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Economics of Disease Prevention: Infectious Kidney Disease

Dramatic advances in the treatment of diseases are for the most part universally welcomed. However, because of economic constraints, differences in philosophical or ethical judgments, and conflicting medical viewpoints concerning the efficacy of alternative methods of disease control, proposals to guarantee unlimited access to such treatments, by whatever means, are usually met with some dissent.

Often, the disagreements are based upon differences in the sources of the arguments rather than on simple differences of view. Three viewpoints may be contrasted. First, there is the uninformed humanitarian who wishes to provide immediate response to urgent problems, and who on that account would always put first the need to keep the dying alive. Second, there is the view of the medical professional whose interest is in the prevention of disease, where possible, and in control and mitigation of its effects. Third, there is the view of the policy-maker who is attracted to competing alternatives, constrained by budget, and devoted to achieving optimal results

from a combination of choices. This paper presents and illustrates a model which permits accommodation of the analysis of the medical and economic professionals with that of social preference by combining consideration of medical and economic data in a way that permits explicit recognition of social preferences.

Variation of opinion within the medical community concerning the most effective means of controlling the morbidity and mortality associated with kidney diseases provides a case in point. There have been advances in artificial kidney therapy (and in other forms of dialysis), and in kidney transplantation; and recent proposals have suggested an expansion of governmental financing of "kidney centers" in order to eventually insure treatment for all persons with otherwise terminal chronic kidney failure.

A lack of consensus on such proposals can be ascribed to differing viewpoints concerning:

1 The feasibility as well as the ethical implications of employing costly procedures involving artificial and borrowed organs to prolong for an uncertain period of time the lives of a limited number of selected individuals with terminal chronic kidney failure; and

2 The effectiveness of medical treatment administered earlier in the kidney disease process in terms of its ability to prevent chronic kidney disease and thereby reduce the need for treatment facilities in the future.

One view contends that the "prevention" of chronic kidney disease is not a viable

alternative to providing facilities for treating persons with kidney failure; and that kidney disease control programs should, therefore, emphasize the "treatment" rather than the "prevention" of kidney disease. The contrary view holds that the costs of a large-scale dialysis and kidney transplantation program would be "excessive" because its success—measured in terms not only of patient survival but also of their medical and vocational rehabilitation—is not assured, especially if treatment is offered to "unselected" patients; and because its drain on both human and non-human medical resources is severe at a time when such resources appear to be in critically short supply. The implication, of course, is that expenditures by the Federal government for dialysis and transplantation would be more wisely invested in a broadly based medical program for "preventing" kidney disease by detecting and treating it in the early stages of its natural history.

This paper will attempt to clarify discussion of this issue by presenting a framework for determining the effectiveness of medical programs designed to "prevent" infectious kidney disease. This particular type of kidney disease was chosen because it is one of the major types, causing about one-fourth of the morbidity and mortality associated with kidney diseases; and is considered to be more susceptible to "prevention," based on its prevalence, natural history, and other factors, than the other major types. It should be stressed at the outset that the effectiveness of disease control programs should not be considered in terms of an all-or-nothing "prevention" as opposed to "treatment" framework. It is conceivable that prevention is so costly and its effect on reducing the flow of patients requiring dialysis and/or transplantation so insignificant as to render it an unreasonable alternative under certain conditions. But it is more likely that the choice confronting decision-makers is one between incremental changes in the allocations among alternatives for disease control, with some being spent for dialysis and transplantation and some for preven-

tion—and the question is how much more for one or the other. After presenting an analysis of infectious kidney disease prevention programs, we will consider how the analysis could be extended to assist the development of an optimal strategy for allocating the infectious kidney disease budget among the various alternatives for controlling the morbidity, mortality, and treatment costs associated with this disease.

Methodology

One criterion for evaluating the effectiveness of a proposed medical program is to compare its costs with its expected benefits. The costs would be based on the costs of detecting the disease and the costs of administering medical treatment. The benefits would be related to the sequence of events—the morbidity, mortality, and treatment costs—that would be prevented as a result of the program. The benefits can be stated either in physical magnitudes, such as the number of deaths or bed-days of sickness that have been avoided, or in terms of a specified *numeraire,* such as dollars. The program's benefits can then be compared with its costs to facilitate policy choice.

Several methodological and analytical problems accompany the use of benefit and cost analysis. Some relate to the implications as well as the applicability of cost-benefit analyses; some to determining the quantitative magnitudes of certain costs and benefits ("measurement" problems); and others to assigning a dollar measure to the quantitative estimates of costs and benefits ("valuation" problems). Discussion of these problems is warranted since they have received substantial attention and affect the merits of the present study.

One commonly voiced objection is that selecting among different types of health programs by comparing their costs and benefits is contrary to physicians' attitudes in the care of individual patients. Nevertheless, such decisions are constantly made. Prior decisions concerning the allocation of health resources affect the current mix of health programs; and, given

the scarcity of health resources, it seems desirable to base such decisions on an explicitly enumerated set of criteria.

Specification of Criteria

This leads to a fundamental set of methodological issues: those related to the specification of criteria for program selection. Not only must the relevant criteria be identified, but weights must be assigned to a given level of achievement for each criterion. Criteria frequently suggested for selecting among health programs include:

1 The relative magnitudes of the various disease problems;
2 The effectiveness of the budgetary allotments among different types of health problems;
3 The differences between the costs and benefits of the proposed programs;
4 The impact of the costs and benefits of the various alternatives upon the income distribution of the population.

