Cost-Effectiveness of Screening and Early Treatment of Nephropathy in Patients With Insulin-Dependent Diabetes Mellitus

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ABSTRACT

Studies have demonstrated that "antihypertensive" treatment with angiotensin-converting enzyme inhibitors (ACEI) may retard the progress of nephropathy in patients with insulin-dependent diabetes mellitus. To obtain an indication of the potential effect of ACEI treatment and as a guide to future research, the effects of screening and early ACEI treatment programs were estimated using cost-effectiveness models. The preliminary analysis suggests that the early treatment of insulin-dependent diabetes mellitus patients with ACEI is likely to be a very cost-effective use of health care resources. The cost-effectiveness ratio for screening and treatment at the stage of microalbuminuria ($7,900 to $16,500 per year of life saved) compares favorably with those of other medical life-saving interventions. Less-aggressive programs (screening followed by treatment at the stage of proteinuria) would improve life expectancy to a lesser extent but could save net health care costs as well as years of life. Although more exact and comprehensive cost-effectiveness analysis must await clinical trials, these illustrative results demonstrate the range of cost-effectiveness that can be expected from these programs and identify data needed for more decisive policy conclusions.

Key Words: Cost-effectiveness, nephropathy, insulin-dependent diabetes mellitus, antihypertensive treatment

ASSUMPTIONS AND METHODS

Analytic Model

We use a semi-Markov model to simulate the progression of renal complications in a cohort of newly diagnosed IDDM patients. The model consists of mu-
Onset of IDDM

Onset of Microalbuminuria

Onset of Signif. Microalbuminuria

Onset of Overt Proteinuria

Onset of Renal Failure

DEATH

Figure 1. Model of stages of nephropathy in IDDM. The model illustrates the stages of nephropathy, beginning at the time of the diagnosis of IDDM. Rectangles represent states of health; arrows represent the possible transitions between health states. Patients may progress from an initial stage with no nephropathy to microalbuminuria, significant (signif.) microalbuminuria, proteinuria, and renal failure. Those with renal failure ultimately die of renal failure or CAD. Patients in all other states may die of CAD or another cause unrelated to diabetes. Arrows from a rectangle that circle back upon the same rectangle indicate that a patient can remain in that state for more than one follow-up interval. The expected course of nephropathy is simulated in a Markov model using the number of cohort members in any given state and the probabilities of transition to each other state (Table 2).
### TABLE 1. Standard and new programs of antihypertensive treatment in IDDM

<table>
<thead>
<tr>
<th>Program</th>
<th>Screening Method</th>
<th>Antihypertensive Treatment Initiated at Stage</th>
<th>Antihypertensive Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Therapy (No New Program)</td>
<td>None</td>
<td>BP $\geq 140/90$</td>
<td>Hydrochlorothiazide/Lasix</td>
</tr>
<tr>
<td>Program 1</td>
<td>Albustix</td>
<td>Proteinuria ($\geq 300$ $\mu$g/min)</td>
<td>Enalapril</td>
</tr>
<tr>
<td>Program 2</td>
<td>Urinalysis</td>
<td>Significant microalbuminuria ($\geq 100$ $\mu$g/min)</td>
<td>Enalapril</td>
</tr>
<tr>
<td>Program 3</td>
<td>Urinalysis</td>
<td>Microalbuminuria ($\geq 20$ $\mu$g/min)</td>
<td>Enalapril</td>
</tr>
</tbody>
</table>

### TABLE 2. Natural history of nephropathy in a cohort of newly diagnosed juvenile-onset IDDM Patients under standard program of antihypertensive treatment

<table>
<thead>
<tr>
<th>Transition From</th>
<th>Transition To</th>
<th>%</th>
<th>Median Time (yr)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDDM Onset</td>
<td>Microalbuminuria&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.60</td>
<td>12</td>
<td>3–25</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>Significant Microalbuminuria&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.75</td>
<td>4</td>
<td>2–8</td>
</tr>
<tr>
<td>Significant Microalbuminuria</td>
<td>Proteinuria&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.75</td>
<td>4</td>
<td>2–8</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>Renal Failure</td>
<td>0.50</td>
<td>10</td>
<td>3–18</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>CAD</td>
<td>0.66</td>
<td>10</td>
<td>5–20</td>
</tr>
</tbody>
</table>

<sup>a</sup> Mortality from causes other than CAD and renal failure is assumed to be the same as for the general population (age adjusted). Including this mortality in the simulations, 32% of the cohort eventually develop proteinuria under standard treatment. Of these, 50% die of CAD, 30% die of renal failure, and 20% die of other causes.

