The Cost Effects of Improved Kidney Transplantation

Jerome Aroesty, Richard A. Rettig
The research described in this report was supported in part by a grant from the National Institutes of Health, in part by an unrestricted grant from the Sandoz Corporation, and in part by The Rand Corporation in accordance with its program of public service.

The Rand Publication Series: The Report is the principal publication documenting and transmitting Rand's major research findings and final research results. The Rand Note reports other outputs of sponsored research for general distribution. Publications of The Rand Corporation do not necessarily reflect the opinions or policies of the sponsors of Rand research.

Published by The Rand Corporation
The Cost Effects of Improved Kidney Transplantation

Jerome Aroesty, Richard A. Rettig

February 1984
PREFACE

Transplant centers report major advances in preventing the rejection of transplanted organs. Should these advances be realizable in wider practice, then organ transplantation's role will be expanded in the treatment of patients with end-stage disease of the kidney, heart, lung, liver, pancreas, and bone marrow. This expansion poses a number of questions, some of them significant in policy terms. Within the federal government, the End-Stage Renal Disease program (ESRD) of Medicare has a special interest in improved transplantation because it finances renal replacement therapy for Americans with chronic kidney failure. In 1982 Medicare expended $1.8 billion for ESRD health care costs, including 5000 kidney transplants and dialysis treatment for 60,000 beneficiaries.

Many observers have speculated on the extent to which improved transplant outcomes and an increased rate of kidney transplantation might yield cost savings to Medicare while also improving the quality of life for many patients. This report uses an analytic model, supported by current and historical data, to quantify these speculations realistically and to bound the potential cost effects to the federal government of improved transplantation.

Two earlier Rand publications by Richard A. Rettig, assisted by E. Marks, describe the background and implementation of the ESRD program: Implementing the End-Stage Renal Disease Program of Medicare, R-2505-HCFA/HEW, September 1980, and The Federal Government and Social Planning for End-Stage Renal Disease, N-1922-NCHSR, February 1983.

The research described in this report was supported by the National Institutes of Health Biomedical Research Support Program, an unrestricted grant from the Sandoz Corporation, and Rand Corporation research funds.
SUMMARY

Recent developments in preventing the rejection of transplanted organs have focused public attention on whole organ transplantation. Liver transplantation in children receives the most publicity, but kidney transplantation also draws substantial interest for several reasons: Annual kidney transplants number in the thousands, not the hundreds or tens; if successful, they effectively substitute for the more cumbersome and more costly treatment of kidney failure by dialysis; and the federal government plays a prominent role in financing both transplantation and dialysis for most Americans with End-Stage Renal Disease (ESRD).

Within the past decade, the survival rate for transplant patients has improved markedly. Until recently, however, survival of the transplanted kidney (graft survival) for cadaver kidney transplants, which account for 70 percent of the total, has hovered around 50 percent at the one-year post-transplant milestone. Although various new techniques have brought about incremental improvements, the most significant improvement in graft survival, at least in early clinical trials, has come through the introduction of Cyclosporine—a new immunosuppressive compound. Many in the transplant community firmly believe that transplantation is on the threshold of a new era of effectiveness.

As policy analysts, we recognize that only clinical trials and additional experience will define the specific efficacy of the new means of preventing rejection. Consequently, this report uses the conditional throughout. If there is an advance in immunosuppression, we ask, then what cost effects will flow from improved transplantation outcomes? We are not predicting any specific cost effects. Rather, we project a range of cost effects under a set of assumptions guided by the early results of clinical trials, as modified by historical data on the outcomes and costs of kidney transplantation. If our assumptions are poorly based, or if the constraints of limited data and analytical models do not serve us well, actual experience will obviously vary from our projections. Despite these limitations, we have sought to bound, realistically, the issue of potential cost effects of improved kidney transplantation.

Total national expenditures for medical care and income maintenance of victims of kidney failure clearly exceed $2 billion annually, and probably fall between $2.5 billion and $3.0 billion. The direct cost to Medicare alone is estimated at $1.8 billion for 1982. Improved kidney transplantation therefore raises the expectation that the overall
cost burden of the Medicare ESRD program can be reduced. The analysis described in this report supports that expectation; it finds that cost savings will come from doing transplantation better and from shifting patients from dialysis to transplantation.

Doing transplantation better will produce two results. First, the costs of successful transplants will decline, primarily because of shorter hospital stays by recipients. (We note, parenthetically, that the financial incentives of Medicare’s new diagnostic-related groups (DRGs) will reinforce this clinical development.)

Second, the frequency and severity of kidney transplant failure will decline, and the costs of treating failure will be reduced. All transplant recipients incur the costs of organ acquisition and the transplant procedure itself. If the body attempts to reject the transplanted kidney, three outcomes can occur: Rejection can be successfully treated and the transplant maintained; rejection can lead to a failure of the transplant and the patient’s return to dialysis; or the patient can die. Even successful rejection treatment exposes the patient to increased risks of morbidity and complication.

The failure modes are expensive: They require additional days of hospitalization; the failed kidney may have to be removed (by a nephrectomy); and intensive anti-rejection protocols may be administered. Further, patients who must return to dialysis may incur costs that exceed those of the average dialysis patient who has not received a transplant. Reducing the frequency and severity of kidney transplant failure, therefore, will reduce both human and monetary costs.

We employed a range of outcomes and costs suggested by recent clinical trials and historical data to quantify the effects of improved transplants. We used a five-year projection interval and three levels of efficacy, “current,” “medium,” and “excellent,” represented by one-year graft survivals (averaged over all transplant recipients) of 61 percent, 74 percent, and 89 percent. We found that the typical recipient transplanted today under current protocols will require dialysis support for 30 percent of the next five years of life; that figure drops to 20 percent if “medium” efficacy is realized, and to 6 percent if efficacy is “excellent.” In terms of five-year savings to the Health Care Financing Administration (HCFA) from adopting improved protocols, this translates into cost savings per transplant recipient (in 1979 dollars) that vary between $8000 and $30,000. Projected savings are sensitive to such factors as outcomes, costs of primary and rejection treatment, and changes in ESRD coverage policy for transplant recipients.

The analysis also suggests that HCFA will save between $30,000 and $66,000 over a five-year period for each suitable dialysis patient who shifts to transplantation, the specific magnitude again depending on several factors.
To translate these individual savings into an ESRD programmatic projection, we performed an idealized analysis for a five-year period, 1982-1987, during which HCFA-financed transplants are assumed to rise abruptly to 8000/year and remain at that level, for a total of 40,000 procedures. This pattern, admittedly unrealistic, was selected to explore the consequences of a hypothetical increase in transplant activity during a period where projections about the ESRD program may be reasonably supported by data and analysis. We compared this situation with a baseline case that extrapolates recent ESRD history and corresponds to 24,400 HCFA-financed procedures over five years. In terms of social cost savings, we found that although 15,600 more transplants are performed during the hypothetical five-year period, "medium" efficacy leads to 1300 additional transplant failures who must return to dialysis, beyond the baseline of 11,600 failures, while "excellent" efficacy reduces failures by 5300 below baseline. In terms of person-years with a functioning graft, "medium" efficacy increases over baseline by 36,000, and "excellent" efficacy by 51,000. Furthermore, there are corresponding declines of 25,000 and 37,000 person-years in maintenance dialysis. At the end of the five-year period, the baseline estimate of 21 percent of ESRD beneficiaries with a functioning graft increases to 32 percent in the "medium" case and 38 percent in the "excellent" case. The improvements in outcome are responsible for cumulative savings to HCFA (in 1979 dollars) of between $300 million and $570 million, depending on the level of efficacy that is achieved. Since 300,000 to 340,000 person-years of dialysis will occur during this interval, the cost savings constitute 5 percent to 10 percent of ESRD expenditures.

Consistent with these procedures is our judgment that a doubling of all kidney transplant procedures (both HCFA and non-HCFA financed) may be feasible, from over 5000 in 1982 to 10,000 in 1987. Such an increase may be limited by the availability of kidneys, though the number of retrieved kidneys has increased steadily each year for the past five years, and improved results may stimulate still more donation and acquisition.

Our analysis, although still preliminary, suggests that cost savings, both human and financial, will be positive but that aggregate cost savings to the government will be modest in the initial five years of the "new era" of transplantation for three reasons:

- Expenditures for transplantation account for only a small portion of the Medicare ESRD program, which is, and will remain, primarily a dialysis treatment program.
• The major costs of transplantation—both successes and failures—occur in the year of the procedure, while cost savings accrue in later years.
• The rate of adoption of new protocols is likely to be more gradual than we have assumed.