In the absence of a "social objective" function, which would essentially identify the goals of society and weight the criteria appropriately—so as to make likely the choice of the "best" mix of health programs—choices are made within a certain political decision-making process with legislative actions presumably revealing social preferences. It must be concluded, therefore, that a cost-benefit comparison provides pertinent and valuable information to facilitate choice; and there is a presumption that projects "passing" a benefit-cost test should be preferred to those that "fail." However, such a test need not provide fully correct evaluations of costs and benefits in the view of decision-makers voting for their actual preferences.

Even under circumstances where cost and benefit calculations seem particularly applicable, the actual calculation of costs and benefits introduces many complex problems. "Measurement" problems arise because it is difficult or impossible (and therefore costly) to attempt to measure the quantitative significance of certain costs and benefits due to uncertainty, lack of knowledge about future events, and spillovers of benefits and costs to third parties. For example, it is difficult to predict with certainty the number of deaths that an infectious kidney disease program will prevent; it is impossible to measure the contributions of kidney transplantation and hemodialysis to the general stock of medical knowledge. Failure to include explicit estimates of such benefits and costs results in a decision reflecting implicit judgments as to their quantitative significance.

"Valuation" problems result from difficulties in expressing certain disparate costs and benefits in terms of a common measure of value. For example, the detection, treatment, and permanent cure of infectious kidney disease in an early stage will eliminate the costs associated with morbidity, mortality, and treatment—including the pain, discomfort, and fear of incapacitating illness—that would have accompanied subsequent stages of the disease process. While analysts can readily measure and assign dollar values to the avoided medical costs (assuming knowledge of the disease's natural history), they may be unwilling or unable to express the reductions in morbidity, mortality and pain costs in terms of dollar values. This difficulty arises not because societies and individuals do not, at least implicitly, place valuations on human lives, but because of diverse opinions concerning the specific value to be assigned. Under these circumstances the customary procedure in a cost-benefit analysis is to either assign an "appropriate" value to the benefits or costs,[1] or to present the full array of expected results without expressing them in the form of a single index of value.

Problems associated with the measurement and valuation of costs and benefits can be circumvented to some extent so as to make policy assessment more conscious and systematic and more nearly in accord with a society's range of preferences. This can be done by incorporating within the analysis a range of alternative estimates, for the magnitude of certain "immeasur-

able" benefits and costs, or for the value of certain expected results, and showing how the costs, benefits, and conclusions of the analysis would thereby be affected. For example, if the mortality rate associated with a certain disease is not known precisely, alternative estimates can be used to demonstrate how the costs and benefits would be affected. If certain "immeasurable" external benefits are expected to result from a proposed course of action, it might be worthwhile (as a way to make them explicit) to show how the benefits would vary with alternative estimates of their quantitative magnitude. The costs of a proposed medical program could be estimated using alternative assumptions about costs of medicine, laboratory fees, incidence of the disease, or other key variables, with some indication as to how policy conclusions would be altered with different assumptions. If the "correct" discount rate for converting future costs and benefits to their present values is not known, alternative rates yielding different results should be provided. If there are diverse opinions regarding the specific "value" of certain expected results, such as preventing illness or prolonging an individual's life, the analysis should include an evaluation of the policy implications using alternative valuations of the expected results. Such a procedure would tend to forestall criticism concerning the "correctness" of particular assumptions that have been employed, enhance the applicability and conclusions of the analysis, and make explicit any judgments as to the quantitative significance of certain "immeasurable" costs and benefits as well as the relative valuations of expected outcomes.

Infectious Kidney Disease Prevention Program

Based on medical data presented elsewhere,[2] the following assumptions pertaining to the infectious kidney disease process underlie the basic model:

1 The natural history of infectious kidney disease is comprised of four basic stages: uncomplicated urinary tract infection (UTI); urinary tract infection involving the kidneys (KI); chronic kidney disease (CKD); and chronic irreversible kidney failure (CKF).

2 Especially in the first two stages, but also in the third, the disease is frequently asymptomatic so that individuals must be screened for the disease if it is to be detected.

3 Unless administered early in the first stage, medical treatment is ineffective in permanently halting the progression of the disease process although it may result in short-term eradication of the infection.

4 The disease becomes symptomatic in the fourth stage and unless some form of long-term palliative treatment (either dialysis or transplantation) is used to relieve the symptoms that accompany this stage of the disease, the patient will die.

5 There is, therefore, a certain probability that unless the disease process is halted in either the first or second stage it will progress over a certain time span to the stage of chronic irreversible kidney failure.

Costs of a Disease "Prevention" Program

Infectious kidney disease is frequently asymptomatic in its first two stages (UTI and KI), so its presence can only be determined by detection programs in certain population cohorts. Once detected, the infection is usually treated with various antibiotics until eradicated. However, since urinary infections are difficult to cure or eradicate permanently—especially if long-standing, and if the kidneys are involved—there is a certain probability of recurrence in subsequent time periods. An infectious kidney disease prevention program would involve, therefore: 1) selecting a target population, 2) screening it for stages 1 and/or 2 of the disease, 3) administering treatment to individuals with infections, and 4) conducting follow-up tests on those with infections—even if "successfully" treated—for a certain time period.

