption made in OTA's analysis, that the incidence of type-specific pneumococcal pneumonia caused by each of the 14 different types of pneumococci represented in the vaccine does not

[7] The 72 percent is an average of the percent of vaccine-type isolates in confirmed and putative cases of pneumonia. Seven-V percent of the 33 confirmed cases and 76 percent of the 17 putative cases were vaccine-type isolates. (See Valenti, 1978).

vary among different age groups, also may be incorrect. At present, however, there exist no age-specific incidence data for type-specific pneumococcal pneumonia which can be used either to validate or invalidate this assumption.

Pneumococcal Vaccine's Rate of Efficacy Against Type-Specific Pneumococcal Pneumonia

The efficacy of pneumococcal vaccine against type-specific pneumococcal pneumonia has been investigated in a number of clinical trials.[8] On the basis of evidence from these trials, in the base case analysis, pneumococcal vaccine was assumed to be 80 percent effective against type-specific pneumococcal pneumonia. In the sensitivity analysis, two different assumptions used for comparative purposes were that: 1) the vaccine's efficacy rate might be as low as 40 percent; or 2) it might be as high as 100 percent.

The 80-percent efficacy rate used in the base case analysis was based mainly on results of clinical trials conducted among South African gold miners (Smit, 1977; Austrian, et al., 1976). These South African trials, some early U.S. studies (Kaufman, 1947), and a study with sickle-cell patients (Ammann, 1977) were used as a basis for the 14-valent pneumococcal vaccine's licensure by the Food and Drug Administration (FDA). Also taken into consideration were data from immunologic studies in which the vaccine consistently increased vaccinees' antibody levels following immunization (Ammann, 1977; Weibel, 1977).

While an 80-percent effectiveness rate for pneumococcal vaccine was fairly well substantiated in the studies conducted in South Africa, this rate was not confirmed in two clinical trials conducted in the United States. In one trial, conducted at the Dorothea Dix Hospital in Raleigh, North Carolina, 608 subjects were immunized with two 6-valent vaccines, and 693 subjects received a saline placebo (Austrian, 1978). There was a 53 percent reduction among vaccinees in radiologically confirmed, vaccine-type pneumonia, but this reduction was only barely statistically significant ($p < .041$). In the other trial, conducted at the San Francisco Kaiser Permanence Medical Center, 6,850 subjects were given a 12-valent vaccine, and 6,750 subjects were given a saline placebo (Austrian, 1978; Austrian, May 1, 1976; Austrain, May 28, 1976). No apparent or statistically significant difference between the incidence among controls and vaccinees of radiologically confirmed, type-specific pneumococcal pneumonia was demonstrated. Difficulties in these two U.S. trials possibly may have resulted from the relatively low incidence of pneumococcal pneumonia in the study groups.

Vaccine Side Effects

Pneumococcal vaccine appears to be generally safe, with minimal side effects reported to date.[9] In one trial in New Guinea, 131 vaccinees were monitored for adverse reactions (Riley, 1977). Seventy-five percent of these 131 vaccinees reported no side effects, 24 percent reported a sore arm; 7 percent, fever; and 3 percent, a swollen arm. In field trials in San Francisco, over 6,000 adults were given the vaccine (Austrian, May 1, 1976; Austrian, et al., 1976). Sixty percent experienced no adverse reactions; 40 percent showed some discomfort; 30 percent developed a local rash; and 3 percent had a mild fever for a day.

Pneumococcal vaccine has been on the market since February 1978. According to the Center for Disease Control (CDC), the number of adverse reactions reported since then has been small. According to CDC'S estimate, between February and September of 1978, less than one case of severe systemic reaction per 100,000 vaccinees was reported (Broome, 1978). There have been few reports of possible anaphylaxis (severe allergic reaction) and no reports of deaths directly attributable to the vaccine.[10]

For OTA's cost-effectiveness analysis in chapter 4 (in both the base case and sensitivity analysis), probabilities of having a systemic reaction to pneumococcal vaccine were developed on the basis of estimates from CDC, while probabilities of experiencing a minor reaction were developed on the basis of data from the trials in New Guinea and San Francisco cited above. The assumption was made that there would be one case of severe systemic reaction per 100,ooo vaccinees and five cases of fever per 100 vacinees. It was assumed that vaccine recipients experiencing severe adverse reactions would spend 2 days in the hospital (2 days of bed disability), at a total cost of $396, and an additional day recuperating at home (1 day of bed disability). For fever, it was assumed that the patient would suffer 1 day of nonbed disability, but would require no special medical attention, The side effects and risk of local reactions (e.g., pain or redness at the site of injection) were considered too minor to alter quality of life or cost considerations, so these were not taken into account.