Despite these limitations, the results appear encouraging: The potential exists for improved treatment and quality of life for more ESRD patients, accompanied by cost savings to Medicare.
ACKNOWLEDGMENTS

Our research has benefited from discussions with many persons too numerous to name here who are active in the End-Stage Renal Disease system. Specifically, we wish to thank C. Brax, D. Gentile, M. McMullen, S. Kappert, M. Weil, and P. Eggers for sharing their data with us. A special acknowledgment is required for Dr. Henry Krakauer, who facilitated our research by providing us with output from a computer-based model of the ESRD treatment system. Thanks are also due to E. Keeler, A. P. Williams, D. Work, R. Freeman, J. Sadler, and others who critiqued our work at various stages during its progress, and to W. Harriss for his editorial contributions.
## CONTENTS

PREFACE ......................................................... iii

SUMMARY ....................................................... v

ACKNOWLEDGMENTS ............................................. ix

TABLES .......................................................... xi

Section
I. INTRODUCTION .................................................. 1

II. OUTCOMES AND COSTS OF RENAL TRANSPLANTATION .......... 5
    Baseline Outcomes—Patient Survival .......................... 6
    Baseline Outcomes—Graft Survival ............................ 6
    Projected Outcomes—Patient Survival ......................... 7
    Projected Outcomes—Graft Survival ............................ 8
    Current Cost Data ............................................. 9
    The Present Situation ......................................... 16

III. COST SAVINGS OF IMPROVED TRANSPLANTATION .............. 18
    Reducing Costs of Success ................................... 18
    Reducing Costs of Failure ................................... 23
    Projected Five-Year Cost Saving Due to Improved Outcomes 24

IV. COST EFFECTS OF SHIFTING PATIENTS FROM DIALYSIS TO TRANSPLANTATION ............. 28

V. CONCLUDING OBSERVATIONS ................................ 36

BIBLIOGRAPHY .................................................. 39
TABLES

1. Average Medicare Reimbursement Per Person-Year by ESRD Treatment ........................................ 10

2. Medicare Reimbursements Per Person-Year by Transplant Type and outcome, 1979 .......................... 11

3. Average Hospital Charges for Transplant Procedures and Rejection Treatment, 1980 ......................... 14

4. First Year Hospitalization for Transplantation (From Moffitt Hospital, San Francisco) ..................... 20

5. Projected Costs to HCFA of a Patient Transplanted in 1982 .......................................................... 26

I. INTRODUCTION

The Social Security amendments of 1972 established Medicare as the primary financier of treatment for end-stage renal disease (ESRD) in the United States, both by dialysis and transplantation. In 1974, the first full calendar year of the new renal program, Medicare expended $228.5 million for renal-related benefits. In calendar 1982, expenditures reached $1.6 billion for bills posted through June 30, 1983, and estimates for the year were $1.8 billion. A total of 5358 transplants were performed during 1982, and the number of patients receiving dialysis at the end of the year totaled 65,765. (The numbers for both transplant and dialysis patients include Medicare and non-Medicare beneficiaries, though the former dominate.)

If we add, to direct Medicare expenditures, funds from all government and private sources for medical benefits (Medicaid, Veterans Administration, state programs, as well as private insurance and personal income expenditures), and for nonmedical benefits (monthly disability payments), the total national cost for the support of ESRD patients exceeds $2 billion and may be as high as $2.5 to $3.0 billion. Obviously, the cost burden to the country for making these life-saving treatments available on essentially a universal basis is substantial.

That burden may ease in the near future, however. Medical science appears to be on the threshold of important advances in the clinical immunosuppression of transplant recipients that will markedly improve outcomes. “Improved outcomes” in this report means the following: no decrease and perhaps some modest increase in the survival rate of transplant recipients; marked increase in graft survival, i.e., survival of the transplanted kidney, especially among patients receiving cadaver organs; and reduced morbidity of transplant recipients.

For a brief review of the basis for optimism, we cite P. J. Morris, President-elect of the International Transplant Society, who has recently surveyed significant developments in renal transplantation since 1980 [1]. After noting that patient survival and graft survival had continued to improve, and that more elderly patients were being transplanted, Morris listed as further advances “matching for HLA-DR, transplantation in the hypersensitized patient, donor-specific transfusions in living related transplantation, the recognition of lymphoid subpopulations both in the blood and in the transplanted kidney with monoclonal antibodies, and improved immunosuppression where Cyclosporine-A (CsA) is maintaining the considerable promise shown previously.” These developments, although not all at the same level of
scientific maturity, promise to improve future outcomes for subgroups of transplant recipients. But one development—improved immunosuppression—has the potential to improve the status of renal transplantation for broad classes of recipients soon enough to enter into policy analyses of the ESRD program during the 1980s.

Although many in the transplant community endorse this view, a residual scepticism remains among some transplant surgeons and transplant oriented nephrologists who have adopted a wait-and-see attitude. This scepticism is strongest among nephrologists, including a number who are highly informed about transplantation and who recall other "advances" which have borne less fruit than promised.

If major improvements are indeed realized, many patients, physicians, and policymakers will wish to know what the cost effects will be. This study addresses that issue. Our analysis suggests that improved transplantation will reduce the total costs of the Medicare ESRD program by reducing the costs of transplant successes and failures, and by shifting patients from dialysis to transplantation. For two reasons, however, it appears that the projected cost savings will be relatively modest for some time to come:

- Because the ESRD program is primarily a dialysis program\(^1\) and will remain so even if the number of kidney transplants doubles within five years, the cost-effects of improved transplantation will occur within a small but perhaps growing part of a much larger dialysis program. It is difficult to forecast the future rate of transplants; however, we estimate that 8,000 to 10,000 potential transplant candidates annually enter the ESRD program, and that the current pool of potential kidney transplant candidates who are medically suitable consists of 22,500 to 25,000 ESRD beneficiaries.
- The high front-end costs of transplantation procedures and kidney acquisition will mask the long-term cost savings of improved transplantation.

For analytic purposes, we employ a range of transplant outcomes and costs that are suggested by the early results of clinical trials of Cy-

\(^1\)We use data from 1979 (the last year for which comprehensive cost data are available) to estimate that 80 to 85 percent of ESRD expenditures are for dialysis patients. ESRD expenditures reached $1.0 billion in 1979. Of this total, $110 million (11 percent) was for transplant-related costs for 4000 Medicare-reimbursed transplant recipients, and $30 to $50 million (3 to 5 percent) was for treating the estimated five to ten thousand pre-1979 kidney recipients whose kidney grafts were still functioning in 1979. The balance ($840 to $860 million) must then be associated with the dialysis side. Furthermore, transplant procedures were performed on less than 10 percent of the 1979 ESRD beneficiary population.
closporine conducted by several major transplant centers. These ongoing trials, it must be noted, are still too limited in scope and too brief in follow-up to provide precise data about protocols, outcomes, and costs for use in a five-year projection for the entire United States; and other new drugs for treating acute rejection are also entering community practice and may alter trends in costs and outcomes. Our analysis attempts to reflect these factors, but the evolutionary course that clinical renal transplantation will follow during the next five years is highly uncertain. Our cost projections must therefore be regarded as preliminary, to be refined by further data as they become available from the transplantation and ESRD treatment systems.

Finally, we note that introduction of new prospective reimbursement regulations for dialysis and the inclusion of transplantation under the new diagnostic-related-group (DRG) system of Medicare prospective payment will influence the cost effects of improved transplantation in ways we cannot yet predict.

The report is organized as follows:

- Section II describes our present knowledge of the costs and outcomes of transplantation, based largely on data obtained from the HCFA Office of Research and several large transplantation data bases.
- Section III discusses cost savings that might stem from the two ways of performing better transplantations—reducing the cost of transplant success and reducing the number and cost of failures.
- Section IV discusses the potential savings from shifting appropriate patients from dialysis to transplantation. Sections III and IV include quantitative analyses based on results of projections using a range of transplant outcomes, policies, and utilization rates.
- Finally, Sec. V discusses factors that remain uncertain, and the implications of our analysis for the future direction of the ESRD program.

Four large databases, reflecting national rather than local or regional data, furnished the information on which we based much of our analysis:

- The UCLA International Transplant Registry, which collects and analyzes data about transplant outcomes and transplant immunology.
- HCFA's Medical Information System of the End Stage Renal Disease program (ESRD-MIS), which collects and manages data on all recipients of ESRD benefits.
• The Medicare data files, which HCFA's Office of Research has
  used to determine Medicare expenditures for ESRD ben-
  eficiaries by treatment category, outcome, and hospital discharge.
• The NIH Kidney Transplant Histocompatibility Study
  (KTHS), a large and well-documented study of the natural his-
  tory of kidney transplantation during the mid- and late 1970s.

In addition to these sources and others described in the text, we also
benefited from a series of calculations performed for us by Dr. Henry
Krakauer of NIH using a preliminary computer-based model of the
ESRD treatment system.
II. OUTCOMES AND COSTS OF RENAL TRANSPLANTATION

This section presents data on the outcomes and costs of transplantation. Later, as we project expenditures for transplantation into the future, costs for current protocols will provide a baseline set of cost elements to be used in estimating cost savings due to "improved" transplantation. Before proceeding with cost considerations, however, it is useful to review the recent status of transplant outcomes, and in this way to infer the "baseline" results that may be expected from current protocols.

We concentrate on patient and graft survival, since timely national data are available for these outcome measures. Morbidity and rejection episodes can be inferred only indirectly from a few published sources. Because no entirely satisfactory single U.S. transplant registry yet exists, we draw on data from several sources (based on patient samples that overlap to an unknown extent). We rely most heavily on data from the UCLA registry analyzed by Terasaki and his associates [2], and the ESRD Medical Information System (ESRD-MIS), analyzed by Krakauer and his associates [3].

Several factors are credited for the improvements in patient and graft survival described below: improved management of immunosuppression (with no fundamental change in drugs that are employed); improved patient management; pretreatment of graft recipients with blood transfusions; and refinements in the technology and precision of laboratory procedures for tissue typing and histocompatibility. Until recently, accurate tissue typing and matching was restricted to the HLA-A,B loci. Therefore, it is still too early for HLA-DR matching to have affected nationwide data significantly. Until more U.S. patients have been accurately typed for HLA-DR, its role in transplantation remains to be defined. However, some transplant centers and organ procurement agencies have already adopted HLA-DR matching as the primary means for matching kidneys to cadaveric recipients.
BASELINE OUTCOMES—PATIENT SURVIVAL

Patient survival has improved markedly in recent years. The last report of the Human Renal Transplant Registry indicated that one-year patient survival for primary cadaveric recipients was nearly 60 percent in 1968 and had reached 72 percent by 1974. The American Society of Transplant Surgeons reported that the figure had risen to nearly 90 percent by 1980 [4]. The UCLA registry [2], which receives data from over 100 transplant centers, mostly in North America, reports that one year cadaveric patient survival improved from 65 percent in 1960 to 90 percent in 1980, with an annual rate of increase of 1.9 percent/year, thus approaching the 97 percent rate for live related donor (LRD) transplants performed in 1980.