The total costs of a medical program to prevent urinary infections from progressing through subsequent stages of the disease would depend, therefore, on four principal elements. First, an important factor is the number of tests needed to detect the urinary infections in the population cohort. The number of tests would be determined by: the size of the target population; the number of tests required to confirm the presence of the disease (individuals who are positive on the initial test are usually re-tested twice subsequently); the number of persons followed and re-tested for either persistence or a recurrence of the disease each year; and the number of times the entire cohort is to be screened in its lifetime. Second, the cost per test would enter the calculation. Third, the average costs of medical treatment, including laboratory fees, urologic examinations, drugs, and doctors' fees would be considered. Fourth, the number of persons treated would be involved. This figure depends on the number of persons initially detected with the disease, the short-term success in eradicating the infection, the probability of recurrences in successfully treated patients, and the success in treating recurrences. The number of persons treated and the number of treatments required per person would thus be related to total treatment costs. Program costs would then include total costs of screening and treatment.[3]

Benefits of a Disease "Prevention" Program

The benefits of a medical program serve as a measure of the observed or simulated willingness of consumers to pay for the services rendered, and thus represent an estimate of the value placed on the reductions in morbidity, mortality, treatment costs and pain costs that result from the program. The benefits are related not only to the sequence of events that would have occurred in the absence of medical treatment, but also to the effectiveness of the treatment in preventing the progression of the disease through its various stages. There are two sets of primary beneficiaries

from an infectious kidney disease prevention program: 1) those in whom the infection has been eliminated and the progression of the disease thereby halted; and 2) those in whom the entire disease process is pushed into the future though the infection is never completely or successfully eradicated as a result of the prevention program.[4] The second group of direct beneficiaries will be ignored and, to this extent, the benefits will be understated.

To estimate the benefits of an infectious kidney disease prevention program, individuals who have been detected with the disease, treated, and permanently cured, will be followed through subsequent stages of the disease process to determine the sequence of events if the "prevention program" had not been administered. It is assumed that the infectious kidney disease process is comprised of four stages—UTI, KI, CKD, and CKF—and that, after an individual develops CKF, either dialysis or transplantation is required to prevent death. It is also assumed that individuals must progress through the infectious kidney disease process sequentially (i.e., stage 1 to 2 to 3 to 4 to dialysis or transplantation). The probabilities of an individual being sick, of his dying or developing the next stage of the disease, or of his being spontaneously cured (and thereby "leaving" the process) are assumed to depend on the particular stage of the disease, the length of time the individual has been in that stage, and his clinical status in previous time periods.

Persons who are cured as a result of the prevention program are classified as having been in either stage 1 (UTI) or stage 2 (KI) at the time of cure. There are certain probabilities that those who were in stage 1 when cured would have been sick or well, developed an infection of the kidneys (stage 2), spontaneously "lost" their UTI, or died during time period 1. Similarly, there are certain probabilities that individuals who were in stage 2 when cured would have been sick or well, developed chronic kidney disease (stage 3), or died during the first time period. During a

second time period, some who were initially in stage 1 will remain there (and either be sick, well, die or spontaneously cured); some will develop stage 2; some will remain in stage 2 (having either been classified initially in this stage or developed it during time period 1); and some will develop stage 3 (CKD). By the fourth time period, some of the cohort detected with UTI and cured would have required medical treatment—dialysis and/or transplantation—for CKF. There are certain probabilities of survival and clinical rehabilitation for persons receiving this treatment.

Assuming certain probabilities — or ranges of probabilities—for these events, the number of persons in each stage of the disease and the number sick, well, dead, and receiving treatment for the final stage of the disease can be estimated for each year the cohort is followed. Additional data are needed to estimate the costs of morbidity and mortality associated with the various stages of the disease. For example, the morbidity losses for persons in stage 2 in the second time period are calculated by: 1) multiplying the number of persons in stage 2 in time period 2 by the probability of sickness to determine the number of sick persons; 2) multiplying the number of sick persons by the average number of bed-days or restricted days per episode of morbidity; and 3) multiplying the total number of bed-days by a dollar value for each bed-day. Then, to express the dollar costs for stage 2 in time period 2 in terms of their present value, the costs must be discounted. Algebraically

$$\begin{pmatrix} \text{Present value} \\ \text{of morbidity} \end{pmatrix} = \begin{pmatrix} \text{Total persons} \\ \text{in stage 2} \end{pmatrix} \times$$

$$\begin{pmatrix} \text{Probability} \\ \text{of sickness} \end{pmatrix} \times \begin{pmatrix} \text{Average bed-days} \\ \text{sick person} \end{pmatrix} \times$$

$$\begin{pmatrix} \text{Dollar value} \\ \text{per bed-day} \end{pmatrix} \times \begin{pmatrix} \text{Discount} \\ \text{rate} \end{pmatrix}$$

Similarly, the present value of mortality is the result of applying the probability of death, an arbitrary current value for each death, and a discount rate to the number of persons in stage 2. The present values of morbidity and mortality are then in common terms and can be combined. The dollar figure that results is the present value of the costs of morbidity and mortality during time period 2 for persons from the original target cohort who would have been in the second stage of the infectious kidney disease process if their infections had not been detected, treated, and cured in the prevention program. To determine the total benefits of the prevention program, similar calculations for each stage of the disease, as well as for the costs associated with the treatment required for stage 4, would be aggregated over a certain time span.

Since the models for estimating costs and benefits explicitly allow the inclusion of alternative arrays of values for certain variables, there are many opportunities for analysis. Alternative assumptions about discount rates, prevention costs, morbidity and mortality rates, treatment costs, and other variables, might be used to determine their effects on cost and benefit estimates. If a given program were not worthwhile (in a cost-benefit sense) under a particular set of assumptions, the analysis could show what changes in assumptions would be necessary to make the program worthwhile. The analysis could also show how new, more effective ways to "prevent" infectious kidney disease or new methods to treat CKF would affect cost and benefit estimates, and how such changes would alter the optimal strategy for controlling the costs associated with this disease.

