A Two-Stage Model for the Control
of Epidemic Influenza

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I. Introduction

Nearly all of the public immunization programs for influenza implemented in the past by the U.S. government have been "limited" programs. The primary objective of these "limited" programs has been to minimize epidemic costs by preventing illness among members of the population who are at higher than average risk of either dying from the disease or developing complications for which the treatment would be costly. High-risk population groups, as they are called, are somewhat arbitrarily constituted, but typically include all individuals over age 65 and also younger persons suffering from chronic diseases regardless of age. Though attack rates for influenza may be somewhat lower among high-risk individuals than others, hospitalization rates and mortality rates are considerably higher, thereby accounting for the greater societal costs when members of the high-risk groups become ill.[1]

An alternative public health strategy for minimizing influenza epidemic costs is to mount a "broad" program which seeks to immunize a sufficiently large and homogeneous segment of the entire population that the epidemic would be averted together. This alternative strategy has been tried only once in recent memory - during 1976, in anticipation of an epidemic of swine influenza that never materialized. Because the 1976 swine influenza immunization program was beset with problems in its implementation and with a higher than expected occurrence of life threatening complications among vaccinated persons, the program is widely believed to have failed.[2] Failure of the swine flu program may have been seen to reflect adversely on the broad-scale immunization strategy, even though the viability of the strategy remained largely untested.

Policy-makers faced with decisions about how best to protect the population against infectious diseases might find useful the capability to compare alternative immunization strategies systematically, in economic terms. We have developed a two-stage model that forms the basis for a decision support system to help predict the circumstances under which specified public immunization strategies for influenza are likely to be best suited to national needs. The first stage of our two-stage model is a deterministic epidemic model, which, when solved numerically, describes the fraction of the population that becomes infective during the course of a hypothetical epidemic. The output from the epidemic model is an important input variable into the second stage, a cost/benefit model which allows the comparison of the expected net economic benefits, in dollars, of alternative public immunization programs. With the assumptions we made, the decision system predicts that despite the wide disenchantment about the success of the 1976 Swine Influenza Immunization Program, broad public immunization programs can, under certain circumstances, be at least as useful in economic terms as limited programs.

II. Structure of the Model

The rate of occurrence of influenza cases among susceptibles is related to the extent of contact with infectives, those persons already able to transmit the disease. Those who are neither susceptible nor infective are immune. This immune protection must have been conferred either by vaccination or by previous exposure to influenza. When an immunization program is mounted, its effect is to raise the fraction of the population which, at baseline, is already immune. The effectiveness of such a program in the prevention of disease depends, of course, on the members of the population who will accept the vaccine when offered. Program effectiveness also depends on the efficacy of vaccine, the probability that an immunized individual will avoid becoming ill.

Four kinds of exogenous variables are required as inputs to the two-stage model that ultimately allows the comparison of alternative immunization program strategies in terms of expected net dollar benefits. These include: information specific to the potential disease threat; details about the immune status of the population under each alternative immunization program; the societal costs, direct and indirect, associated with the outbreak of the disease in epidemic proportion; and the probability that the epidemic will, in fact occur.*

Stage One: The Epidemic Model – Description and Suitability

Since about 1920 deterministic epidemic models have been the object of an academic literature of interest to applied mathematicians and others.[3] Early work addressed the elucidation of factors involved in the causation of disease. Recently, some models of similar form have been proposed and used by researchers as decision aids in the selection from among competing policy alternatives.[4] The epidemic model we used builds upon this recent work.

We chose to adapt the deterministic epidemic model originally proposed by Kermack and McKendrick[5] in 1920. Three states are represented in the epidemic model: susceptible, infective, and immune. These three states describe the entire population at risk . Population is, itself a vector describing seven segments of society according to age and health status. In equations, 1, 2, and 3, below, $\vec{S}$, $\vec{I}$, and $\vec{R}$ are vectors and refer, respectively to the fraction of the population which resides in each of the three states as a function of time. A transition rate β, between

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* Notice that in the absence of a disease outbreak no "benefits" will accrue to the population in terms of societal costs averted. The probability that the epidemic will actually occur is, therefore, a necessary parameter for the computation of the level of expected dollar benefits under each immunization program.

$$\frac{d\vec{S}}{dt} = -\beta \; \vec{S}(t) \cdot \vec{I}(t) \qquad\qquad (1)$$

$$\frac{d\vec{I}}{dt} = \beta \; \vec{S}(t) \cdot \vec{I}(t) \; - \; \gamma \; \vec{I}(t) \qquad (2)$$

$$\frac{d\vec{R}}{dt} = \gamma \; \vec{I}(t) \qquad\qquad (3)$$

susceptibles and infectives, is called the "contact rate" and is related

to the number of individuals in close enough proximity to one another

such that disease could be transmitted if a susceptible contacted an

infective. The transition rate γ , between the infective and the immune

states, is called the "removal rate" and is the inverse of the average

duration of the infective period. Note that since the entire population

must at any point in time be in one of those states, four parameters specify

the model.*

The Kermack-McKendrick Model is considered suitable for this research

in part because it has proven useful in predicting some aspects of the

course of local influenza outbreaks in the Soviet Union[6] and in Great

Britain[7] to within a reasonably close fit. This straightforward model

also offers the practical advantage of being easy to work with and

amenable to solution using numerical methods.