To illustrate the importance of age, sex, race, and disease on outcome of ESRD treatment, we refer to published data [3], from the ESRD-MIS data file on patient survival, experienced from 1977 through 1980 for LRD and cadaveric recipients and for dialysis patients. These data show 95 and 86 percent patient survival, respectively, for LRD and cadaver recipients at the one-year post-transplant milestone, and 91 and 78 percent survival, respectively, at three years. The lowest survival rates are recorded by recipients over fifty years of age and by those whose kidney failure is associated with diabetes. For dialysis patients, whose median age is fully twenty years greater than that of transplant recipients, one-year survival of 81 percent and three-year survival of 56 percent translate into a constant mortality rate of nearly 20 percent per year.

We stress that these survival data should not be used to compare dialysis and transplantation outcomes without accounting for “time to transplantation” bias and known risk factors. Such analyses have been performed for ESRD populations in Montreal [5], Seattle [6], and Michigan [7], but not yet for any national data base.

BASELINE OUTCOMES—GRAFT SURVIVAL

The UCLA report [2] suggests a steady fifteen-year improvement in patient survival following transplantation. Transplanted kidney survival, however, hovered around 50 percent for one-year cadaveric graft survival until quite recently. From UCLA registry data, it appears that one-year cadaveric graft survival declined between 1968 and 1975, but then improved from 44 percent in 1975 to 56 percent in 1980. The same source reports a value of 86 percent one-year graft survival for recipients of kidneys from identical siblings, and 82 percent for recipients of kidneys from parental donors for procedures performed in
1980. Graft survival data from the ESRD-MIS reveal that one-year cadaveric survival rose from 51 percent in 1977 to 61 percent in 1980, and LRD survival rose from 70 percent to 82 percent; that older patients do less well than younger ones; that no significant difference exists between men and women; and that white recipients fare better than blacks.

On the basis of these data, and without accounting for case-mix differences and type of transplant, it appears that a baseline value of 61 percent for a one-year graft survival is consistent with current transplant results in the United States.

PROJECTED OUTCOMES—PATIENT SURVIVAL

In this section and the next, we consider the potential range of proximate improvements in patient and graft survival. It is too early as yet to predict what the precise configuration of results or even protocols will be when the use of Cyclosporine becomes more widespread. However, the transplant centers that participated in early trials are now converging in agreement on the value of combining Cyclosporine with reduced doses of steroids, the tapering of Cyclosporine after a high loading dose, and the need to determine whether reduced kidney function is due to rejection or to Cyclosporine-induced nephrotoxicity. We now summarize the results reported in several trials conducted in the U.S. in Colorado, Pittsburgh, Minnesota, Houston, and in Canada. Although clinical trial data from Europe, Australia, and Japan are now available, the North American results are deemed more suitable for projecting outcomes in the United States. For a recent survey of results see the forthcoming “Proceedings of the First International Congress on Cyclosporine,” held in Houston, Texas on May 16–19, 1983.

A 1979 pilot study initiated at the University of Colorado by Starzl [8], while not a true trial, is now entering its fourth year. Patient survival at the end of year one was 86 percent, a low figure attributed to over-immunosuppression and the failure to distinguish between nephrotoxicity and rejection. Patient survival improved thereafter, and 79 percent of the original 66 patients are still living after 2½ to 3 years. Later results from Starzl and his colleagues, now at the University of Pittsburgh [8], showed 97 percent one-year patient survival, and no difference between Cyclosporine and controls in a group of 99 cadaveric recipients operated during 1981.

The University of Minnesota trials [9] [10], included 161 cadaveric and LRD recipients who were transplanted since 1980. One-year patient survival was 92 percent for recipients in the Cyclosporine group
and 95 percent for the recipients in the control group; two-year patient survival was 89 percent for Cyclosporine and 92 percent for controls. No statistically significant difference was observed.

The University of Texas, Houston studies [11], were based on 100 patients transplanted during 1980, 1981, and 1982. One-year patient survival for Cyclosporine-treated recipients of LRD kidneys was 97 percent; for Cyclosporine-treated recipients of cadaveric kidneys, 94 percent; and for the control group of cadaveric recipients, 91 percent. No control group of LRD recipients was used.

These U.S. trials are single center studies. The Canadian trial [12] differs from the U.S. studies in several ways: It is a multi-center trial involving 210 patients treated at 11 different centers, and it also indicated a statistically important advantage for Cyclosporine in terms of one-year patient survival. At the time of analysis, when only 33 patients had been followed for more than one year, patient survival was found to be 97 percent for the Cyclosporine group, compared with 86 percent for controls.

Despite the Canadian results, which are based on limited follow-up, the consensus that emerges from these reports (and others) is that aggregate patient survival is not expected to improve materially with the entry of Cyclosporine into clinical practice. Causes of death may change, however, away from infection and toward cardiovascular complications, as steroid doses are reduced and older and higher-risk patients are transplanted.

PROJECTED OUTCOMES—GRAFT SURVIVAL

While patient survival shows virtually no further change, the trials suggest that graft survival may improve dramatically.

Starzl's pilot study in Colorado [8], found a one-year graft survival of 79 percent, and a two-year value of 75 percent, for primary cadaveric recipients. The results for such recipients at Pittsburgh [8] show a one-year graft survival of 90 percent for the Cyclosporine group and 50 percent for controls, and a one-year graft survival of 78 percent for cadaveric retransplants—a result twice as good as in historical controls. The Minnesota results showed no significant improvement in graft survival from the already high values obtained for the control groups. One-year graft survival was 88 percent for the Cyclosporine group compared with 80 percent for controls, and two-year survival was 78 percent for Cyclosporine and 80 percent for controls. A further dissection of the Minnesota results [10] shows that cadaveric graft survival slightly favored Cyclosporine, while LRD graft survival favored the control group. The Houston results [11] showed one-year graft
survivals of 55 percent for cadaveric controls, 76 percent for Cyclosporine-treated cadaveric recipients, and 91 percent for Cyclosporine-treated LRD recipients.

The Canadian trials [12] demonstrated a one-year cadaveric graft survival of 80 percent, in contrast to 64 percent for those receiving standard therapy. Three centers participating in the Canadian trials used the Minnesota three-drug regimen (anti-lymphocyte globulin, azathioprine, prednisone) for the control group. For these centers, cadaver graft survival was 81 percent for both treatment and control groups.

The centers engaged in the Cyclosporine trials vary considerably both in the importance they ascribe to tissue typing, and their approach to immunosuppression and rejection. We also note that even for the control groups, some centers now show significant improvement over historical values.

We have used these data on graft survival to estimate that one-year graft survivals of 74 percent and 89 percent should bracket the expected outcomes of improved transplantation for all U.S. transplant centers for a case mix that is roughly similar to the U.S. ESRD transplant population.

CURRENT COST DATA

We may now turn to questions of cost: What are the current costs to Medicare of health care for transplant recipients, how do they compare with dialysis costs, and how may the costs be projected in order to predict fiscal impacts on the federal government? Future costs can be approximated only roughly because of the limited experience with new protocols and the altered future configuration of Medicare reimbursement policy. Current costs can be more firmly established on a national basis because of the ongoing analysis of Medicare and ESRD-MIS files by Dr. P. Eggers in the HCFA Office of Research and Demonstrations.

To support our analyses and projections, we summarize a series of average national costs for subsets of patients undergoing ESRD treatment. Although HCFA data files include more recent patient data, national treatment cost data have been analyzed mainly for 1979 and, in some rare instances, 1980. Therefore, the cost elements are generally specified in 1979 dollars for treatment that was received during 1979. The reimbursements are computed on a patient-year or annualized basis, and encompass all Part A and Part B Medicare-reimbursed treatment costs of both renal and nonrenal origin for 1979, the only year for which linked medical and cost data are currently available.
Accurate linkage between medical and reimbursement files was possible for half the patients.

Despite the incompleteness of the medical data and the broad categories, average ESRD reimbursements based on aggregate data are expected to be representative of the entire U.S. population of ESRD beneficiaries.¹

The magnitude of average Medicare reimbursement for transplant recipients and dialysis patients is shown in Table 1 for 1979. We note from the table that the average transplant recipient incurs Medicare costs less than 25 percent of the average center dialysis patient in each year following the year of transplantation. However, the categories in

| Table 1 |
| AVERAGE MEDICARE REIMBURSEMENT PER PERSON-YEAR |
| BY ESRD TREATMENT: 1979 |
| All Transplants | Dislysis |
| | Operated before 1979 | Operated in 1979 | In Center | In Home |
| Inpatient costs | $21,500 | $3,700 | $5,500 | $4,700 |
| Physicians' reimbursement and supplies | 5,800 | 900 | 3,500 | 7,500 |
| Outpatient costs | 8,300 | 1,000 | 14,600 | 6,500 |
| Average cost to Medicare | $35,600 | $5,600 | $23,600 | $18,700 |

¹Most of the difference between Medicare Part A allowed charges and reimbursements represents unrecoverable charges as specified by Medicare regulations, only a small portion of this difference being accounted for by coinsurance and deductibles. In the case of Part B, coinsurance and deductibles account for the major part of the difference between allowed charges and Medicare reimbursements. Coinsurance and deductible portions of both Part A and Part B are paid by patients, their families, Medicaid, private insurance, state programs, nonprofit organizations, and other sources. Little empirical basis exists for determining the distribution among non-Medicare sources, or the ESRD-specific ratio of reimbursements to approved hospital charges. The ratio of all Medicare Part A reimbursements to approved hospital charges declined from 75 percent in 1974 to less than 70 percent currently, and the ratio of all Part B reimbursements for allowed charges increased from 74 percent in 1974 to 78 percent. We do not know the ESRD-specific ratio, but will assume that ESRD reimbursement ratios are close to those for the entire Medicare program.
Table 1 are too broad to portray the true costs of transplantation. They do not adequately distinguish between success and the cost of failure.