Hypothetical Kidney Disease Medical Program

In this section, the techniques for estimating the costs and benefits of infectious kidney disease control programs will be more fully elaborated and applied to a hypothetical medical program for detecting and treating "kidney infections" in a certain population cohort. This is a purely hypothetical example, and the specific probabilities and dollar values for the various events have been chosen primarily to simplify the exposition of the models.

Table 1. Costs of a hypothetical kidney disease prevention program for a single population cohort

Year	Number screened[a]	Present value of screen costs[b]	Number treated[c]	Number of successes[d]	Present value treatment costs[e]	Present value total costs[f]
1	1,300,000	$13,000,000	50,000	25,000	$5,000,000	$18,000,000
2	50,000	462,950	25,000	12,500	2,314,800	2,777,750
3	50,000	428,650	12,500	6,250	1,071,620	1,500,270
4	50,000	396,900	6,250	3,125	496,120	893,020
5	50,000	367,500	3,125	1,563	229,690	597,190
6	50,000	340,300	1,563	781	106,380	446,680
7	50,000	315,100	781	390	49,220	364,320
8	50,000	291,750	390	195	22,760	314,510
9	50,000	270,150	195	97	10,540	280,690
10	50,000	250,100	98	49	4,900	255,000
11	50,000	231,600	49	25	2,270	233,870
12	50,000	214,450	24	12	1,030	215,480
13	50,000	198,850	12	6	480	119,330
14	50,000	183,800	6	3	220	184,020
15	50,000	170,250	3	1	100	170,350
	Total program cost					$26,432,480

[a] Year 1: $(1 + .15 + .15) \times (1,000,000)$; Year 2 (*et seq.*): $.05 (1,000,000)$.
[b] $10 (discounted at 8 percent to present value) $\times$ column 2.
[c] Year 1: $.05 (1,000,000)$; Year 2 (seq.): .5 of preceding year.
[d] 50 percent of column 4.
[e] $100 (discounted at 8 percent to present value) $\times$ column 4.
[f] Column 6 + column 3.

Costs of Early Detection and Treatment Program

The costs of a medical program to prevent kidney infections from progressing beyond the first two stages of the disease process are based on the costs of detecting and the costs of treating the disease in its early stages. Since infectious kidney disease is usually asymptomatic in its earliest stages (UTI and KI), the target population must be screened to determine the presence of disease. Assume the following: 1) 1,000,000 individuals are to be screened for "kidney infections"; 2) three consecutive positive urine specimens are needed to verify the diagnosis; 3) 15 percent of the group are found to be positive on the first test, two-thirds of whom are positive on the second test, and the overall prevalence after the third test (i.e., the actual UTI prevalence rate as determined by three consecutive positive tests) is 5 percent; 4) all persons in whom a "kidney infection" has been detected are rescreened once per year for 15 years; 5) the cost per test is $10; and 6) the discount rate for converting future costs to their present

value is 8 percent.[5] The number of persons screened per year and the present value of screening costs are shown in Table 1, columns 2 and 3.

Once the infection is detected, the cost of treatment varies depending on the specific medical procedures employed. Some patients are merely given antibacterial therapy and, if the infection is not eradicated within a certain time period, a different drug is prescribed. Others are given an extensive urologic workup in order to determine the extent to which the kidneys are also infected. The cost of treatment also varies with the degree of difficulty in eradicating the infection, with some patients requiring several years of continuous treatment to eradicate the UTI. In other cases, however, the UTI is eradicated with the first round of treatment, though there is still a certain probability of relapse thereafter. Because there is a relatively high frequency of recurrence in persons who are apparently treated "successfully" for UTI, "successful" treatment is assumed to mean short-term eradication of the infection rather than permanent

cure of the infectious kidney disease process. Therefore, there is a certain probability that persons treated "successfully" will have a recurrence of their infection in subsequent time periods; and this, too, will affect the costs of treating "kidney infections" in their early stages.

Assume that 50 percent of the persons entering the treatment program are treated "successfully" initially and that 50 percent of the remainder are treated "successfully" each time period thereafter. Assume also in this example that success means zero probability of future recurrence (i.e., permanent cure). Assuming treatment costs of $100 per episode and a discount rate of 8 percent, the number of patients treated, the number of "successes," and the present value of the treatment costs each year are shown in columns 4, 5 and 6, respectively, of Table 1. Column 7 shows the present value of the treatment and detection costs for each year of this prevention program. The total costs—$26,-432,480—represent the present value of the total costs for an infectious kidney disease control program based on the above assumptions.

Benefits of the Program

It is assumed that unless infectious kidney disease is detected, treated and permanently cured at an early stage, there is a certain probability that the disease will progress from an uncomplicated UTI (stage 1) to chronic irreversible kidney failure (stage 4).[6] Therefore, the benefits of an infectious kidney disease prevention program can be estimated by measuring the morbidity, mortality, and treatment costs that will be avoided as a result of the program.

It was assumed in the prevention program illustrated above that 50 percent of those with UTI were treated successfully the first year and 50 percent of the remainder were successfully treated each year thereafter until all the UTI's were eradicated. It was also assumed that the probability of the infection recurring after

being successfully treated was zero. Thus successful treatment in this example is assumed to result in permanent cure of the UTI and permanent cessation of the disease process. The number of persons successfully treated (permanently cured) per year is shown in column 6, of Table 1. Each year's "successes" must be followed through the infectious kidney disease process to determine what would have occurred if their UTI had not been successfully treated.