<sup>b</sup> Microalbuminuria, $\geq 20$ $\mu$g/min.

<sup>c</sup> Significant microalbuminuria, $\geq 100$ $\mu$g/min.

<sup>d</sup> Proteinuria, $\geq 300$ $\mu$g/min.

artery disease (CAD) among diabetics and life tables to estimate mortality from other causes (16,17).

**New Programs.** "New" in this analysis refers to alternative strategies for implementing early treatment with ACEI. The main objective of each is to detect diabetic nephropathy (regardless of blood pressure level) and to treat with ACEI to delay the onset of renal failure. Three such programs are considered (Programs 1, 2, and 3) in increasing order of aggressiveness (Table 1).

Patients are screened twice a year in each new program. In Program 3, the most aggressive plan, patients identified as having microalbuminuria ($\geq 20$ $\mu$g of albumin/1 mg of urine creatinine in two out of three consecutive urinanalyses) are treated with ACEI. Program 2 differs in that the treatment with ACEI is begun only if patients have significant microalbuminuria ($\geq 100$ $\mu$g of albumin/1 mg of urine creatinine in two out of three consecutive urinanalyses). In Program 1, screened patients are treated only if they have overt proteinuria, which is recognized if two out of three consecutive Albustix tests are positive. Although it is the least aggressive of the new programs, Program 1 is more aggressive than standard treatment because it treats all proteinuric patients with ACEI regardless of their blood pressures.

To control the costs of the new programs, we assume that screening tests will be done during regular clinic visits and that the albumin/creatinine ratio in a random urine specimen is used in Programs 2 and 3 instead of a determination of the albumin excretion rate in a timed urine collection. These modifications avoid requirements for extra time on the part of patients and providers, which would generate significant extra costs.

Because the effectiveness of ACEI in retarding the progression of nephropathy has not been quantified precisely, we estimate their effect on the basis of data from available literature (2–6). We use two estimates of effectiveness, conservative and optimistic. Both assume that ACEI treatment delays—but does not arrest—the progression of nephropathy for those at risk. The first estimate is intended to represent a likely lower bound of ACEI effectiveness. We assume that treatment would postpone the median time for progression to each stage of nephropathy by 50% but would leave the range of time for progression unchanged. Specifically, we assume that the median...
time for progression from microalbuminuria to significant microalbuminuria would be increased by 2 yr., for progression from significant microalbuminuria to proteinuria would be increased by 2 yr., and for progression from proteinuria to renal failure would be increased by 5 yr (Table 3).

The second estimates represent a more optimistic assessment of ACEI effectiveness. Here, we assume that the median time for progression to each stage of nephropathy is increased by 75% relative to standard treatment. In addition, we assume that the range of time for progression is increased by 50% (Table 3).

In both sets of estimates, we assume conservatively that ACEI have no effect on the progression from proteinuria to CAD. However, some delay in CAD development occurs secondarily to the postponement of overt proteinuria.

Cost-Effectiveness Analysis

We compare the progression of nephropathy and medical care costs incurred with the new programs—summarized as life expectancy and lifetime costs—with the same outcomes under standard treatment. Cost-effectiveness is the ratio of the net increase in health-care costs to the net improvement in health outcome (life expectancy). The lower the value of this ratio, the higher the priority of the program. A cost-effectiveness ratio is calculated for each of the new programs relative to the next-less-effective program.

The index of cost-effectiveness may be summarized as:

\[
\frac{\Delta C}{\Delta E} = \frac{\Delta (\text{SCR} + \text{RX} + \text{MORB})}{\Delta Y}
\]

Net Health Care Costs of the New Programs. Net program costs (\(\Delta C\)) include all additional direct medical and health costs related to the new programs. These include the incremental cost of screening (\(\Delta C_{\text{SCR}}\)), which as noted earlier, does not include costs of additional provider visits. In Programs 2 and 3, patients are screened for microalbuminuria at an estimated $50 per person per year (two tests) (Table 4). In Program 1, proteinuria can be identified on the basis of 82 Albusxtx testing every 6 months.