The drawbacks of using this deterministic model for influenza

epidemics lie in the need for making certain simplifying assumptions

whose significance may be testable only after extensive and costly

field research. For example, the country is assumed to be sufficiently

homogenous that the differences among geographic areas in population density

distribution and weather conditions can be ignored. The population

is closed; neither births nor deaths are accounted for in this model.

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* The model is specified by beta, gamma, and two of the following three parameters: the percentage of the population initially susceptible (So), the percentage initially infective (Io), and the percentage initially immune (Ro).

The attack rate for the disease is assumed to be uniform within the susceptible population. People must either be immune, susceptible, or infected, and variation is not permitted in the degree of immunity, the level of susceptibility, or the virulence of one's infective state. Finally, an individual who recovers from the disease is treated as immune for the duration of the epidemic.

A consequence of the structure and assumptions of the epidemic model is that non-immunized individuals benefit each time an additional susceptible accepts vaccine. Logically extended, this implies it should be possible to avert the outbreak of an epidemic, altogether, without the need to immunize everyone. Whether this observation has practical significance in influenza control could, in theory, only be determined through field research.

Stage Two: The Cost/Benefit Model

We now describe the cost/benefit model employed as the second stage of this analysis.* Expected net benefits associated with a particular

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$$* \quad E(NB) = P(E) \times \left\{ \sum_{i=1}^{6} DC_i^{NP} - \sum_{i=1}^{6} DC_i^{P} \right\} - \sum_{j=1}^{2} SEC_j - PC$$

$E(NB) =$ Expected net benefits of program;

$DC_i^{P} =$ Expected disease – related costs associated with resource i, given the inoculation program and the occurrence of the epidemic;

$DC_i^{NP} =$ Expected disease – related costs associated with resource i, given <u>no</u> inoculation program and the occurrence of the epidemic;

$SEC_j =$ Expected side effects costs associated with resource j, given the inoculation program;

$PC =$ Program expenditures for production and administration of the vaccine;

$P(E) =$ Probability of epidemic occurring;

$i =$ The six categories of disease – related costs: hospitalization, inpatient physician, outpatient physician, prescription drugs, lost productivity due to restricted activity and premature mortality

$j =$ The two components of side effects costs: minor and major.

public immunization program for influenza are expressed as the difference between the expected benefits (i.e., expected reduction of societal costs) due to the immunization program and the costs associated with the implementation of the program. The expected benefits are written as a function of both the probability of occurrence of an epidemic and the difference in expected disease-related costs as a result of having implemented as compared to not having implemented an immunization program. Costs include hospitalization costs, the costs of physician services rendered to both hospitalized and ambulatory patients, and the cost of drugs used to treat complications. Costs also encompass the indirect costs associated with excess premature mortality as well as the loss of productivity associated with days of restricted activity due to the disease.[8,9] The costs of premature mortality are evaluated via a foregone earnings approach.*

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* A foregone earnings approach also known as the "human capital approach", calculates the present value of the expected foregone earnings stream of a person dying at age ℓ , as:

$$PVE = \sum_{n=\ell}^{85} P_{\ell,s}(n) \quad x \quad Y_s(n) \quad x \quad E_s(n) \quad x \quad \left(\frac{1+\gamma}{1+r}\right)^{n-\ell} \text{ for } \ell > 16$$

(for ℓ <16, start summation at n = 16)

where,

ℓ = age at death, s = sex of individual, γ = average annual rate of increase in labor productivity; r = discount rate;

$P_{\ell,s}(n)$ = probability of a person in the general population of age ℓ, and sex s, surviving to a subsequent age n;

$Y_s(n)$ = mean annual earnings of employed people and homemakers in the general population of age n and sex s, measured at base year (1976) levels;

$E_s(n)$ = proportion of the general population of age n, and sex s, employed in the labor force or engaged in housekeeping tasks;

PVE = present value of an individual's expected foregone earnings discounted back to the base year.

Those of lost productivity associated with restricted activity are based upon estimates of disease-related restricted activity derived from a schedule generated by the National Center for Health Statistics.[10] The costs of implementing an immunization program are seen to include the public expenditures for manufacturing and distributing the vaccine as well as the cost of side effects due to the vaccine. In our analysis, side affects costs are limited to the costs of minor systemic reactions from the vaccine shot as reflected in restricted-activity days and the cost of life-threatening vaccine complications resulting in premature mortality.

III. Calibration of the Model

Disease Parameters

A baseline run of our deterministic epidemic model was possible once values were specified for the initial population of infectives (I_o), the initial population of immunes (R_o), the contact rate (β), and the removal rate (γ). Sensitivity of results to alternative values will be considered later. The value for one of these, I_o, was by definition assigned to be arbitarily small, in this case 0.1%.