[8] Studies used to evaluate the efficacy of pneumococcal vaccine are discussed in ch. 3 and described more fully in app. 3.5 and 3.6.

[9] Studies used to evaluate the safety of pneumococcal vaccine are discussed inch. 3 and described more fully in app. 3.5 and 3.6.

[10] See discussion of postmarketing data regarding the safety of pneumococcal vaccine in ch. 3.

In the base case analysis, it was assumed that the neurological disorder Guillain-Barre Syndrome (GBS)[11] would not be among the adverse reactions caused by pneumococcal vaccine. GBS has been observed as an adverse reaction to rabies, DPT, polio, and most notably, swine flu vaccine; however, these are all whole cell vaccines. Pneumococcal vaccine is a polysaccharide vaccine, and therefore is more pure (i.e., free from contaminants) than whole cell virus vaccines; at least theoretically, this vaccine may be less likely to cause GBS (Hill, 1978),

In the sensitivity analysis, the assumption was made that GBS would sometimes be a side effect. It was assumed that the incidence of GBS associated with pneumococcal vaccination would be comparable to the excess incidence of GBS among swine flu vaccinees (Schoenberger, 1979).12 For persons under 18 years of age, no excess incidence was reported. For persons 18 to 24, an increased incidence of four cases per million doses of vaccine was observed. For persons over 24 years old, the increased incidence was found to be 9 or 10 cases per million.

Knowledge regarding the effects of GBS is limited, although a few data do exist. Patients with GBS are initially treated at an acute hospital. One neurologist estimates that the average patient is hospitalized for 21½ months, but that following initial hospitalization, he or she usually needs no further medical or special home care (Asbury, 1978). According to some estimates, however, about 5 to 10 percent of GBS patients discharged from hospitals do have some lasting residual impairment after their release (Asbury, 1978). Approximately 5 percent of patients who develop GBS do die from the disease. Available data from the swine flu program indicate that GBS mortality rates are different for particular age categories. GBS mortality rates by age groups under the 1976 swine flu program were as follows: age 18-24, 3.5 percent; age 25-44, 2.4 percent; age 45-64, 5.8 percent; and age 65 and over, 12.7 percent (Schoenberger, 1978). No pattern as to the timing of death in the course of the illness has been described.

For purposes of the sensitivity analysis, it was assumed that vaccinees developing GBS would be hospitalized for an average of 75 days (75 days of bed disability) at a total cost of $15,640. Estimates of the probability of some GBS patients' dying following hospital discharge were based on mortality rates reported during the swine flu program. The assumption was made that 10 percent of the vaccinees developing GBS would have a residual disability (comparable to a permanent, restricted activity, nonbed disability). GBS survivors were assumed not to require additional special care subsequent to their hospital discharge.

Duration of Immunity Conferred by Pneumococcal Vaccine

The duration of immunity conferred by pneumococcal vaccine is not known. No clinical investigators to date have followed their vaccinated subjects for more than 8 years to establish a clinically based estimate of the duration of the protection conferred by the vaccine against death from pneumococcal pneumonia.

In a recent study in New Guinea, investigators found that pneumococcal vaccine afforded some protection against lower respiratory tract infection (LRTI) for a minimum of 3 years (Riley, 1977). Investigators in this study, however, did not attempt to demonstrate the maximum period during which immunity would last.

A study conducted in the 1940's using 3- and 6-valent vaccines demonstrated that these vaccines produced sustained serum antibody levels, and hence, possibly afforded protection, 8 years after vaccination (Heidelberger, 1953). In that study, the antibody levels in subjects' blood sera were examined at periodic intervals following vaccination. Antibody levels among subjects who had been vaccinated from 3 to 6 years previously ranged from one-fifth to one-half or more of their maximum value, and abundant residual antibodies remained in the blood of the few subjects who had been vaccinated 8 years previously.

Some scientists maintain that pneumococcal vaccine might provide protection for even longer intervals than 8 years (Hill, 1978; Robbins, 1978). Their estimates—ranging from 20 years to a lifetime—are based, not on observed cases, however, but on biological evidence and intuitive reasoning.

In the base case analysis in chapter 4, pneumococcal vaccine was assumed to offer protection for an average of 8 years. It seemed reasonable to assume that the duration of immunity would vary slightly for different individuals, so an assumption was arbitrarily made that duration of immunity would follow a normal distribution with the standard deviation equal to the square root of the mean. In the sensitivity analysis, two different assumptions regarding the duration of immunity were used: 1) that immunity would last only 3 years; and 2) that it would last for 72 years (a lifetime).

[11] Guillain Barre Syndrome (GBS) is discussed in app. 5.1.

[12] See discussion of the excess incidence of GBS among swine flu vaccinees in app. 5.1.

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