For patients identified during screening, there are new costs for early antihypertensive treatment (\(\Delta C_{\text{RX}}\)). Patients are prescribed ACEI (enalapril, 10 mg/day). Although the drug prescription is the same in the three prototype programs, total treatment costs vary because progressively more patients are treated in Programs 1, 2, and 3. Some patients who do not need treatment—that is, who would not have progressed to proteinuria even without treatment—are also prescribed antihypertensive drugs in Programs 2 and 3. Costs for these cases are included as induced program costs.

\(\Delta C_{\text{MORB}}\) represents savings in health care costs due to the reductions in morbidity accomplished by the new programs. We consider reductions in renal failure and indirect reductions in CAD for the new programs relative to standard treatment. An avoided or postponed case of renal failure is estimated to save $36,433 ($1991) annually. This is the 1987 per capita Medicare cost for patients in the ESRD program (18) adjusted to 1991 dollars using the medical care consumer price index. This figure reflects costs of both dialysis and transplant.

The cost of CAD is based on estimates of the discounted lifetime direct costs (treatment, hospitalization, physician services) associated with cardiac events (19). The estimates are weighted to reflect the relative frequency of various clinical manifestations in a general population (17), converted to 1991 dol-

<table>
<thead>
<tr>
<th>TRANSITION</th>
<th>STANDARD PROGRAM</th>
<th>CONSERVATIVE ESTIMATE</th>
<th>OPTIMISTIC ESTIMATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDDM Onset</td>
<td>Microalbuminuria</td>
<td>12 (3-25)</td>
<td>12 (3-25)</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>Significant Microalbuminuria</td>
<td>4 (2-8)</td>
<td>6 (2-8)</td>
</tr>
<tr>
<td>Significant Microalbuminuria</td>
<td>Proteinuria</td>
<td>4 (2-8)</td>
<td>6 (2-8)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>Renal Failure</td>
<td>10 (3-18)</td>
<td>15 (3-18)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>CADb</td>
<td>10 (5-20)</td>
<td>10 (5-20)</td>
</tr>
</tbody>
</table>

a Microalbuminuria, \(\geq 20 \mu g/min\).

b Transition not affected by new programs.

c Significant microalbuminuria, \(\geq 100 \mu g/min\).

d Proteinuria, \(\geq 300 \mu g/min\).
TABLE 4. Medical care cost assumptions

<table>
<thead>
<tr>
<th>Type</th>
<th>Unit Cost</th>
<th>Cost* ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albustix</td>
<td>Per test</td>
<td>2</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>Per test</td>
<td>25</td>
</tr>
<tr>
<td>Antihypertensive Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enalapril</td>
<td>Annual</td>
<td>259</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Annual</td>
<td>22</td>
</tr>
<tr>
<td>Lasix</td>
<td>Annual</td>
<td>13</td>
</tr>
<tr>
<td>Medical Care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESRD</td>
<td>Annual</td>
<td>36,433</td>
</tr>
<tr>
<td>CAD</td>
<td>Lifetime</td>
<td>25,116</td>
</tr>
</tbody>
</table>

* Costs in 1991 dollars.
* Costs for Vasotec (Merck, Sharp and Dohme, West Point, PA), 10 mg/day. Source: Boston retail pharmacies.

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Journal of the American Society of Nephrology

standard treatment are estimated separately by modeling the course of diabetes from diagnosis until death in the hypothetical cohort of IDDM patients. We then calculate the cost-effectiveness of the various new programs (the incremental net cost of the program per additional year of life saved) by comparing overall costs and life expectancy under each scenario.

All costs are discounted at 5% per annum. Discounted costs represent the amount of current dollars that, if invested at the 5% rate, would be needed to cover the costs of "antihypertensive treatment" for a 15-yr-old newly diagnosed IDDM patient over the course of his/her lifetime. Life years are reported without discounting, but cost-effectiveness ratios incorporate discounting of costs and life years. The effect of discounting is to give less weight to costs and health consequences that occur in the future, relative to present costs (9–11).