We make this distinction in Table 2, where 1979 Medicare reimbursement by transplant type and outcome are presented. In this table, we designate a transplant recipient with a functioning kidney graft as a success. By failure, we mean either a transplant recipient whose graft has rejected or a transplant recipient who has died. (The HCFA data do not discriminate among different causes of death.)

In this way we begin to underscore the cost-penalties of failure. From Table 2 we see that graft failures in 1979, the year of the transplant, entails additional reimbursements of $10,600 for cadaveric recipients, $19,400 for LRD recipients, and $12,700 for all transplant types. Furthermore, the additional costs associated with treating a dying transplant recipient approach $16,000 to $18,000 per person-year over those required for graft failure.

If a pre-1979 transplant recipient fails in 1979 by either rejection or death, additional Medicare reimbursements of $26,000 to $28,000 are associated with failure, presumably for rejection treatment, dialysis, and acute care. In terms of hospital days per person-year, the pre-1979 recipient with functioning graft required 9 days of care, the pre-1979 recipient who failed by rejection required 41 days of care, and failure that resulted in death required 70 days of hospital care.

Table 2

<table>
<thead>
<tr>
<th>Transplant Group</th>
<th>Success Alive, with Functioning Kidney</th>
<th>Failure Alive, Kidney Rejected</th>
<th>Failure Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>All transplants in 1979</td>
<td>$32,000</td>
<td>$44,700</td>
<td>$62,900</td>
</tr>
<tr>
<td>LRD transplants in 1979</td>
<td>29,800</td>
<td>49,200</td>
<td>65,000</td>
</tr>
<tr>
<td>CAD transplants in 1979</td>
<td>33,400</td>
<td>44,000</td>
<td>61,100</td>
</tr>
<tr>
<td>All transplants before 1979</td>
<td>4,100</td>
<td>30,200</td>
<td>32,200</td>
</tr>
</tbody>
</table>
Costs and Risks

Current and historical national data cannot provide a detailed portrayal of the relationships among costs, risks and transplant type. We can only sketch a qualitative picture, using data from different centers and different time periods. Because of differences in protocol, charge rates, and cost methodologies, data from individual centers are not comparable. The few centers that report such data classify patient risk using two criteria: the source of the kidney (LRD or cadaveric) and whether the patient is diabetic. Outcome is mainly specified in terms of graft and patient survival and, occasionally, in terms of rejection episodes.

For example, yearly treatment costs for Moffitt Hospital transplant recipients [13] during 1976–1977 were:

- Living related donor ....................... $17,600
- Cadaveric donor .......................... 22,000
- Cadaveric donor, diabetic ................. 27,800
- Cadaveric donor, two rejections, graft loss .... 26,300

Another example is based on published average cost data from the University of Wisconsin [14], after including kidney procurement costs, surgeons' fees, and anesthesia:

<table>
<thead>
<tr>
<th>Donor</th>
<th>Cost of Transplant</th>
<th>Additional First-Year Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Living related donor (nondiabetic)</td>
<td>$14,500</td>
<td>$2,000</td>
</tr>
<tr>
<td>Living related donor (diabetic)</td>
<td>16,000</td>
<td>4,100</td>
</tr>
<tr>
<td>Cadaveric donor (nondiabetic)</td>
<td>16,500</td>
<td>4,700</td>
</tr>
<tr>
<td>Cadaveric donor (diabetic)</td>
<td>9,200</td>
<td>7,600</td>
</tr>
</tbody>
</table>

The Wisconsin data exhibited greatest variation in the additional first-year costs for diabetics (mean costs of $5300, standard deviation of $8200, and a range of $32,000). To further illustrate the cost penalties of failure, we cite recent data on the cost experience of 29 transplant patients at Massachusetts General Hospital [14]. The 20 patients who retained their kidneys incurred average costs of $20,940, with a median cost of about $15,000; 9 patients who lost function
through rejection incurred average costs of $45,000, with a median cost of about $40,000; and the average cost for all transplants, independent of outcome, was $28,000. (Amounts are based on total health care costs during three months following transplantation.)

Hospital Charges

Another more detailed comparison is in terms of transplant-related hospital charges. These are shown in Table 3 for three categories of treatment: transplant procedure, additional rejection treatment, and nephrectomy after graft failure. Since some patients require rejection treatment during the initial hospital stay for transplantation, some costs of rejection treatment are included within the first category. For consistency, we compare costs in terms of the fiscal impact on Medicare—$16,800 for the transplant hospital stay, $3700 for additional rejection treatment (when required), and $10,000 for nephrectomy (also when required by surgical practice).

Table 3 also presents data and cost center charge distributions for the various treatment categories. The charge data are from the 1980 Medpar file, a 20 percent random sample of Medicare hospital discharges. The Medpar file has no distinct charge center for kidney acquisition costs and does not distinguish between cadaveric and LRD grafts. Kidney costs are included in the ancillary category, along with dialysis, physical therapy, and other unspecified services. The average 1980 transplant (without regard to outcome of procedure) incurred hospital charges of $24,000. (The average hospital stay was thirty days, with four days in the ICU-CCU.) To that figure should be added surgical fees of $2000 to $2500 for transplantation and $1000 for live donor nephrectomy (when required); anesthetist’s fees of $600; and other physicians’ fees, to bring the 1980 total charges to $27,100. Part A reimbursement is estimated to be $16,800 using the 1980 Medicare reimbursement-to-charge ratio of 70 percent. However, kidney costs are not subject to coinsurance and deductibles. Therefore, the average 1980 HCFA Part A reimbursement for transplantation may be closer to $19,000, leaving perhaps one thousand dollars to be provided by other sources.

Kidney Acquisition Costs

Kidney acquisition charges are identified separately in the Annual Report to Congress and other HCFA sources. During 1980, the average kidney acquisition charge was $7000 for a kidney from a cadaveric donor, and $7600 for a kidney from a living donor, with an average
Table 3
AVERAGE HOSPITAL CHARGES FOR TRANSPLANT PROCEDURES
AND REJECTION TREATMENT, 1980

<table>
<thead>
<tr>
<th>Category</th>
<th>Charges for Transplant Procedures</th>
<th>Rejection Treatment</th>
<th>Nephrectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accommodations</td>
<td>$5,300</td>
<td>$1,700</td>
<td>$4,500</td>
</tr>
<tr>
<td>ICU and CCU</td>
<td>1,500</td>
<td>200</td>
<td>400</td>
</tr>
<tr>
<td>Operating room</td>
<td>1,600</td>
<td>200</td>
<td>1,000</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>1,800</td>
<td>400</td>
<td>1,000</td>
</tr>
<tr>
<td>Laboratory</td>
<td>4,100</td>
<td>1,000</td>
<td>2,000</td>
</tr>
<tr>
<td>Radiology</td>
<td>900</td>
<td>300</td>
<td>500</td>
</tr>
<tr>
<td>Medical supplies</td>
<td>600</td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>300</td>
<td>&lt; 100</td>
<td>200</td>
</tr>
<tr>
<td>Ancillary(^a) (dialysis, physical therapy, or other services including kidney acquisition)</td>
<td>8,100</td>
<td>700</td>
<td>2,900</td>
</tr>
<tr>
<td>Total per discharge(^b)</td>
<td>$24,100</td>
<td>$4,600</td>
<td>$12,000</td>
</tr>
<tr>
<td>Average length of stay</td>
<td>30 days</td>
<td>10 days</td>
<td>21 days</td>
</tr>
<tr>
<td>Estimated HCFA reimbursement</td>
<td>$16,800</td>
<td>$3,700</td>
<td>$10,000</td>
</tr>
</tbody>
</table>

\(^a\)No separate category in file for kidney acquisition costs (included within ancillary).

\(^b\)Charges per stay for transplantation increased by 10 percent between 1979 and 1980.

cost/charge ratio of 0.83. The corresponding 1981 estimates are $7200 and $7600, with a cost/charge ratio of 1.0, and the 1982 charges are $8800 and $9000 respectively. The range of kidney acquisition costs is large, depending on type of donor, agency, and the costs of donor management, both for LRD and cadaveric kidneys.
Transplant Cost Model

The cost data presented above may be used to develop a preliminary national cost model for transplantation. The average combined Part A + Part B cost per patient-year for a person transplanted in 1979 was $35,600, broken down in the following way. The average transplant procedure consisted of inpatient costs to HCFA of $15,700 (including kidney acquisition), and costs for surgical services of $1500 to $2000, for a total of about $17,500. If one assumes that the average transplant occurs at midyear, then the average 1979 period of dialysis before transplantation is less than six months, based on the KTHS observation that 35 percent of all kidney recipients (25 percent of cadaver kidney recipients) had less than six prior months of dialysis. In the absence of precise data, we assume that the average 1979 transplant recipient received 4.5 months of dialysis in 1979 before surgery, for associated prorated reimbursements by HCFA of $10,000. On this basis, the average 1979 recipient had incurred costs of $27,500 by the time of transplant discharge. The remaining $8100 consists of the various post-transplant costs for treatment complications, death, rejection episodes, etc., and may be further dissected using estimates of graft survival, patient survival, and treatment costs.

The high cost of failure is demonstrated by the $12,600 annual difference between graft failure and success, and by the high annualized cost of treating patients who die after transplantation. The annualized cost overestimates the differences for patients who die after transplantation. Such patients, on the average, survive for one month after surgery if the average procedure occurs at midyear. Pre-1979 transplants provide further examples of the economies of success and the costs of failure: A functioning graft entails $4100 in HCFA costs, a graft failing before 1979 entails $23,000 in HCFA costs, and a graft failing in 1979 entails $30,200.