Assigning values to two other paramters, γ and R_o, required an interpretive search of the published literature.[10,11,12,13] A large number of published sources offer empirical data from previous outbreaks of influenza in the U.S. The various data sources are uneven in quality and do not reflect readily comparable study designs and data collection methodologies. Because of these differences, the use of statistical estimating procedures in a meaningful fashion would have proven difficult to defend. The most important data have been reviewed in

the context of public policy implications for the control of influenza.[10]

From the best data available, we intentionally derived a value for γ which, when run in the model, should have made broad-scale immunization programs look less favorable compared to limited programs. In this fashion, if our results justified broad-scale programs using these conservative assumptions, then the conclusions should not change when those conservative assumptions are relaxed. The removal rate γ is the reciprocal of the average number of days during which an infective is able to spread the disease. Although the commonly reported duration of the infective period of influenza ranges from 1 to 5 days, the removal rate is also influenced by the number of influenza infectives who happen to isolate themselves from contact with others in the population before their infection dies out. A value for the removal rate equal to 0.5, the reciprocal of two days, has been used in this work.

To arrive at a value for Ro, the fraction of the population already in the immune state at baseline, empirical data were reviewed from previous flu epidemics. Previously published work has defended the selection of a value for Ro that appropriately reflected the severity of the perceived impending threat at the time when the 1976 public immunization program for swine influenza was launched.[1] Age-specific values for the fraction of the population initially immune have been chosen and are presented in Table 1 along with a summary of other baseline parameters calibrations. The average

value selected for the fraction initially immune in the entire population in 1976 is 19%.

Determining a value for β, the contact rate, proved most difficult. Once the numerical values for Io, Ro, and γ were decided upon, a value for β, equal to 0.75, was selected both for compatibility with empirical data reported for actual influenza epidemics occurring in 1957 and 1968 and for internal consistency with the values selected for the other three parameters described above.[10,11,12,13]

An estimate of the probability that an influenza epidemic would actually occur was also needed. Prior to sensitivity analysis, we estimated that probability to be 10%. This is consistent with the estimate made by other researchers who used the Delphi technique to ascertain the concensus of experts in infectious diseases concerning the likelihood of a swine flu epidemic occurring in the U.S. in 1976.[1]

Cost Parameters

Cost parameters were also calibrated with the aid of published estimates emanating from attempts to anticipate an impending 1976 swine influenza threat.[1,10,12,14] The assignment of initial values for these cost parameters (sensitivity analysis will be described later) reflected the long-standing belief held by many medical practitioners, researchers, and decision-makers that if an influenza epidemic materialized, the largest fraction of the costs incurred by society would be those generated by members of high-risk groups. Table 2 identifies the categories of costs accounted for in our model and also offers estimates for dollar

costs attributed to high- and low-risk population groups. According to our estimates, high-risk individuals would be expected to account for approximately 44.0 percent of the $21.1 billion (1976 dollars) in epidemic-related costs.

As mentioned previously, the entire U.S. population has been divided into seven population segments. Each is characterized according to the age and risk status of the group of individuals involved. The different segments are characterized in Table 3 which summarizes the values assumed in our baseline case for the cost parameters. Notice that although, as mentioned above, population groupings designated high-risk generated 44.0 percent of epidemic-related costs, they account for only 24.6 percent of the entire population.

IV. Results and Discussion

General Findings

The approach used for this analysis was to specify characteristics of several hypothetical public influenza prevention or control programs and to use our model to compare the resulting net benefits in dollar terms. Because the original context for our analysis was the swine influenza immunization program, we generated the expected net dollar benefits associated with three alternative public influenza immunization programs that were actually considered by decision-makers in 1976. Two of the programs , Programs A and B, are broad population programs that address the issue of eliminating epidemic-associated costs by averting the epidemic altogether. Program A would have offered vaccine to the entire U.S. population. Program B excluded only those children under 16 years of age who had not been identified as high-risk. The third alternative, Program C, refers to a limited immunization program

that would have reached only the high-risk segment of the population,

accounting for 24.6 percent of the total population. The results of

our analysis are summarized in Table 4. On an expected net benefit

basis, each of the three programs easily pays for itself. However, the

expected net benefits under both broad Programs A and B significantly

exceed those under limited Program C because of the former programs'

ability to avert all anticipated consequences of the epidemic. Program

B's total expected net benefits ($997.1 million) are in the same range

as those of Program A ($944.1 million).

Sensitivity Analysis and Discussion

To test the robustness of our results, a sensitivity analysis was

performed on nearly all of the baseline values assumed for the model's

input parameters. Results from the sensitivity analysis concerning

three specific parameters warrant special mention because of the range

of uncertainty in the actual value of each of them. These parameters are:

acceptance rate of the vaccine; efficacy rate of the vaccine, and prior

probability of an outbreak of influenza.

Figure 1 considers the variation in expected net benefits from the

alternative programs as a function of the acceptance rate of the

vaccine. The acceptance rate is difficult to specify because there may

have been insufficient experience with public immunization programs for

influenza to make a reliable prediction of public willingness to submit

to immunization. From Figure 1 one sees that, assuming a constant efficacy

rate of the vaccine of 70%, immunization Programs A and B achieve their

maximum expected net benefits with 20-30% of the target population

accepting vaccine. With Program C, however, over 80% of the target

population is required to accept vaccine in order to achieve the same level of expected net dollar benefits as is reached by the other programs at far lower acceptance rates. Even though, for Program C, 80% of the targeted high-risk population translates to only 20% of the whole U.S. population, this result could be significant. Strategies for the marketing of immunization programs might be very different if the goal was a representative 30% of an entire population as opposed to 80% of a special high-risk group. Furthermore, the mechanism for cost savings in these examples is different. Cost savings in limited Program C would result primarily from minimizing premature mortality costs and the costs of treating the disease and its complications among the high-risk population. The largest component of the costs averted in broad Programs A and B is the indirect cost due to the productivity loss among younger members of the population who, on a per capita basis, suffer less disability and miss less work.