Persons who have been permanently cured are initially classified as having been in either stage 1 (UTI) or stage 2 (KI) at the time of cure. Each group is then followed through the remainder of the disease process. During the first time period, a certain number of those permanently cured would have been sick; some would have remained well;[7] in some the UTI may have spontaneously cured; some would have developed a kidney infection; and a certain number would have died. In time period 2, persons remaining in stage 1 (i.e., those who were either sick or well during period 1) must be followed for morbidity, mortality, spontaneous cure, or a worsening of the disease. Since the probability of these events is assumed to be related to medical status in previous time periods, those who were sick in the first time period are more likely to be sick, die, or develop stage 2, and less likely to be spontaneously cured or well, than those who had remained well. Similarly, the probability of morbidity differs in time period 3 and subsequent periods, with totals for these periods calculated over the entire cohort.

Since it has been assumed that some, but not all, persons being treated for "kidney infections" (UTI or KI) are cured in the first year of treatment, new "permanently cured" persons enter the benefit flow over an extended time span.[8] Therefore the total number of UTI's who would have been sick, well, cured, dead, or developed KI in a certain time period would be an aggregate based on the UTI's from previous time periods' cohorts who are still

Table 2. The first stage of the kidney disease process: number of persons
morbid, dead, well, spontaneously cured, and developing stage 2 each year

Year	Enter stage 1 (UTI)[a]	Enter stage 2 (KI)[b]	UTI Morbidity[c]	UTI Okay[d]	UTI Cured[e]	UTI Mortality[f]
1	12,500	17,500	2,500	1,250	2,500	1,250
2	6,250	9,688	2,000	1,187	1,875	1,500
3	3,125	5,172	1,244	809	1,181	1,031
4	1,563	2,701	704	483	680	610
5	782	1,391	381	269	372	338
6	391	709	200	144	197	180
7	195	359	104	76	102	94
8	98	181	53	39	53	48
9	49	91	27	20	27	25
10	25	46	14	10	14	13
11	13	23	7	5	7	6
12	6	11	3	3	3	3
13	3	6	2	1	2	2
14	2	3	1	1	1	1
15	1	1	....	....	....	....

[a] 50 percent of "successes" (Table 1, column 5).
[b] Year 1: 50 percent of successes + 40 percent of column 2; Year 2 (*et seq.*): 50 percent of successes + certain percentages of previous years' UTI cohorts (see text).
[c] Year 1: 20 percent of column 2; Year 2 (*et seq.*): 20 percent of column 2 + certain percentages of previous years' UTI's in columns 4 and 5.
[d] Same as column 4, with different probabilities (see text). Persons who remain well still have the disease, but suffer no morbidity or mortality, are not cured, and do not worsen in that time period.
[e] Same as column 4, with different probabilities (see text). Persons who are "cured" have spontaneously cured themselves of the disease.
[f] Same as column 4, with different probabilities (see text).

being followed plus the UTI cohort that entered the benefit flow in that particular time period. For example, by the fourth time period, four separate cohorts would have entered the benefit flow: the initial cohort, comprised of those whose "kidney infections" were permanently cured the first year of the prevention program, would be in their fourth year in the UTI stage; the cohort which was cured in the second year of the prevention program would be in its third year; the third year's "permanent cures" would be in their second year in the benefit flow; and those who were treated successfully (in this example, permanently cured) in time period 4 would be in their first year.

Table 2 shows the number of UTI's sick, well, spontaneously cured, dead and developing KI each year, and is based on the following assumptions:

1 Fifty percent of the persons cured each year are initially found to have a kidney infection (stage 2 of the disease process);

2 During the first year, 20, 10, 20, 40, and 10 percent of each entering UTI group are sick, well, spontaneously cured, moved to stage 2, and dead, respectively;

3 Each year thereafter there are probabilities of 25, 10, 10, 25 and 30 percent that a person who was sick in the previous period will be sick, well, spontaneously cured, develop stage 2 and dead, respectively; and probabilities of 10, 25, 30, 25, and 10 percent that one who was well in the previous period will be sick, well, cured, develop KI, and dead, respectively.[9]

Each year's figures are an aggregate comprised of each of the UTI groups being followed in that year. For example, the morbidity for year 3 is comprised of the number of UTI's morbid in each of the three groups being followed in that year, including the third year's morbidity for the 12,500 UTI's from year 1 (representing 50 percent of those permanently cured the first year of the program), plus the second year's morbidity for the 6,250 UTI's

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Table 3. Total morbidity and mortality losses associated with stage 1 (UTI) of the infectious kidney disease process for the original population cohort

Year	Bed-days[a]	Morbidity losses[b]	Mortality losses[c]	Total indirect losses, stage 1[d]	Present value total indirect losses[e]
1	2,500	$25,000	$1,250,000	$1,275,000	$1,275,000
2	2,000	20,000	1,500,000	1,520,000	1,407,368
3	1,244	12,440	1,031,000	1,043,000	894,541
4	704	7,040	610,040	617,000	489,806
5	381	3,810	338,000	341,810	251,230
6	200	2,000	180,000	182,000	123,869
7	104	1,040	94,000	95,040	59,894
8	53	530	48,000	48,530	28,317
9	27	270	25,000	25,270	13,653
10	14	140	13,000	13,140	6,573
11	7	70	6,000	6,070	2,812
12	3	30	3,000	3,030	1,300
13	2	20	2,000	2,020	802
14	1	10	1,000	1,010	371
Total benefits if stage 1 were prevented					$4,555,536

[a] UTI morbidity (Table 2, column 4) × 1 day (representing average length of illness for each episode of morbidity).
[b] Column 1 × $10 (representing average "value" per bed-day of illness).
[c] UTI mortality (Table 2, column 7) × $1000 (representing average "value" of each death).
[d] Column 3 + column 4.
[e] Column 5 discounted at 8 percent to present value.

who were successfully treated in year 2, plus the first year's morbidity for the 3,125 UTI's who entered the benefit flow in year 3.