For purposes of analysis, we thus assume that the first-year costs to Medicare for a transplant, kidney acquisition, and successful rejection treatment are $21,000 (in 1979 dollars). It is also estimated that a transplant recipient who died entailed costs of $15,000, compared with $5000 for a dialysis death, and that annual maintenance for a successful transplant recipient entails HCFA costs of $4100.¹

¹For concreteness, we refer treatment costs to 1979 values in our analyses. Suitable data for tracking and predicting temporal changes in the detailed costs of ESRD related goods and services are not readily available. For reference, we note that health-care-related consumer price indices increased in the following proportions between 1979 and 1982: medical care, 37 percent; physician services, 33 percent; hospital services, 49 percent; and all prescription drugs, 38 percent. These compare with a 27 percent rise in the overall Consumer Price Index.
If a transplant fails and the recipient returns to dialysis, we also assume that unsuccessful treatment of rejection with a nephrectomy of the failed kidney costs $12,000, that each hospital treatment for acute rejection (without nephrectomy) costs $3700, and that health-care costs for maintenance dialysis are estimated at $23,000 per year, or as much as $3000 per year more than the costs for the never-transplanted average dialysis patient. (These are again estimated costs to HCFA in constant 1979 dollars.)

This picture is qualitatively consistent with earlier studies by Stange and Sumner [16], and Roberts et al. [17]. For a transplant failure, they estimated first-year costs of $24,000 to $25,000 compared with HCFA costs of $20,000 for the basic transplant procedure and subsequent treatment; failure costs of $9000 to $10,000 for rejection, compared with HCFA costs of $7000; and between $13,000 and $25,000 annual costs for dialysis compared with HCFA costs of $10,000 to $19,000, depending on whether treatment is home-based or center-based.

THE PRESENT SITUATION

Before exploring the potential cost effects of improved transplantation, it is useful to outline the present situation, with regard to the relative costs of success and failure.

For concreteness, we consider the 4883 transplant procedures performed in 1981, of which 3425 were cadaveric transplants. The latter included about 3000 first transplants and 400 second or subsequent transplants. If we restrict ourselves to first transplants only, since data are better for these, we can develop a profile of the costs of transplant failure.

Of the patients with first transplants, about 10 percent, or 300, died; about 60 percent, or 1800, were alive with a functioning kidney one year post transplant; and about 30 percent, or 900 patients, had experienced transplant failure and returned to dialysis. (These numbers are best estimates, not actual counts.)

In collaboration with Dr. H. Krakauer of NIH, we have used a preliminary mathematical model of the transplantation system that incorporates realistic estimates of graft and patient survival and costs to HCFA to deduce the following facts about the nearly 5000 transplant recipients in 1981:

- About 30 percent of these recipients will experience failure within the first year after transplantation and will then require maintenance dialysis.
• Only 70 percent of patient-life-years during the five years following transplantation will be with restored kidney function; the remaining 30 percent will be lived on dialysis.

• The expected average treatment costs to HCFA for each recipient (in 1979 dollars) will be $27,000 for the first year after transplant and $8500 for each additional year of life, including the costs of failure. These figures are based upon the current three-year limit on eligibility for Medicare benefits for successful transplants.

• For these nearly 5000 transplant recipients of 1981, fully 50 percent of the costs borne by the HCFA during the following five years will represent the “costs of failure”—treatment of rejection, nephrectomies of failed kidneys, and increased annual chronic maintenance dialysis costs.
III. COST SAVINGS OF IMPROVED TRANSPLANTATION

How, we ask, will improved outcomes reduce the costs of transplantation? Improvement will shift transplant recipients away from failures and toward successes, and will involve reduced length of stay for initial hospitalization, fewer or less acute episodes of rejection and thus fewer days of hospitalization for rejection treatment, fewer nephrectomies for failed kidneys, and, of course, fewer transplant recipients returning to dialysis—all of which directly reduce costs. Cyclosporine is likely to reduce the dosage of standard immunosuppressives such as azathioprine and steroids but the net cost effect of drug use remains unclear, since Cyclosporine is expected to cost more than current drugs. Clinical ease of use, and long-term side effects of Cyclosporine including nephrotoxicity also remain to be determined.

The cost savings from improved outcomes, it should be pointed out, are not contingent upon increasing the supply of cadaveric kidneys. Instead, the reduction in the costs of success and the penalties of failure will be captured by those patients now receiving transplantation, and without reference to shifting patients from dialysis to transplant. However, the maximal effect is achieved by transplanting suitable ESRD patients who might otherwise be managed by dialysis.

REDUCING COSTS OF SUCCESS

Hospitalization of the transplant recipient accounts for a large portion of transplant costs. The average transplant recipient in the United States spends 30 days in the hospital for the initial procedure. The range of hospital length-of-stays is unusually wide, though data on this matter are inadequate.¹

Major reasons for hospitalization beyond the initial procedure, recovery, and complications are to treat rejection of the transplanted kidney or to perform a nephrectomy in the event of graft failure (see Table 3).

¹Confirming the variability in hospital length-of-stays under current transplantation protocols, the New Jersey prospective payment system based on Diagnostic Related Groups (DRGs) allows “normal” stays of between 20 and 60 days (an exceptionally long interval by DRG standards). It should be remembered that all procedures for a given DRG will eventually be reimbursed at a single standard rate.
We believe that the large variability in the initial transplant hospital stay is related to both successful and unsuccessful inpatient treatment of rejection episodes occurring during the initial hospitalization. From the limited published data for transplants performed during the mid- and late 1970s, we found that both LRD and cadaveric recipients share a greater than 0.5 probability of rejection during the initial hospital stay, and the cadaveric recipient who rejects once has perhaps a 0.4 or 0.5 probability of rejection again during the first year.

Table 4 underscores the penalty in increased morbidity associated with multiple rejections and graft failure. It exhibits the range in admission rates and lengths of stay for LRD and cadaveric recipients at Moffitt Hospital, San Francisco [13]. The data may not be entirely typical of current practice because protocols now tend toward less aggressive treatment of rejection when an interval of diminished kidney function is sandwiched between two rejection episodes. Transplant success leads to shorter hospital stays and fewer admissions during the second year: Recipients with functioning kidneys at two years experienced a second-year admission rate of 0.08/year for LRD grafts and 0.3/year for grafts from cadavers, with average lengths of stay of 0.7 and 4.5 days for successful recipients. The average time of onset for rejection (when it occurred) was 19 days for recipients of cadaveric organs, but 20 percent of cadaveric recipients received no treatment for rejection during their first year.

For the KTHS sample [19], an average of 1.3 and 1.0 rejection episodes per patient occurred for cadaveric and LRD recipients; 16 percent of cadaveric recipients and 30 percent of LRD recipients experienced no rejection episodes during the entire period of follow-up; 68 percent of cadaveric and 50 percent of LRD recipients experienced initial rejection within 30 days; 77 percent of cadaveric and 62 percent of LRD recipients experienced their initial rejection within 60 days of transplantation; and the median time of initial rejection was 14 days for all patients.

Many successful recipients undergo setbacks. Supportive dialysis treatment was required by 30 percent of Moffitt cadaveric recipients during their first year. For the KTHS sample, over 50 percent of cadaveric recipients and 27 percent of LRD recipients required dialysis support during the study's follow-up period (up to five years). Results from the Cyclosporine trials are promising, but are not yet sufficiently detailed to permit detailed comparison with these historical results. Anecdotal reports emphasize the need for careful patient management and monitoring to obtain a maximum benefit from improved immunosuppression.
Table 4
FIRST YEAR HOSPITALIZATION FOR TRANSPLANTATION
(FROM MOFFITT HOSPITAL, SAN FRANCISCO)

<table>
<thead>
<tr>
<th>Category</th>
<th>Admissions/Year</th>
<th>Average Length of Stay (Days/Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Living Related Donor</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Success</td>
<td>1.45</td>
<td>33</td>
</tr>
<tr>
<td>Failure</td>
<td>2.00</td>
<td>48</td>
</tr>
<tr>
<td>Total</td>
<td>1.48</td>
<td>34</td>
</tr>
</tbody>
</table>

| **Cadaveric donor**    |                 |                                   |
| Success                |                 |                                   |
| No rejection treated   | 1.49            | 31                                |
| One rejection treated  | 1.89            | 42                                |
| Two rejections treated | 2.43            | 48                                |
| All success            | 1.94            | 40                                |
| Failure                |                 |                                   |
| No rejection treated   | 1.50            | 39                                |
| One rejection treated  | 1.50            | 43                                |
| Two rejections treated | 2.37            | 63                                |
| All failure            | 1.95            | 52                                |
| Total                  | 1.94            | 46                                |

Two transplantation centers in this country that are using Cyclosporine report reduced initial hospitalization. Data from the University of Minnesota [20] show that the initial length of hospital stay is reduced by an average of 38 percent for patients on an immunosuppressive regime that includes Cyclosporine, when compared with their standard regime of anti-lymphoblastic serum, azathioprine, and prednisone. The Minnesota data also show that the frequency of hospital readmissions is reduced by 52 percent during the first year and the costs of readmission are reduced by 59 percent. Rejection episodes are fewer and are more easily managed, and patients using Cyclosporine require an average of 80 percent fewer days of post-transplant hospitalization for complications. Data from the University of Pittsburgh are consistent with this experience [21], where Starzl suggests that hospital treatment costs have decreased by 50 percent due to reduced
length of stay. The Canadian trials, on the other hand, suggest little difference in rejection episodes or length of stay.