Figure 2 is a mapping of the locus of vaccine efficacy rate and acceptance rate combinations over which alternative immunization Programs A, B, or C would be expected to yield the highest expected net economic benefits. Like the acceptance rate, the efficacy rate of flu vaccine has proven difficult to specify, in advance. As can be observed from Figure 2, there exists a large domain of values for the efficacy rate and acceptance rate over which broad immunization programs which target the entire population dominate limited Program C, which targets only the high-risk segments.

Finally, from Figure 3, we observe that large scale inoculation programs can be attractive from the standpoint of expected net benefit criteria even at estimates for the probability of occurrence of an epidemic which are considerably lower than the 10% initially assumed, and become even more

attractive as the probability estimates increase from 10%.

This work suggests that there may be real situations in which broad public immunization programs for influenza aimed at the entire population are preferable to limited programs directed at specific high-risk segments of the population. In the context of the assumptions called for in our model, we are led to ask under what circumstances it would be easier to gain an acceptance rate of 20-30% of the whole population as opposed to 80% of a high-risk group. As long as there continues to be broad recognition by medical specialists of the importance of protecting a high-risk group, then one possible policy might be to gain as high an acceptance rate as possible from among the limited Program C population and to attempt to supplement this group with other population members in order to attain 20-30% of the whole population required in broad Programs A and B. There has been some recent attention in the published literature of medicine and public health that questions the value of making the distinction of a high-risk grouping for influenza.[15,16] While the controversy is far from resolved, if those arguments were to be accepted, the attractiveness of broader public immunization programs for influenza epidemic prevention and control would be enhanced.

Yet to be raised is the issue of whether the findings of our work, which assumes a severe flu threat as was anticipated in 1976 would hold for less severe epidemics. When the model was calibrated with alternative, understated values for the key parameters, a considerably less severe epidemic, in economic terms, was simulated. Even when the epidemic is mild the findings suggest that the broad population programs continue to compare favorably to the more limited ones.

Sensitivity analysis was also performed using the cost parameters discussed earlier including the side effects costs and indirect costs

indirect costs were caluculated using two different rates (6 and 10 percent),
Over a broad range of reasonable values, the major result described above
remained unchanged: broad Program A and B were clearly perferable to
limited Program C on an expected net dollar benefit basis.

V. Validation of the Model

The results of the sensitivity analysis described above offer support
for the contention that broad-scale immunization programs should be worthy
of consideration when flu epidemics are anticipated. The significance
of this observation would be greatly enhanced if it were possible to
gain some empirical evidence of the applicability of the underlying epidemic model.

Ideally, it would be desirable to effect an empirical test of the
Kermack-McKendrick model comparing its predictions with data with the data
from the epidemics of influenza that occurred in the U.S. during 1957 and
1968. However, the quality of the data that are available from these
years makes it difficult to defensibly carry out such a test.

An important theoretical consequence of the epidemic model should be
amenable to verification. The structure and basic assumptions of the
model predict that non-immunized individuals should benefit each time an
additional susceptible accepts vaccine. Integrating over time, it should
be possible to avert an outbreak of disease altogether if less than the
whole population has been protected by immunization. The level of
immunity to the prevailing varieties of influenza virus can be
determined by blood tests conducted in a serology laboratory. When
influenza vaccine is made available voluntarily, one expects a
distribution of vaccine acceptance rates across the large number of
local communities offering the vaccine. It should be possible to design
a prospective field study that could give correlative data regarding a
community's level of protection against influenza and its "performance"

during an upcoming epidemic year. If the findings were consistent with
the predictions of the epidemic model, then strong support would have
been gained for the validity of the current application.

VI. Implementation of the Model

We now speculate about how our two-stage model might potentially
influence public policy toward the prevention and control of epidemic
influenza. Models such as this one can offer decision-makers an opportunity
to improve the effectiveness of immunization as a tool in reducing disease.

Decision makers did not, so far as we know, have access to an explicit
model at the time alternative policies for Swine Influenza were under consider-
ation in 1976. On the basis of our analysis, the decision to mount a broad-
scale immunization program was not unreasonable. Failure of the program did
not, as some unfortunately believe, imply failure of the broad program strategy.
Had a high percentage of the public accepted the swine flu vaccine and had
there been no outbreak of disease, it might have proven difficult to decide
whether the epidemic had been averted or whether there had never been any
real threat of one.

Our model predicts that if an outbreak of virulent disease is feared,
broad-scale immunization programs might be warranted even at lower epidemic
probabilities than had been assumed in anticipating the swine flu. But,
if a decision-maker recommends and implements such a program and then
appears to have "cried wolf," the success of future immunization policies
may be threatened.