In Table 3, a certain number of bed-days are assigned each episode of morbidity, certain values are attributed to each death and to each bed-day of morbidity, and the present value of the total morbidity and mortality losses associated with stage 1 of infectious kidney disease are estimated, based on the foregoing assumptions.[10] The present values of each year's total losses are calculated using an 8 percent discount rate. The present value of the total morbidity and mortality losses—$4,555,536—represents the benefits if stage 1 were prevented from occurring as a result of an infectious kidney disease prevention program.

The same procedure can be used to estimate the benefits expected to result from the prevention of the second and third stages of infectious kidney disease in a certain cohort. Over a certain time duration, persons are in stage 2 (KI) either because they had a kidney infection when permanently cured or had advanced to stage 2 from the first stage of the disease. For any particular year the total number of KI's sick, well, dead, and advancing to stage 3 (CKD) would be based on the number of persons entering and remaining in stage 2 as of that year. The same is true for individuals in the third stage of the disease. The primary difference between the different stages of the disease process would be in the probabilities of the various events, which would be directly related to the severity (stage) of the disease. The total indirect losses associated with the second and third stages of the disease process — representing the benefits expected to result if these stages were prevented from occurring — are presented below.[11]

Chronic Irreversible Kidney Failure

The fourth stage of the infectious kidney disease process is chronic irreversible kidney failure (CKF). After progressing to this stage of the disease, persons either die within a short time period or are selected to receive some form of long-term treatment—either dialysis or transplantation. The number of persons entering CKF

Table 4. Results for patients requiring long-term treatment for CKF

Year	Enter long-term treatment[a]	Total on HD[b]	HD patients fully rehabilitated[c]	HD mortality[d]	Total receiving transplants[e]
4	4,288	2,144	1,286	429	2,573
5	4,868	3,720	2,232	742	3,178
6	3,452	3,959	2,375	792	2,519
7	2,053	3,402	2,041	680	1,707
8	1,128	2,569	1,563	521	1,085
9	597	1,862	1,117	372	671
10	309	1,272	763	254	409
11	158	842	505	168	247
12	80	545	327	109	149
13	40	347	208	69	89
14	21	219	132	44	55
15	10	137	82	27	32
16	4	84	51	17	19
17	....	51	31	10	10
18	....	31	18	6	6
19	....	18	11	4	4
20	....	11	7	2	2

[a] Certain percentage of persons with CKF (see footnote 12).
[b] Year 4: 50 percent of column 2; Year 5 (*et seq.*): 50 percent of column 2 + 60 percent of the previous year's column 3.
[c] 60 percent of column 3. Additional columns to account for partial rehabilitation and inactive cases should be added where information permits or assumptions require them.
[d] 20 percent of column 3.
[e] 50 percent of column 2 + 20 percent of column 3.

in any time period is related to the number of persons sick or well with CKD in the previous time period.[12] The total benefits if stage 4 were prevented from occurring are presented below.

Persons who have progressed through the four stages of the infectious kidney disease process and have been selected to receive long-term treatment for CKF must also be followed to determine the treatment costs and indirect losses associated with treatment for CKF, since these could have been avoided if the disease had been prevented in the original population cohort. Each year a certain number of persons are selected from those with chronic kidney failure and are either put on dialysis therapy or given a kidney transplant. Thereafter, dialysis patients will either remain alive on dialysis, be given a transplant, or die; and patients who are alive on dialysis will be either fully or partially rehabilitated or totally inactive. The probabilities of full and partial rehabilitation, inactivity, death, and receiving a transplant are assumed to depend on the patient's clinical status in the preceding

period.[13, 14] Table 4 presents data on the flow of patients from the original population cohort, showing the number selected each year to receive treatment, the total on dialysis, and the numbers fully rehabilitated, dying, and given transplants. Table 5 shows the direct and indirect costs associated with dialysis treatment, based on the above assumptions, and discounted at 8 percent. The total annual direct costs of dialysis are a function of the number of persons being maintained on home dialysis (HD) and the cost per patient per year. The column entitled "rehabilitation losses" would include an estimate of the losses associated with incomplete rehabilitation. The present value of the direct and indirect losses represent an approximation of the "costs" associated with dialysis therapy which could have been avoided with a disease prevention program for the original population cohort.

The direct and indirect costs associated with kidney transplants must also be determined. Since survival rates depend on whether the graft is from a related living donor, unrelated living donor, or cadaver,

transplant recipients are initially classified according to the source of their graft and then followed to determine the subsequent course of events. During their first year with a transplant, recipients will either remain alive with the transplant, die, or be given dialysis therapy after transplant failure. During the second year, recipients of transplants are classified into one of the following groups: 1) alive with the same transplant; 2) alive with a second transplant; 3) alive, but due to transplant failure, given dialysis therapy; or 4) dead due to transplant failure. Patients transferred back to dialysis must also be followed. To simplify this illustration, it is assumed that patients whose transplants fail simply die rather than receive another transplant or dialysis therapy. The mortality rate is assumed to be 50 percent per year; each transplant is assumed to cost $1,000; each death "costs" $1,000; and costs are discounted using an 8 percent discount rate. The total costs associated with kidney transplantation, representing the benefits if the disease process were prevented in the original population cohort, are shown in Table 6.