The final step is to conduct sensitivity analyses, changing assumptions used in the model to test their effects on the conclusions.

RESULTS

Standard Treatment

Under standard antihypertensive treatment, our model gives a cohort of 15-yr-old patients with IDDM a median life expectancy of 44.9 yr, i.e., survival to age 60 on average (Table 5). The lifetime costs of medical care for antihypertensive treatment (including treatment of renal complications and CAD) is $4,700 (discounted) per person. This is an average; those developing renal failure incur very high costs, but these are greatly diluted by averaging them with the much lower costs of the rest of the cohort.

New Programs

Under our most conservative assumptions regarding ACEI effectiveness, life expectancy improves marginally with the new programs (Table 5). From 2 to 4% of renal failure cases are avoided, depending on the aggressiveness of the program. For Program 1, the least aggressive intervention, life expectancy increases to 45.1 yr, a slight improvement over standard treatment. Costs are $4,600 (discounted) per person—actually lower than costs with no program. The relatively modest expense of Program 1 is offset by decreases in medical care costs for renal failure. Programs 2 and 3, which involve screening for earlier stages of nephropathy (microalbuminuria) and earlier treatment with ACEI, would increase costs to $5,500 and $5,900 per person, respectively. Life expectancy increases to 45.3 yr in Program 2 and 45.5 yr in Program 3.

With more optimistic assumptions regarding ACEI
TABLE 5. Incremental cost-effectiveness analysis: conservative assumptions of ACEI effectiveness

<table>
<thead>
<tr>
<th>Programs</th>
<th>Antihypertensive Treatment Initiated at Stage</th>
<th>Program Costs ($</th>
<th>Program LE (yr)</th>
<th>Cost-Effectiveness Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Discounted</td>
<td>Not Discounted</td>
<td>Discounted</td>
</tr>
<tr>
<td>Standard</td>
<td>BP ≥ 140/90</td>
<td>$4,706</td>
<td>$24,934</td>
<td>17.4</td>
</tr>
<tr>
<td>New</td>
<td>Proteinuria</td>
<td>$4,643</td>
<td>$25,794</td>
<td>17.4</td>
</tr>
<tr>
<td></td>
<td>Significant Microalbuminuria</td>
<td>$5,542</td>
<td>$28,582</td>
<td>17.5</td>
</tr>
<tr>
<td></td>
<td>Microalbuminuria</td>
<td>$6,927</td>
<td>$30,056</td>
<td>17.5</td>
</tr>
</tbody>
</table>

° Discounted at 5% per year.

Incremental cost-effectiveness ratio: ΔC (discounted)/ΔLE (discounted). Ratio may differ from ΔC/ΔLE in table because of rounding. See Text for abbreviations.

A "no program" option is not recommended. Costs are greater than those under Program 1, but life expectancy is lower.

Program 2 compared with Program 1 has higher incremental cost per incremental life year saved than the incremental cost effectiveness of Program 3 compared with Program 2. This result indicates that Program 3 could achieve the same benefits as Program 2 at a lower cost. Program 2 is said to be dominated—it is not a cost-effective option. (See reference 23 for further discussion.) Program 3 is therefore compared with Program 1 in the table.

effectiveness, the early intervention programs would prevent from 4 to 13% of the cases of renal failure. Under these assumptions, costs for all programs are lower and life expectancy is higher (Table 6). Under Program 1, patients would live an expected 45.4 yr, half a year longer than with no program. Expected medical costs would be $4,400 (discounted). Under Programs 2 and 3, life expectancy would improve to 45.8 and 46.1 yr, respectively, whereas costs would increase to $5,200 and $5,500.

Cost-Effectiveness

Incremental cost-effectiveness analysis compares each program with the next-less-expensive option to determine the additional investment required for increased benefit. Ordinarily, the least expensive new program would be compared with current standard treatment. However, because Program 1 results in lower total costs than standard treatment and also improves life expectancy, it is superior to a "no program" option and is substituted as the baseline program (Tables 5 and 6). Our standard for comparison is therefore a program that improves life expectancy an estimated 2 to 6 months over current practice.