Fortunately, the threat of epidemics of virulent influenza occurs
only once in a great while. A model such as the one used here need have
utility for the kind of decisions that are less dramatic and are faced
more frequently. Annually, there are choices to be made about the
allocation of limited stockpiles of vaccine and a model provides the

capability of shedding light on the preferred strategy. Frequently, more information is available than had been the case in anticipation of the swine flu outbreak.

A model can also assist policy-makers by providing a framework to test radical new strategies that had been proposed, but not previously used for influenza. It has been suggested, for example, that immunizing school age children might prove effective in preventing and controlling the disease.[17] School children, it is argued, are a readily identifiable group and can be expected to show a relatively high acceptance rate. Advocates of this approach support their arguments with results from limited empirical field trials.[18,19] When the model is used to analyze this alternative, our finding is that this approach would have less to offer than vaccinating only the high-risk and elderly population. The model predicts that an epidemic will still occur even at very favorable levels of vaccine acceptance among school children. Yet, the elderly and high-risk group has essentially been left unprotected from the consequences of influenza. However, this alternative may deserve further investigation.

Finally, it is worth considering whether models could successfully be developed to evaluate alternatives for the control of potentially a wide range of infectious diseases through immunization. There has recently been renewed recognition of the favorable economic benefits that accrue from preventing disease instead of curing it.[20] Immunization has proven useful in eradicating, through prevention, diseases such as small pox, and polio. The utility of models in decision-making lies in the real possibility that, in conjunction with empirical field research, they can improve the effectiveness with which immunization programs are implemented.

TABLE 1   BASE CASE VALUES FOR DISEASE DESCRIPTION AND INOCULATION PROGRAM DESCRIPTION

SYSTEM PARAMETERS BY POPULATION SUBGROUP+

| | Population Subgroup | | | | | | | |
| | High-Risk People | | | | Low-Risk People | | | |
Parameter	less than 16 yrs.	16-44 yrs.	45-64 yrs.	65+ yrs.	less than 16 yrs.	16-44 yrs.	45-64 yrs.	Total Population
I . Population Fraction(%)	1.946	7.377	4.632	10.666	24.432	35.264	15.682	100%
II Disease Description								
CONTACT RATE (β)	.75	.75	.75	.75	.75	.75	.75	.75
REMOVAL RATE (γ)	.50	.50	.50	.50	.50	.50	.50	.50
III Inoculation Program Description								
TARGETED FOR IN-OCULATION*(%)	*	*	*	*	*	*	*	*
ACCEPTANCE RATE**	63	66	60	60	63	66	60	64%
EFFICACY RATE (%)	70	70	70	70	70	70	70	70%
INITIAL INFECTIVES(%)	.100	.100	.100	.100	.100	.100	.100	.100%
INITIALLY IMMUNE (Before Program)	9	14	31	41	9	14	31	19%

Notes: *Depends on inoculation program.
**For inoculation program oriented towards high-risk groups only, the acceptance rates change to 46%, 52%, 50%, and 70% for high-risk people 16 yrs., 16-44 yrs., and 65+ yrs., respectively.
+Values assumed with the help of references 1, 8, 9, 10, 11, 12

TABLE 2

ESTIMATED COSTS OF AN UNPREVENTED SWINE INFLUENZA

EPIDEMIC FOR THE LOW-RISK, HIGH-RISK

AND TOTAL POPULATION:*+

Cost Category	Low-Risk Population ($000,000)	High-Risk Population ($000,000)	Total Population ($000,000)
Direct Costs:			
Physician Services			
Outpatient	$ 196	$ 53	$ 249
In Hospital	33	64	97
Hospital Services	327	727	1,054
Prescription Drugs	80	23	103
Total Direct	$ 636	$ 867	$1,503
Indirect Costs:			
Premature Mortality	1,714	3,109	4,823
Lost Productivity due to Restricted Activity	4,425	1,342	5,767
Total Indirect	$6,139	$4,451	$10,590
Total, Direct and Indirect	$6,775	$5,318	$12,093

*Using base case value for model's input parameters. All costs expressed in 1976 dollars.
+Adapted from references 6, 7, 8.

TABLE 3: BASE-CASE VALUES FOR COST AND MEDICAL RESOURCE UTILIZATION SYSTEM PARAMETERS BY POPULATION SUBGROUP+

Parameter	High-Risk People				Low-Risk People		
	less than 16 yrs.	16-44 yrs.	45-64 yrs.	65+ yrs.	less than 16 yrs.	16-44 yrs.	45-64 yrs.
Case hospitalization rate (%)	2.33	1.97	3.51	6.80	.74	.7	1.55
# days hospitalized/hospitalized case	8	7	8	12	7	5	6
# in-hospital doctor visits/hospitalized case	10	9	10	14	9	7	8
# outpatient doctor vistis/case	.417	.417	.417	.417	.417	.417	.417
Cost per doctor visit($)	10.40	10.40	10.40	10.40	10.40	10.40	10.40
Hospitalization costs per day ($)	139.50	139.50	139.50	139.50	139.50	139.50	139.50
Drug costs/prescription ($)*	4.25	4.25	4.25	4.25	4.25	4.25	4.25
Value of statistical human life ($)**	135,530.	195,290.	80,150.	7,930.	135,530.	195,290.	80,150.
# days restricted activity/case	5.0	5.0	8.9	11.5	5.0	5.0	8.9
Value of a day of restricted activity($)	0	24.	26.	5.	0	24.	26.
# days restricted activity/shot due to vaccine side effects	.04	.02	.02	.02	.04	.02	.02
Complication costs/shot due to Guillain-Barre Syndrome ($)***	0.014	0.078	0.024	0.003	0.014	0.078	0.024