It should be stressed, however, that the Cyclosporine data are from only two of the more than 160 transplant centers currently operating in the United States and that centers differ in their treatment procedure. Thus, length of stay may vary substantially from center to center and the prospects for reduced length of stay will vary accordingly.

If Cyclosporine reduces the frequency of acute rejection of the transplanted kidney, it may therefore reduce the costs of successful transplants. The cost savings will occur as reduced rejection shortens hospitalization and reduces reliance upon steroids and other immunosuppressives for treating rejection. The offsetting factor may be the effect of the costs of Cyclosporine on the cost of the total immunosuppressive regime, including the diagnosis and treatment of Cyclosporine's side effects.

First-year medication costs for transplant recipients undergoing conventional treatment have been about $3000 to $4000, including immunosuppressive drugs, antiacids, and antihypertensives, and all hospital pharmacy charges. Annual drug maintenance costs thereafter for a functioning graft, not currently borne by Medicare, are in the $1000 to $2000 range.

Medicare reimburses the costs of anti-rejection drugs that are administered in an inpatient setting or are not self-administered. From Table 3, we see that historical hospital charges for treating an acute rejection episode approach $5000, with medication contributing up to 10 percent of the total. The 1980 costs shown in Table 3 may change dramatically as a result of the FDA's 1981 approval of ATGAM for treating acute rejection. ATGAM, Upjohn's proprietary antithymocyte globulin (ATG), is administered intravenously during a 14-day (or longer) hospital course of treatment and costs an estimated $5000 to $7000 per rejection episode. The total cost for each course of treatment (up to two per patient) may be several times greater than the figures shown in Table 3. In addition to ATGAM's recent FDA approval, other developments in treating acute rejection are under way.

For example, the University of Minnesota has used its own preparation (antilymphoblast globulin (ALG)) since 1967, and several other centers now use it as part of a therapeutic trial. ALG is currently under consideration for approval by the FDA. ALG, like ATG, is not specific to the portions of the immune system causing rejection and may affect a wider variety of lymphocytes than required for effective immunosuppression.
Monoclonal antibodies, when perfected, promise to eliminate this lack of specificity. Currently, limited trials are being conducted with both commercial and laboratory-made monoclonals, but the results are not yet conclusive. Should appropriate monoclonal antibodies be developed, they could, like Cyclosporine, alter the status of clinical immunosuppression. We have not explicitly included increased costs for any of these new antirejection drugs in our subsequent analysis.

For the most part, Cyclosporine will add to drug costs, although it could simultaneously reduce the need for other antirejection drugs. One major unresolved issue is the appropriate maintenance dose of Cyclosporine required in the years following transplantation. The Minnesota trials [22] suggest that dose reductions over time are required to maintain adequate kidney function, leading to a halving of the dose at the end of one year, to less than 6 mg/kg/day. Starzl (personal communication) has suggested that a tapering of the Cyclosporine dose from 10 mg/kg/day to 1 mg/kg/day may be required to balance nephrotoxicity against immunosuppression during maintenance. It was found during the Canadian trials that doses as low as 2 mg/kg/day could maintain therapeutic blood levels in some patients [23], and some have recommended that long-term use of Cyclosporine may be limited to rather low doses.

Thus the true cost increment associated with Cyclosporine use is not yet settled. Moreover, since the drug will be administered for maintenance purposes by patients themselves in the outpatient setting, for which Medicare does not reimburse, much of the cost will fall directly on the patient. At a cost to the patient of about $150 for a five-gram bottle and an 8 mg/kg/day dose, each year of treatment, including the first, entails Cyclosporine costs of about $6000. If the unit price does not change, then the costs of maintenance treatment will be roughly proportional to dose, and a maintenance dose of less than 4 mg/kg/day may cost under $3000/year. Transplant centers now inform prospective Cyclosporine recipients that they should anticipate drug charges in the $5000 to $6000 range annually.

Overall, then, we may experience cost-saving effects to Medicare, but not, perhaps, to the patient, from reducing the costs of successful transplantation. More significant, though, in our view, are the cost savings that are likely to result from reduced kidney transplant failure.

\[\text{Doses are specified in mg of drug/kilogram of body weight/day.}\]
REDUCING COSTS OF FAILURE

Two modes of transplant failure exist: death, and rejection of a transplant that results in the patient's return to dialysis. It is of critical importance to recognize that substantial human and financial costs result from both types of failures. Loss of life is a heavy human cost, although "cost savings" occur by decisively removing a patient from treatment. But transplant failure that results in a return to dialysis is costly in both human and financial terms. These costs, part of the true costs of transplantation, usually remain unrecognized because the transplant community has preferred to advertise the benefits of success rather than the costs of failure. Consequently, definitive data and thorough analyses of the costs of kidney transplant failure do not exist.

We can make some rough estimates of the costs of transplant failure on the basis of information from a few centers, from analysts at the National Institutes of Health and Health Care Financing Administration, and from other studies, but few data exist about patient with failed grafts who must return to dialysis: the KTHS collected minimal information on such patients; and they are generally lost to follow-up by transplant centers and scattered among dialysis patients. Furthermore, the shift toward less aggressive immunosuppression may lead to patterns of morbidity and mortality that differ from those seen in the mid-1970s [22].

The few literature and anecdotal reports generally support the notion that a successful transplant recipient is better rehabilitated medically and psychiatrically than either a person undergoing chronic dialysis or a recipient whose graft has failed. This view, however, has been challenged by a recent report [23], from the Rogosin Kidney Center indicating that the same high level of psychiatric impairment exists for both dialysis patients and successful transplant recipients.

Several other reports suggest that transplant failure by rejection is associated with psychological instability and suicide [24]; diminished quality of life, as judged by the patients and others [25]; and an employment and functional status comparable to center dialysis patients (whose median age was 20 years greater than the transplant failure group) [26].

Shifting away from the human costs of transplant failure, we cite anecdotal data that portrays the financial penalties for failure, primarily during the initial period following graft rejection.

Orange County. Patient records from St. Joseph Hospital in Orange County, California, for example, show that current treatment costs are $21,000 greater for patients whose grafts fail during the initial hospital stay. In addition, transplant recipients with a functioning kidney entail average first-year annual costs of $7300 for follow-up and
rejection treatment, and $8500 for further hospitalization following a successful graft procedure.

**Boston.** The cost experience at Massachusetts General Hospital is consistent with this picture [15]. The average cost of a failed transplant, in a three-month period following the procedure, exceeds the comparable cost of success by $25,000!

**San Francisco.** Similarly, data from the University of California Hospital [13] show a penalty, in first-year length of stay, of between 12 and 30 days for graft failures, depending on the number of treated rejection episodes. This clearly translates into increased treatment costs.

From national data obtained by HCFA in 1979, we find the average surviving LRD recipient whose graft failed required 23 additional days of hospital care compared with the average successful LRD recipient; and the average surviving cadaveric kidney recipient whose graft failed required 13 more hospital days than the average successful cadaveric recipient.

In Table 3, we indicate the hospital charge categories that pertain to this discussion. It can be clearly seen that the charges for rejection treatment, without nephrectomy, fall primarily in accommodations, laboratory tests, and ancillary services (mostly dialysis) categories. If rejection treatment fails, and requires a nephrectomy, then accommodation charges are trebled on the average, and charges for additional surgery, rejection indication, laboratory tests, and ancillary services all jump substantially.

If advances in immunosuppression occur that act with greater specificity against rejection, as Cyclosporine appears to do, then the cost-saving implications come into sharper focus. There will be fewer instances of rejection and the episodes of rejection may be less severe. The results will be fewer days of hospitalization and lower charges for surgery, antirejection medication, laboratory tests, and ancillary services.

**PROJECTED FIVE-YEAR COST SAVING DUE TO IMPROVED OUTCOMES**

As mentioned at the beginning of this section, savings from reducing the costs of success and the penalties of failure will accrue from improved efficacy of transplantation without reference to shifting patients from dialysis, and without being contingent on an increased supply of kidneys. To explore this point and to illustrate the magnitude of such savings, we have projected the expected five-year costs to HCFA for a single transplant recipient using three different
assumptions about graft survival, consistent with the UCLA and ESRD-MIS results described earlier, and with graft-survival data reported in Cyclosporine clinical trials. For current baseline, we assumed 61 percent graft survival at the end of one year, and an annual failure rate of 9 percent for later years.

We cannot predict exactly how much improvement will occur when the use of Cyclosporine moves beyond clinical trials. But we have chosen two hypothetical levels of outcome to bracket our projections based upon data from the early studies. The first of these ("medium") corresponds to a 74 percent one-year survival post transplant, with an annual failure rate of 5 percent for subsequent years; the second ("excellent") corresponds to an 89 percent graft survival one year post-transplant, and a 2 percent annual failure rate. We based our projections on calculations provided by Dr. H. Krakauer of NIH, which we then modified to reflect alternative treatment cost estimates and potential changes in reimbursement policy.³

The three levels of transplant outcome have corresponding levels of patient life years requiring dialysis. The baseline ("current") outcome results in an expected 30 percent of patient life-years requiring maintenance dialysis; the 74-percent ("medium") outcome results in 20 percent of patient life-years on dialysis, and the 89 percent outcome ("high") results in 6 percent of patient life-years requiring dialysis, using a five-year projection frame. If there is no "catchup" effect, the decreased reliance on dialysis support should extend beyond the five-year interval.

We examined the following three cases:

Case A: (1) Current government policy prevails, which limits ESRD benefits to three years for successful transplant recipients and restricts coverage of immunosuppressive drugs to inpatient treatment; and (2) treatment costs remain unchanged for all three levels of outcome.

Case B: (1) Current government policy prevails; and (2) new transplantation treatment costs decline 25 percent from baseline costs, a magnitude consistent with results from trials reported by Pittsburgh and Minnesota.