Relative to Program 1, Program 2 offers additional life savings at an additional cost; however, it is not a cost-effective option. The substantial increase in screening and treatment costs is not offset by a sufficient increase in life expectancy. Program 3, which intervenes at an earlier stage than Program 2, accomplishes the benefits of Program 2 at a lower cost.

Because Program 2 is not a recommended option, Program 3 is the only alternative to Program 1. This early intervention program saves an additional 5 to 8 months of life expectancy as compared with the less-aggressive Program 1. Its incremental cost-effectiveness ratio is $87,900 to $16,500 (discounted) per additional year of life saved (Tables 5 and 6).

Sensitivity Analysis

In addition to ACEI treatment effectiveness, the cost-effectiveness of the programs we consider is affected by the costs of screening and treatment and the avoided costs of ESRD treatment. We conduct sensitivity analyses on alternative estimates of these costs to test the robustness of our results.

The annual costs for the detection of microalbuminuria have a direct effect on the cost-effectiveness of screening programs. If screening costs more than our estimated $50 annually, the cost-effectiveness ratio of Program 3 will increase. For example, if the test costs $100 annually, the additional cost per year of life saved in Program 3 increases from $16,500 to $24,600 under our conservative assumptions of ACEI effectiveness. If screening costs are significantly lower than we expect (e.g., $20 annually), then the relative desirability of the programs changes. At this point, Program 2 becomes a viable program option. The cost of screening all patients for $50 per year is not justified if only those with significant microalbuminuria are treated; however, if screening costs could be substantially reduced, then this program would be cost-effective.

Screening and treatment costs for all programs are offset by reductions in the renal complications of IDDM, the most expensive of which is ESRD treat-
Table 6. Incremental cost-effectiveness analysis: optimistic assumptions of ACEI effectiveness

<table>
<thead>
<tr>
<th>Programs</th>
<th>Antihypertensive Treatment Initiated at Stage</th>
<th>Program Costs ($)</th>
<th>Program LE (yr)</th>
<th>Cost-Effectiveness Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Discounted Not</td>
<td>Discounted Not</td>
<td>(\Delta C) (\Delta LE)</td>
</tr>
<tr>
<td>Standard BP ≥ 140/90</td>
<td></td>
<td>4,706 24,934</td>
<td>17.4</td>
<td>44.9</td>
</tr>
<tr>
<td>New Proteinuria</td>
<td></td>
<td>4,401 25,537</td>
<td>17.5</td>
<td>45.4</td>
</tr>
<tr>
<td>New Significant Microalbuminuria</td>
<td></td>
<td>5,179 28,119</td>
<td>17.5</td>
<td>45.8</td>
</tr>
<tr>
<td>New Microalbuminuria</td>
<td></td>
<td>5,465 29,340</td>
<td>17.6</td>
<td>46.1</td>
</tr>
</tbody>
</table>

\(a\) Discounted at 5% per year.

\(b\) Incremental cost-effectiveness ratio: \(\Delta C\) (discounted)/\(\Delta LE\) (discounted). Ratio may differ from \(\Delta C/\Delta LE\) in table because of rounding. See Text for abbreviations.

Program 3, the earliest intervention program, has the highest initial costs because of a more expensive screening protocol and more widespread treatment. However, Program 3 avoids at least twice as many cases of renal failure as Program 1, thus offsetting program expenses to some degree as well as increasing life expectancy. Program 3 also reduces early CAD death among proteinuric patients because of its effects during early nephropathy. This program offers substantial benefit and would be the preferred choice, resources permitting. Program 2, for which costs and benefits fall between those of Programs 1 and 3, does not improve patient outcome sufficiently relative to Program 3 to justify its expenses. It would become a viable option only if screening costs could be reduced.

Discontinuing. ESRD costs are subject to change, because, for example, of the evolution of transplant technology and the changing locus of dialysis treatment.

We examined a plausible range of annual ESRD costs, $10,000 to $60,000. An increase in ESRD costs will increase the savings from preventing or delaying renal failure, improving cost-effectiveness. A decrease in ESRD costs has the opposite effect making the new programs less cost-effective. If ESRD costs are below $30,000 per year, Program 1 no longer saves money relative to standard treatment under our conservative assumptions of ACEI effectiveness, although its cost-effectiveness ratio would be very low. Otherwise, annual ESRD costs in this range do not substantially change our results.