TABLE 3: Continued

Parameters	16 yrs.	16-44 yrs.	45-64 yrs.	65+ yrs.	16 yrs.	16-44 yrs.	45-64 yrs.
Unit program cost/ individual in targeted population ($)	1	1	1	1	1	1	1
Fixed program costs($)	0	0	0	0	0	0	0
Population size of sub-group (in thousands)	4,186	15,871	9,965	22,947	52,565	75,869	33,739

Notes:

*Notice that average drug costs/case can be obtained by multiplying drug costs/prescription by average number of outpatient doctor visits/case, assuming implicity that 1 prescription is written per doctor visit.

**These values assume a 6% discount rate. Use of a 10% discount rate results in values of $53,310, $126,550, $65,280, and $6,850, for a human life in age groups: less than 16 years, 16-44 years, 45-64 years, and 65+ years.

***These values assume a 6% discount rate. Use of a 10% discount rate results in complications costs/shot of $0.005, $0.051, $0.020, $0.003 for individuals in age groups: less than 16 years, 16-44 years, 45-64 years, and 65+ years, respectively.

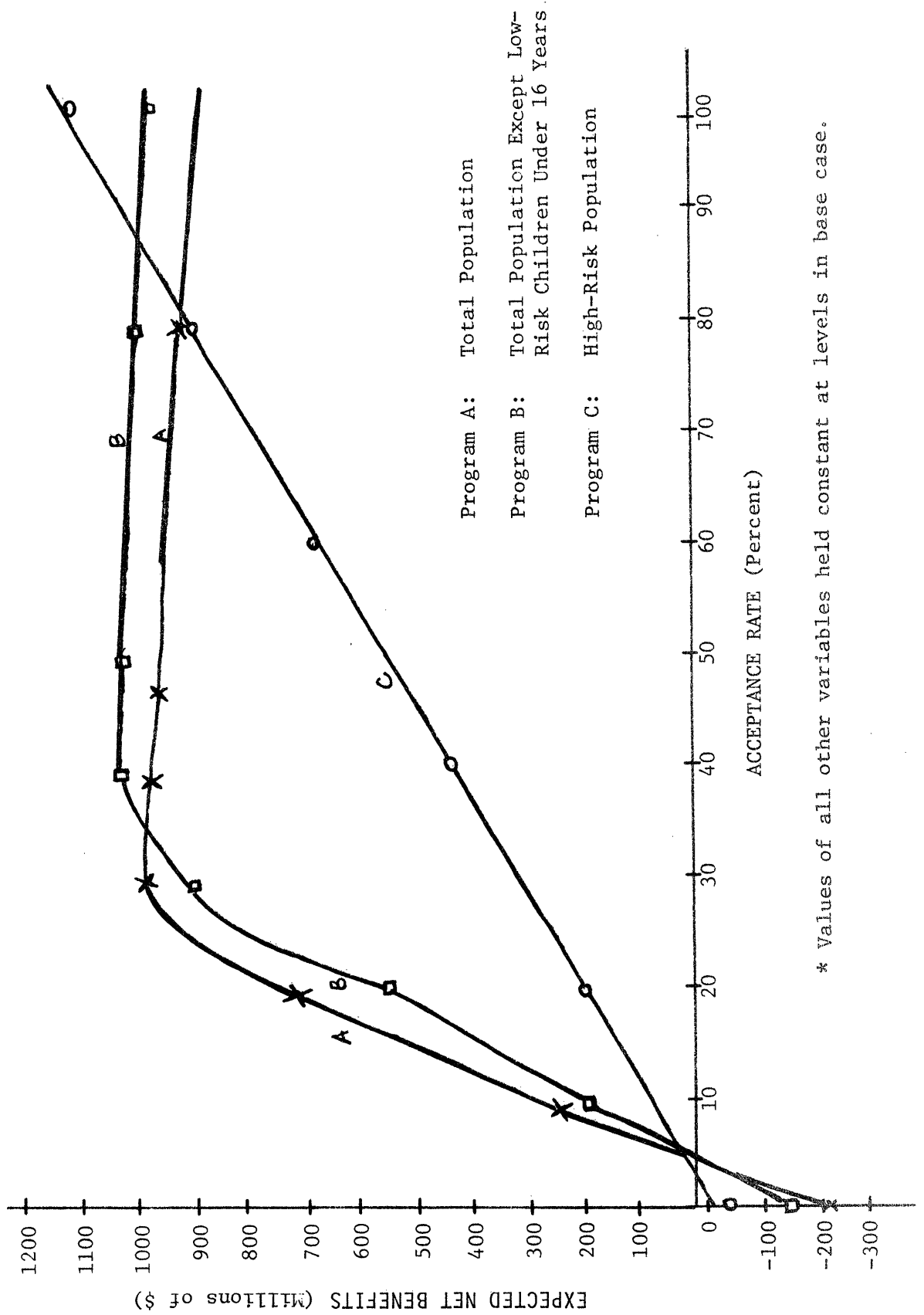+Estimated with the help of references 1, 6, 7, 8, 12.