³The costs of transplantation are largely "front-end," while the benefits accrue over time. This contrasts with dialysis, where costs and benefits occur simultaneously. Despite these differences, we believe that it would be premature to introduce such concepts as discounting and quality-adjusted life-years, given our genuine uncertainty over the configuration of costs and outcomes to be achieved in community transplant centers. Therefore, all our projections are based on simple cost estimates (in 1979 dollars) without discounting or other refinements. The cost elements for current treatment are largely based on 1979 reimbursements by Medicare and do not, therefore, reflect any significant costs for ATGAM treatment of rejection.
Case C: (1) Government policy changes, with the three-year benefit restriction eliminated and coverage extended to immunosuppressive drugs administered in the outpatient setting; (2) drug costs of $1000 per year are incurred for baseline outcomes; and (3) improved transplantation costs are reduced 25 percent, offset by an additional $4000 in drug costs in the first year and $2000 in each successive year. These projected drug costs account for both a tapering of dose and a correction to 1979 cost levels.

The five-year projections are displayed in Table 5. They show that all cases, including Case C, which makes several cost-increasing policy changes, result in lower five-year costs than the approximately

<table>
<thead>
<tr>
<th>Cases</th>
<th>One-Year Graft Survival</th>
<th>α(1)</th>
<th>β(2)</th>
<th>Projected Five-Year Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (current)</td>
<td>61%</td>
<td>$27,000</td>
<td>$8,500</td>
<td>$70,000</td>
</tr>
<tr>
<td>Medium (new)</td>
<td>74%</td>
<td>25,000</td>
<td>6,600</td>
<td>58,000</td>
</tr>
<tr>
<td>High (new)</td>
<td>89%</td>
<td>23,000</td>
<td>3,800</td>
<td>42,000</td>
</tr>
<tr>
<td>Low (Case B)</td>
<td>61%</td>
<td>$27,000</td>
<td>$8,500</td>
<td>$70,000</td>
</tr>
<tr>
<td>Medium</td>
<td>74%</td>
<td>20,000</td>
<td>6,600</td>
<td>53,000</td>
</tr>
<tr>
<td>High</td>
<td>89%</td>
<td>18,000</td>
<td>3,800</td>
<td>37,000</td>
</tr>
<tr>
<td>Low (Case C)</td>
<td>61%</td>
<td>$27,000</td>
<td>$10,000</td>
<td>$78,000</td>
</tr>
<tr>
<td>Medium</td>
<td>74%</td>
<td>20,000</td>
<td>9,900</td>
<td>70,000</td>
</tr>
<tr>
<td>High</td>
<td>89%</td>
<td>18,000</td>
<td>7,300</td>
<td>54,000</td>
</tr>
</tbody>
</table>

NOTES:

(1) α = Expected value of treatment cost for transplantation, including cost of rejection and treatment failure.

(2) β = Expected value of annual maintenance costs, including dialysis (should it be required).

(3) Cost per patient = α + β × T, where T = years of treatment.
$100,000 costs that would be incurred by a dialysis-only patient over the same period.

Cases B and C, with medium and high graft survival rates, represent the range of potential cost savings if current clinical trial data for Cyclosporine are realized more broadly. Because coverage policy is unchanged in Case B (no expenditures by HCFA for outpatient use of immunosuppressives), the saving compared with current regimens for each person transplanted using the new protocol ranges from $17,000 to $33,000 for five years of treatment, and the cumulative savings due to transplanting a suitable dialysis patient are between $47,000 and $66,000.

Case C reflects the influence of changes in coverage policy. The modifications remove the three-year post-transplant limit and cover immunosuppressive costs at the standard Medicare rate. Even for this case, there are projected five-year cost savings of $8000 to $24,000 for the new protocol, and savings over dialysis treatment of $30,000 to $46,000.

Thus, the projections confirm that there is genuine potential for cost savings over the lifetime of transplant recipients—savings associated with improved efficacy and reduced morbidity.
IV. COST EFFECTS OF SHIFTING PATIENTS
FROM DIALYSIS TO TRANSPLANTATION

Many physicians and analysts expect that the major cost effect of improved transplantation outcomes will flow from shifting ESRD patients from dialysis treatment to transplantation. The Gottschalk Report of 1967 projected such an effect. A decade later, in 1978, Stange and Sumner [16] made the same argument. They calculated that:

- A shift of 1000 patients from center dialysis to transplantation would yield ten-year savings of $279 million to $370 million, at the human cost of an estimated reduction of 7 to 17 percent in life expectancy.
- A shift of 1000 patients from home dialysis to transplantation would reduce costs by $103 million to $142 million, despite an estimated 10 to 20 percent reduction in life expectancy.

Patient survival today has improved in many centers since Stange and Sumner’s work was published. As discussed earlier, data from the ESRD-MIS indicate patient survival rates for transplant recipients that are now often comparable to those of age-matched dialysis patients. The UCLA registry reports improvements in one-year cadaveric patient survival rates to 90 percent for first grafts in 1981, an improvement of between 12 and 23 percent over the survival estimates used by Stange and Sumner. Partly this results from a philosophic shift in treating rejection—letting the transplanted kidney go but saving the patient—and partly from choosing recipients with risk of death no greater than on dialysis. Although further significant increase in patient survival is not expected, the present situation represents substantial improvement over that of a few years ago.

In addition to improvements in patient survival, the rising curve of graft survival since the mid-1970’s for kidney recipients is illustrated by the UCLA and ESRD-MIS data, and by the improved values of graft survival observed for control groups during the recent Cyclosporine trials. We believe that the Stange and Sumner study, were it to be repeated today, would project greater savings in both lives and costs than were estimated in 1978, because of improvements in graft and patient survival. Roberts and colleagues [17] supported this hypothesis in a recent analytical study of the ESRD program. They projected that improved survival rates for cadaveric transplant patients could reduce
annual medical care costs to the level of the least costly dialysis treatment group.

Dr. H. Krakauer of NIH has also studied the fiscal effects of improved transplant outcomes on the ESRD program using a mathematical model, based on differential equations, that incorporates HCFA and KTHS data [27]. The Krakauer model is an aggregated three-state mathematical model of the ESRD treatment population. Patients enter the ESRD treatment system from the general population at a rate consistent with recent HCFA experience. The three treatment states are: alive and treated by dialysis; alive, with a functioning kidney graft; and death. These states are linked by appropriate transition rates. The preliminary model does not classify patients by type of dialysis treatment, type of transplant, or age and the other risk factors that influence outcome. Furthermore, as described in Sec. III, the mortality rate for dialysis is assumed constant, and outcome patterns for transplantation are represented by realistic time-dependent graft-failure and mortality functions. These functions derive from patterns observed for subsets of patients who were followed during the five years of KTHS follow-up.

Dr. Krakauer arrived at the rather conservative conclusion that improvements in transplant efficacy, coupled with growth in the number of transplant recipients, should give "significant medical and social benefits without increasing costs."

Although not surprised by these results, we wished to explore alternative projections and therefore requested that Dr. Krakauer perform additional calculations under a revised set of hypotheses. He originally estimated total treatment costs, but because total ESRD program costs are highly sensitive to the costs of treating dialysis patients, we preferred to project outcomes and costs in terms of their differences from baseline. We also used treatment outcomes and cost estimates that were suggested by results from the Cyclosporine trials. Furthermore, where Dr. Krakauer estimated cost effects over a ten-year period, we restricted ourselves to five years as representing the maximum interval permitted by the available data for transplant outcomes, the possibility of new initiatives for preventing ESRD, the likelihood of major changes in treatment outcomes and costs for both dialysis and transplantation, and the inappropriateness of using linear extrapolation of ESRD incidence rates over longer periods.

Four different cases were used for purposes of projecting the simple cost effects (neglecting discounting) of improved transplant outcomes for the five-year interval. (All cases assume a yearly rate of increase of 1000 patients entering the ESRD program and assume no change in current reimbursement policy for transplantation.)
• **Case 1 (Baseline):** Transplant procedures funded by HCFA grow at the rate of 192/year, starting with 4400 procedures in 1981, resulting in a total of 24,400 procedures over five years; graft survival is 61 percent at one-year post-transplant; and a 9 percent annual failure rate occurs.

• **Case 2:** HCFA finances 8000 transplants per year (nearly twice the number financed in 1981), for a total of 40,000 over five years; graft survival remains at 61 percent.

• **Case 3:** HCFA finances 8000 transplants per year; expected graft survival of 74 percent one-year post-transplant is realized; and the annual graft failure rate drops to 5 percent.

• **Case 4:** HCFA finances 8000 transplants per year; the expected graft survival improves further to 89 percent one-year post-transplant, and an annual graft failure rate of 2 percent is realized.

These cases and a five-year planning horizon have been chosen to illustrate the fiscal and human impacts on the ESRD program of improved outcomes and accelerating transplant procedures.

In Table 6 we project the effects of Cases 2, 3, and 4 in comparison with the baseline case. Five-year totals are presented for the ESRD program in terms of

• Transplants performed,
• Transplant failures,
• Number of person-years with a functioning graft,
• Number of person-years requiring maintenance dialysis, and
• Fraction of patients with functioning graft at the end of five years.

For purposes of illustration, we compare Case 4, which has the most favorable hypothetical outcomes, with the baseline case. The baseline 5-year projection is based on 24,400 Medicare-financed procedures and a one-year graft survival of 61 percent. This leads to 11,600 transplant failures returning to dialysis; 90,000 person-years with a functioning graft; 340,000 person years of dialysis; and 21 percent of the ESRD population alive with a functioning graft at the end of the five-year interval (of whom 10 percent remain eligible for Medicare benefits).