Table 6. Present values of costs and benefits of a hypothetical disease control program for a single population cohort

	Total
Stage 1 (UTI)	$ 4,555,536
Stage 2 (KI)	10,231,673
Stage 3 (CKD)	18,437,808
Stage 4 (CKF)	3,961,684
Dialysis	16,035,607
Transplantation	16,662,042
Program benefits	$69,884,350
Program costs	$26,432,480

Table 6 totals the indirect losses expected to be incurred in each stage of the disease process and the indirect losses and direct costs of treatment for CKF to arrive at the present in Table 1. Obviously the costs and benefits of the program depend on the particular assumptions that have been made; but, based on this illustrative comparison of costs and benefits, the program would be worthwhile.

Table 5. Present value of the direct and indirect losses associated with dialysis treatment for CKF (stage 4)

Year	Total costs of HD[a] (in 000's)	Mortality losses, HD[b] (in 000's)	Rehabilitation losses[c]	Total losses[d] (in 000's)	Present value total dialysis losses[e]
4	$2,144	$429	....	$2,573	$2,042,447
5	3,720	742	....	4,462	3,279,570
6	3,959	792	....	4,751	3,233,530
7	3 402	680	....	4,082	2,572,478
8	2,569	521	....	3,090	1,803,015
9	1,862	372	....	2,234	1,207,030
10	1,272	254	....	1,526	763,305
11	842	168	....	1,010	467,832
12	545	109	....	654	280,501
13	347	69	....	416	165,194
14	219	44	....	263	96,705
15	137	27	....	164	55,842
16	84	17	....	101	31,835
17	51	10	....	61	17,806
18	31	6	....	37	10,001
19	18	4	....	22	5,504
20	11	2	....	13	3,012
Total benefits if HD were avoided					$16,035,607

[a]Total on HD (Table 4, column 3) × $1,000.
[b]HD mortality (Table 4, column 5) × $1,000.
[c]In this illustration, all dialysis patients are assumed to be fully rehabilitated.
[d]Column 2 + column 3.
[e]Column 5 discounted at 8 percent to present value.

Conclusions

The preceding section illustrated the application of various models for estimating the costs and benefits of infectious kidney disease prevention programs. In this section, the implications as well as limitations of the models will be discussed.

The most important limitation of the preceding analysis, and of the cost-benefit technique per se, is the assumption that what consumers should be willing to pay for a service (because of its expected benefits) represents its "value." In this study, the benefits are assumed to be based on the morbidity, mortality, and treatment costs that would have been necessary had the prevention program not been administered. As was stressed earlier, difficult problems arise not only with respect to the criterion itself (i.e., the use of attributed "willingness to pay" as a proxy for a service's value), but also in determining the specific dollar amount that consumers would be willing to offer for the provision of a certain service. There will, after all, be very little information on the probabilities of a *particular* person going on to the next stage of the disease (or becoming ill) even if he is aware of its presence. Further, the choice of treatment alternatives is limited to what may be prescribed. Therefore, a model must substitute assumption for information on cost parameters as well as value.

The model could be extended to determine the costs and benefits of preventing infectious kidney disease in successive cohorts over an extended time span. For example, it might be proposed that all females be screened for "kidney infections" on their fifth birthday, and thereafter as necessitated by the initial findings. The annual costs of such a program would be based on the number of persons screened in each of the cohorts that have entered and are being followed as of that year. The costs and benefits that are estimated for a single entering cohort could not, however, be merely multiplied by the number of entering cohorts to determine the aggregate costs and benefits because the co-horts would be entering the program in different time periods.[15]

As a means of by-passing the important problems associated with the estimation of benefits and costs, the model has treated many of the relevant parameters as variables rather than as certain specified values. While space limitations preclude further illustration, different dollar estimates could be assumed for each episode of morbidity and mortality, alternative discount rates could be utilized, different dollar "values" could be used to estimate the costs associated with the partial rehabilitation of dialysis patients, and different probabilities could be associated with stages of the disease. For example, if it is thought that a certain society "prefers" to direct the bulk of its medical care resources to caring for the aged, weights that appropriately reflect such preferences could be used in estimating a medical program's benefits for different age groups. Thus social preferences could be reflected in the assessment of candidate programs for government support. Or, if each bed-day of morbidity is thought to be "worth" $100, the indirect losses associated with morbidity could be estimated using $100 as the value that consumers would have placed on preventing a bed-day of morbidity from occurring. Better clinical and economic data could make the assumptions more realistic, and uniform application to different medical programs of comparable data would permit comparison among programs.

Applicability to Other Disease Control Programs

The specific models that have been presented pertain to infectious kidney disease. With simple modifications these models could be used to analyze the effectiveness of other kidney disease control programs as well. More important, however, the basic analysis—not necessarily "cost-benefit," but simply the method of viewing a disease as a process which begins at some point in time and "progresses" to more advanced stages—can be applied to the analysis of medical programs for any disease

if the disease can be thought of in analogous terms. For example, concern has been voiced recently about the procedure of routinely vaccinating children against smallpox in view of the frequency of the complications (including death) associated with the administration of the smallpox vaccine.[16] One way of analyzing whether routine smallpox vaccinations are worthwhile would be to utilize a cost-benefit framework and to weigh the expected costs of routine vaccination against the expected benefits. The "costs" would include: 1) the cost of administering the vaccination, which would depend on the size of the population cohort and the cost per vaccination; 2) the effectiveness of the vaccination in preventing smallpox from occurring; and 3) the estimated total indirect losses due to the morbidity and mortality that result from the vaccination.[17] Various estimates of morbidity, mortality, discount rates, and other key variables could be postulated to determine how the costs of smallpox control programs would be affected.