Discussion

Although preliminary, our analysis suggests that the early treatment of IDDM patients with ACEI is likely to be a very cost-effective use of health care resources. The cost-effectiveness ratio for our Program 3 ($7,900 to $16,500 per year of life saved) compares favorably with the cost-effectiveness of treating hypertension in the general population (20). Screening and treatment programs offer life savings for IDDM patients at a low cost, even under conservative estimates of ACEI effectiveness.

The analysis identifies two particularly promising strategies for ACEI treatment. The least expensive option intervenes among patients with overt proteinuria, our Program 1. Direct costs are lowest in Program 1 because of the less-expensive Albustix screening, the limited number of patients treated with ACEI, and the shorter duration of treatment. Although life savings are limited with this program, benefits are achieved at a comparatively low cost.

Program 3, the earliest intervention program, has the highest initial costs because of a more expensive screening protocol and more widespread treatment. However, Program 3 avoids at least twice as many cases of renal failure as Program 1, thus offsetting program expenses to some degree as well as increasing life expectancy. Program 3 also reduces early CAD death among proteinuric patients because of its effects during early nephropathy. This program offers substantial benefit and would be the preferred choice, resources permitting. Program 2, for which costs and benefits fall between those of Programs 1 and 3, does not improve patient outcome sufficiently relative to Program 3 to justify its expenses. It would become a viable option only if screening costs could be reduced.

The results of our analysis hinge on the effectiveness of ACEI in delaying or arresting the course of nephropathy in IDDM. Clinical trials are needed to confirm the effects demonstrated in preliminary research. Our analysis indicates that priority should be given to trials of ACEI in two distinct target populations: patients with established proteinuria and patients with early microalbuminuria. It is possible that greater effectiveness would result from initiating treatment even earlier, on the basis of markers of susceptibility. One-time screening for genetic susceptibility might also be less costly than repeated screening for microalbuminuria.

In addition to these trials, knowledge of the effectiveness of ACEI in postponing CAD is critical to the development of treatment strategies. It is well documented that patients with IDDM and proteinuria have a very high risk of developing and dying from CAD (16,21). In our analysis, we assumed that ACEI have no direct effect on the progression of coronary disease. High CAD mortality among patients who
avoid renal failure places an upper limit on the life-saving potential of any program that solely addresses renal failure. Treatment with ACEI may actually have an ameliorating effect on atherosclerosis, independent of the effect of treatment on the progression of proteinuria. Such an effect would greatly improve the effectiveness and cost-effectiveness of Programs 1 and 3. Alternatively, antihypertensive treatment programs may need to include a component directed toward lowering serum lipid levels to have an effect on CAD mortality.

Several additional factors may influence the cost-effectiveness of antihypertensive treatment programs for IDDM patients. In our analysis, we measured the health effectiveness of new programs as the net change in life expectancy, ignoring their effect on the quality of life. Although quantification of these effects is beyond the scope of this analysis, it is obvious that patients would consider extra years without hemodialysis or transplant a significant positive effect. If quality of life were included in our analysis, greater effectiveness would be attributed to the new programs.

Of factors that might negatively affect the cost-effectiveness of ACEI treatment programs, two deserve special consideration. First, lifelong treatment with ACEI will result in some incidence of side effects. Although complications may be infrequent, they will diminish the program effectiveness and require treatment, which generates additional costs. Second, antihypertensive treatment programs will be less effective in practice if they are implemented among patients already at a relatively low risk. It has been shown that patients who are nonattenders to the clinic have a high risk of renal complications (1,22). Effective methods for enrolling these patients in screening programs for microalbuminuria and subsequent therapeutic programs will critically influence the overall program success and should be addressed in clinical trials.

This cost-effectiveness analysis addresses broad questions about the potential of antihypertensive treatment programs in IDDM. Although more exact and comprehensive cost-effectiveness results must await clinical trials, our illustrative results demonstrate the range of cost-effectiveness that can be expected from these programs, indicating that treatment programs that offer even small improvements in the risk of renal complications can be very cost-effective.

ACKNOWLEDGMENT

Supported in part by grant RO1 DK 41526 from the NIH to A.S. Krolevski.

REFERENCES