TABLE 4:

SAVINGS IN COSTS AND EXPECTED NET BENEFITS THROUGH
INFLUENZA IMMUNIZATION PROGRAMS (HYPOTHETICAL) A, B, AND C*+

|	Program A ($000,000)	Program B ($000,000)	Program C ($000,000)
Direct Costs			
●Physician Services			
Outpatient	$ 249	$ 249	$ 139
In-Hospital	97	97	64
●Hospital Services	1,054	1,054	702
●Prescription Drugs	103	103	58
Indirect Costs			
●Premature Mortality	4,823	4,823	3,043
●Lost Productivity due to Restricted Activity	5,768	5,768	3,225
Estimated Total Cost Savings Given Epidemic	12,094	12,094	7,231
●Expected Benefit of Program (with likelihood of epidemic at 10%)	1,209.4	1,209.4	723.1
Program Costs	215.1	162.6	53.0
Side Effects Costs	50.2	49.7	9.0
●Expected Net Benefits of Program	944.1	997.1	661.1

*All costs expressed in 1976 dollars.
+Output from simulation.

FIGURE 1.   EXPECTED NET BENEFITS AS A FUNCTION OF ACCEPTANCE
RATE WITHIN TARGET POPULATION - 70% EFFICACY*

Program A: Total Population

Program B: Total Population Except Low-
Risk Children Under 16 Years

Program C: High-Risk Population

ACCEPTANCE RATE (Percent)

EXPECTED NET BENEFITS (Millions of $)

* Values of all other variables held constant at levels in base case.

FIGURE 2 :   PROGRAM WITH HIGHEST EXPECTED NET
BENEFITS AS A FUNCTION OF ACCEPTANCE
RATE AND EFFICACY RATE*
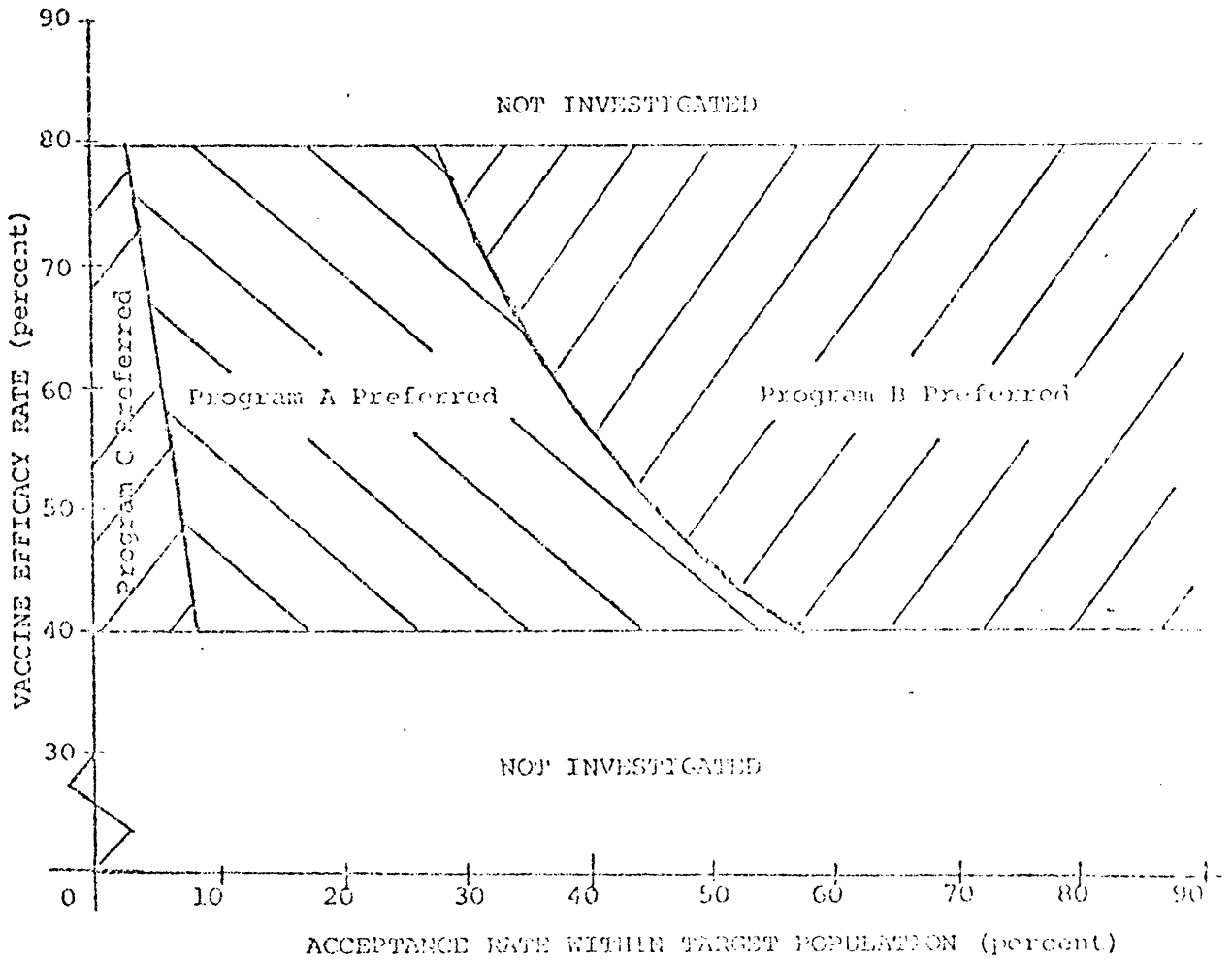
*Values of all other variables held constant at
levels in base case.