The "benefits" of a smallpox vaccination program would be the decrease in morbidity, mortality, and treatment costs that would be expected to result from the program.[18] Assuming that vaccinations permanently halt the smallpox disease process, individuals who are given the vaccination could be followed through the natural history of the disease in order to determine the number of persons who would have been sick or died if the vaccination program had not been administered. If the expected benefits of the smallpox vaccination program exceed its costs, the program would—using the cost-benefit criterion— be judged worthwhile. If not, the recommendation would be to discontinue the routine vaccination of children against smallpox.

Allocation of Resources

To conclude that a medical program is worthwhile does not necessarily mean, however, that it should be undertaken. For one thing, the cost-benefit basis for evaluating the effectiveness of alternate medical programs is only one of many criteria that are used by decision-makers in choosing between various policy proposals. Even if a program were worthwhile by the cost-benefit criterion, this does not necessarily lead to the conclusion that the program should be adopted. First, "health" is only one of many competitors for scarce resources. Second, "disease control" is only one method for utilizing funds that have been allotted for purposes of "health." Funds might also be used for research to find new methods for treating chronic renal failure, additional ways to detect urinary tract infections, or more effective treatment for UTI.

Finally, if the "disease control" budget is to be effectively allocated among various diseases, the medical programs for these diseases must be evaluated in terms of their *relative* effectiveness in reducing the morbidity, mortality, and treatment costs associated with each of the diseases. This is most simply illustrated in a two-disease case. For example, assume 1) that smallpox and infectious kidney diseases are the only diseases that exist; 2) that programs to prevent each would be worthwhile according to the cost-benefit criterion; and 3) that resource limitations require a choice between the two programs. The choice as to the appropriate expenditure levels for each program should depend on a comparison of their relative effectiveness in reducing the direct and indirect losses that result from the advanced stages of the two diseases.

It is interesting that the Federal government—as well as several state governments—are providing funds for establishing artificial kidney centers to treat individuals with chronic kidney failure. In terms of the framework discussed above, this implies, first, that they put a higher priority on reducing the morbidity and mortality resulting from kidney disease than for certain other diseases; and, second, that the "kidney disease budget" is more effectively used to prevent the morbidity and mortality caused by CKF than to prevent the morbidity and mortality

caused by other stages of the kidney disease process (and thereby to avoid CKF). There remains the question of whether the present budgetary allotment is the most effective way to distribute the kidney disease budget among the various stages of the disease. An analysis of this question would include a comparison of the marginal costs and benefits associated with the expenditure of funds in each of the stages. Maximum benefits will occur when such costs and benefits are equated at the margin. Since the benefits are reflections of the reduction of the morbidity, mortality, and treatment costs caused by kidney disease, the budget should be distributed among the stages of the disease in a way that will maximize the total benefits expected from the overall expenditure.

If the problem were reduced to that of determining the most effective allocation of the kidney disease budget between the "prevention" of the disease, on the one hand, and its "treatment," on the other, the marginal costs and benefits associated with expenditures for "preventing" the disease in a certain cohort would have to be compared with the marginal costs and benefits associated with "treating" the disease in that cohort. In this study a model was developed and applied to estimate the costs and benefits of "prevention" pro-grams. Using the same framework, the marginal costs and benefits of various "treatment" programs could also be determined if treatment for chronic renal failure is viewed as a means by which life is prolonged in certain individuals. The costs would be comprised of the expenditures for dialysis and transplantation facilities, and the benefits would be the reductions in morbidity and mortality expected to result from the provision of such facilities. Integrating such data with that in this study would give an indication of how the kidney disease budget should be allocated if total benefits are to be maximized.

These elements involved in achieving maximum efficiency and approaching optimal use of certain budget are well established in economic literature. They have been explored in recent discussions of planning-programming-budgeting systems (PPBS), for example.[19] It is time for the integration of such economic analysis with the knowledge of disease management and control. Application of models that relate them can lead to informed choices for government's health agenda, choices that give proper weight to urgent needs, such as treatment of CKF, and that give proper (discounted) weight to the values of disease prevention.

References and Notes

1 For example, the present value of expected lifetime earnings is frequently used as a proxy for an individual's "value" to society. This procedure tends to weight programs in favor of wealthy, young, able-bodied Caucasian males.

2 See Chapter 2, pages 33-75, of the author's dissertation, *An Economic Analysis of Disease Control Programs,* unpublished, University of Virginia, 1970.

3 Treatment-caused complications, such as drug reactions, will be ignored in cost estimates since they occur infrequently, and when they do are easily controlled by either reducing the dosage or by changing drugs.

4 There are secondary beneficiaries as well. Preventive programs may lead to the discovery of other previously undetected diseases and may also prevent certain other kidney-disease-caused disorders from occurring.

5 It should be emphasized that it is assumed here that the entire population is screened only once and only those found to have UTI's initially will be rescreened yearly thereafter. This is for purposes of simplification only. Those who were initially negative might also be rescreened over a certain time span, or a new target population might be screened each year. If so, the costs as well as the benefits would differ, but the logical framework of these models would still apply.

6 Based on the following: 1) until the third and fourth stages, infectious kidney disease is asymptomatic and will, therefore, not be detected until the kidneys have suffered permanent and irreversible damage, and 2) as the disease worsens, medical treatment becomes progressively less effective in eliminating the infection and halting damage to the kidneys (see footnote 2).

7 Persons who remain well are still in the UTI stage of the disease process but are not sick in that particular time period; persons who are "spon-

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