Program A: Total Population

Program B: Total Population Except Low-Risk Children
Under 16 Years

Program C: High-Risk Population

FIGURE 3 : EXPECTED NET BENEFITS AS A FUNCTION OF PROBABILITY OF EPIDEMIC*

Program A: Total Population

Program B: Total Population except low-risk children.

Program C: High-risk Population

EXPECTED NET BENEFITS ($ MILLIONS)
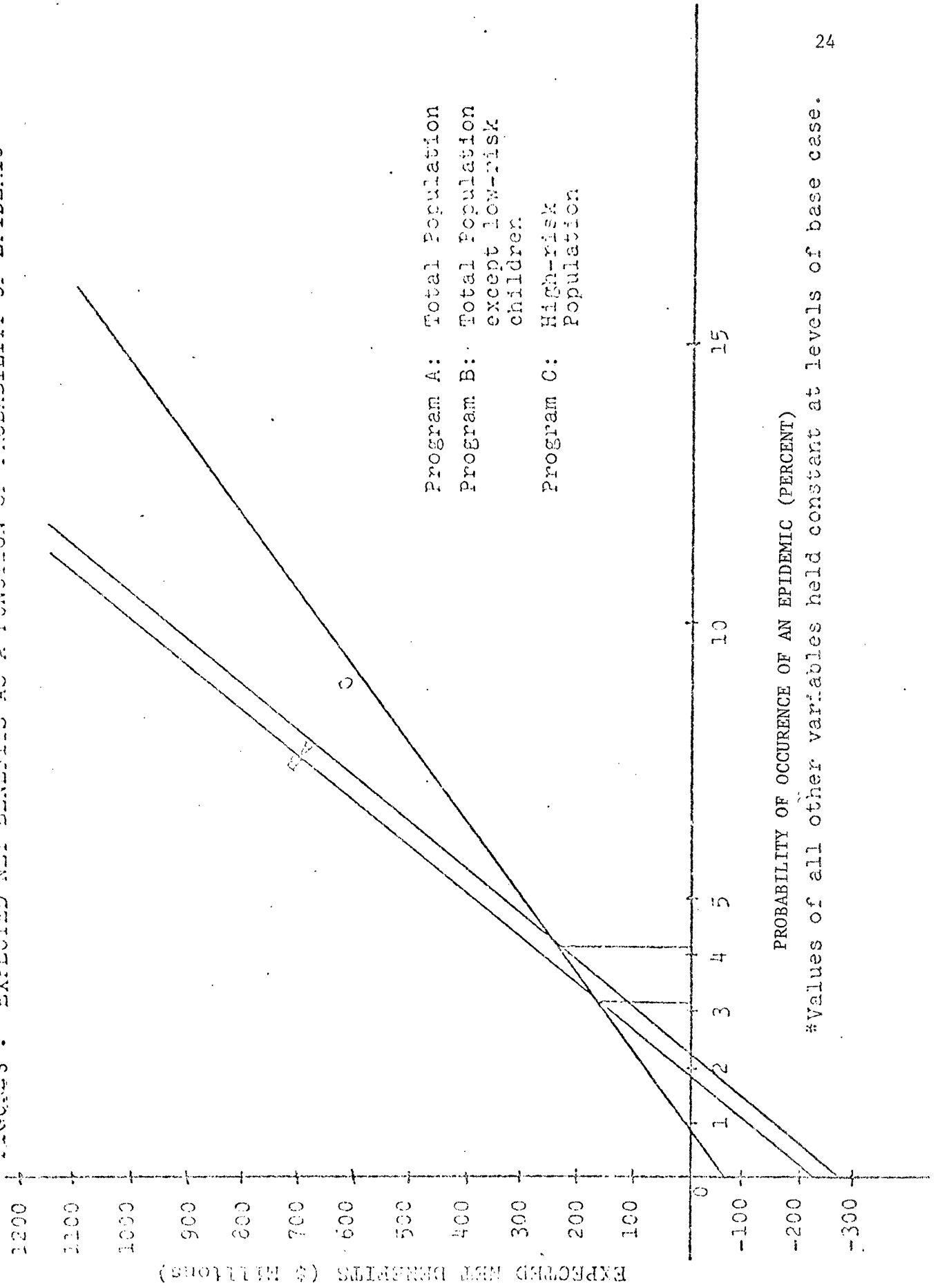
PROBABILITY OF OCCURENCE OF AN EPIDEMIC (PERCENT)

*Values of all other variables held constant at levels of base case.

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