Case 4 assumes 40,000 Medicare-financed transplant procedures take place during the five-year period and that one-year graft survival of 89 percent is reached. The 15,600 additional transplants result in 6300 transplant failures, or 5300 fewer than baseline. Case 4 also leads to 141,000 person years with a functioning graft (an improvement of 51,000 over baseline), 303,000 person years on dialysis (a reduction of
Table 6

HYPOTHETICAL EFFECTS ON ESRD POPULATION IN THE
FIVE-YEAR INTERVAL 1982-1986

<table>
<thead>
<tr>
<th>Item</th>
<th>Baseline</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of transplants performed</td>
<td>24,400</td>
<td>40,000</td>
<td>40,000</td>
<td>40,000</td>
</tr>
<tr>
<td>(difference from baseline)</td>
<td>(15,600)</td>
<td>(15,600)</td>
<td>(15,600)</td>
<td>(15,600)</td>
</tr>
<tr>
<td>Transplant outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year graft survival</td>
<td>61%</td>
<td>61%</td>
<td>74%</td>
<td>89%</td>
</tr>
<tr>
<td>Transplant failures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>returning to dialysis</td>
<td>11,600</td>
<td>17,200</td>
<td>12,900</td>
<td>6,300</td>
</tr>
<tr>
<td>(difference from baseline)</td>
<td>(5,600)</td>
<td>(1,300)</td>
<td>(-5,300)</td>
<td>(5,300)</td>
</tr>
<tr>
<td>Person-years with</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>functioning transplant</td>
<td>90,000</td>
<td>111,000</td>
<td>126,000</td>
<td>141,000</td>
</tr>
<tr>
<td>(difference from baseline)</td>
<td>(21,000)</td>
<td>(36,000)</td>
<td>(51,000)</td>
<td>(51,000)</td>
</tr>
<tr>
<td>Person-years of dialysis</td>
<td>340,000</td>
<td>323,000</td>
<td>315,000</td>
<td>303,000</td>
</tr>
<tr>
<td>(difference from baseline)</td>
<td>(-17,000)</td>
<td>(-25,000)</td>
<td>(-37,000)</td>
<td>(-37,000)</td>
</tr>
<tr>
<td>Percent of ESRD population</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>with functioning transplant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>as of January 1, 1987,</td>
<td>21%</td>
<td>28%</td>
<td>32%</td>
<td>38%</td>
</tr>
<tr>
<td>within three-year eligibility limit</td>
<td>10%</td>
<td>15%</td>
<td>19%</td>
<td>23%</td>
</tr>
</tbody>
</table>

37,000 from baseline), and 38 percent of the ESRD population alive with a functioning graft (of whom 23 percent remain eligible for Medicare benefits for transplantation).

Case 2 demonstrates an implausible situation where transplant rates increase with no underlying improvement in outcome: In the absence of improved outcomes, increasing the rate to 8000/year would increase the number of transplant failures by 5600 compared with only 1300 transplant failures for Case 3 and a decrease of 5300 failures for Case 4. The increase in patient-years with a functioning graft ranges from 21,000 (Case 2) to 51,000 (Case 4) and the number of dialysis-patient-years compared with the baseline decreases from -17,000 (Case 2) to -37,000 (Case 4). Finally, the fraction of the ESRD population with a functioning graft, currently estimated at 21 percent, grows to 32 percent (Case 3) or 38 percent (Case 4) after five years of intensive
transplant activity. Thus, if improvements in outcomes occur and are coupled with intensive transplant activity, the result will be more patients with improved kidney function, fewer transplant failures, and reduced reliance on dialysis.

The savings in ESRD program resource requirements for the best case, then, are equivalent to roughly a 10 percent decrease in dialysis utilization over the five-year period. Because the aggregated Krakauer model does not reflect the altered composition of the dialysis population, both with regard to age and treatment mix, further analysis is required to define the true impact of the changing dialysis population on overall program costs.

To estimate the cost effects of the above projection, we use the following estimated health care costs to HCFA (in 1979 dollars). We have assumed that new protocols will cost somewhat less, in terms of both initial costs and the costs of maintenance in the event of failure, based on our current understanding of Cyclosporine's clinical impact.

<table>
<thead>
<tr>
<th>Costs</th>
<th>Case 2</th>
<th>Cases 3 &amp; 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-year of maintenance dialysis</td>
<td>$20,000</td>
<td>$20,000</td>
</tr>
<tr>
<td>Initial transplantation costs</td>
<td>21,000</td>
<td>16,000</td>
</tr>
<tr>
<td>Patient-year of maintenance with functioning graft</td>
<td>4,000</td>
<td>4,000</td>
</tr>
<tr>
<td>Transplant failure costs</td>
<td>12,000</td>
<td>12,000</td>
</tr>
<tr>
<td>Patient-year of maintenance dialysis after transplant failure</td>
<td>23,000</td>
<td>20,000</td>
</tr>
</tbody>
</table>

Using these cost elements and current coverage policy, we find that increasing the number of transplant recipients without improving transplantation outcomes (Case 2) actually costs an additional $170 million above the baseline over five years, due mainly to the effects of returning transplant failures to dialysis. On the other hand, if transplant outcomes improve to either 74 percent or 89 percent, as hypothesized in Cases 3 and 4, the estimated five-year savings to Medicare (in 1979 dollars) are $300 million or $570 million, respectively.

These estimated cost savings to Medicare of improved transplantation outcomes represent 5 to 10 percent of the costs of dialysis over the projected five-year period. The number of dialysis patient-years, from
baseline through Case 4, proceeds from 340,000 to 323,000 to 315,000 to 303,000. Total health care costs to HCFA (in 1979 dollars) for patients receiving dialysis under these several scenarios, then, fall in a $6 billion to $7 billion range. Several further caveats about this analysis bear repeating.

First, our estimates of future treatment costs, although suggested by the early results from Cyclosporine trials, still rely heavily on 1979 costs and treatment patterns. They do not yet reflect the influence of such factors as the approval of ATGAM or other drugs, which may alter the costs of hospital-based rejection treatment, changes in the costs of acquiring kidneys, or the shift to prospective payment of transplantation services.

Second, the assumption of an abrupt increase in the number of Medicare-financed transplant procedures performed from 4400 per year in the 1981 baseline case to 8000 annually in Cases 2, 3, and 4 deserves elaboration. Obviously, a near doubling in one year is infeasible, a gradual increase being more realistic. The abrupt increase is used for simplicity and concreteness, and to provide a preliminary range of estimates. But we believe that the 8000 transplant per year level is attainable by 1986 for the following reasons. If, as suggested by recent data, Medicare finances nine out of ten transplants performed in the United States, then the current annual rate of growth in HCFA-supported transplants is close to 500 procedures annually, based on data from 1981, 1982, and the first half of 1983. If this annual increment is maintained through 1986 (a conservative estimate), then the total in that year will be 7000, and a slight acceleration would easily lead to the 8000 procedures projected here, and still not reach limits set by the size of the pool of potential transplant candidates.

We also believe that the rate of organ acquisition is likely to increase for several reasons. Increased public concern for transplantation is likely to increase the number of kidneys obtained. Increased scrutiny of organ procurement is apt to result in greater efficiency of organ procurement agencies. Improved transplantation outcomes will probably stimulate increased levels of organ acquisition; that is, the number of acquired kidneys has been performance-limited, not simply limited by physical scarcity.

Third, the values of 74 and 89 percent graft survival require comment. These values are suggested by early clinical trials with Cyclosporine. But the efficacy of this new compound, including a detailed assessment of its side effects, has yet to be established widely. In addition, details are limited for patients who have been followed for more than one year. Moreover, the drugs will not be adopted immediately but over some period of time. Nevertheless, for analytic purpose, the
values have a basis in early clinical trials and usefully bracket the future possibilities.

Fourth, it may be asked, Why expect outcomes to remain level as the volume of patients increases after the initial transition? For one thing, surveys of ESRD patient records lead us to conclude that the individuals who would constitute the pool from which additional transplant candidates would be drawn over a five-year period are not, in age and medical status, at significantly greater risk than current transplant recipients. For another, immunosuppression and not surgery appears to limit successful outcomes. Furthermore, no data exist to definitively support a relationship between patient characteristics, transplant center characteristics including volume and treatment regime, and transplant outcomes. Studies of other surgical procedures suggest that outcomes are likely to improve as volume increases, but this effect, should it also occur in kidney transplantation, may be balanced by the broadening of selection criteria for potential recipients to include high-risk patients. It is still premature, we believe, to use more complex models of transplant outcome than the simple bracketing by average values chosen here. Later, as data are gathered for new protocols and the distribution of risk factors for large subgroups of potential patients, including transplant type, age, race, immune status, existing disease state, etc., these factors may be included as part of a more detailed analysis.

One further remark about the model's limitations is required. The Krakauer model employs outcome patterns that exhibit simultaneous improvements in both patient and graft survival. This contrasts with patterns observed during the early Cyclosporine trials, where graft survival did not appear to be accompanied by important improvements in patient mortality. Therefore, the depiction of patient survival is not as realistic as other aspects of the model. For this reason, we have omitted any projection of differences in patient survival among the cases summarized in Table 6.

In Sec. III we indicated that, with current or improved graft survival rates, cost savings of $30,000 to $63,000 could be expected over a five-year period for a transplant recipient compared with a dialysis patient. In the immediately preceding discussion, however, the projections for an aggressive transplantation effort based upon significant improvements in outcomes, and an immediate doubling of transplants resulting in 38 percent of ESRD patients having a functioning graft in the fifth year, yield less than a 10 percent reduction in estimated ESRD program costs over the five-year period.

Two reasons underlie these apparently modest cost effects:
• Suitable transplant recipients and costs for transplantation constitute only a small portion of the ESRD program. About 80 to 85 percent of current expenditures are for dialysis patients. The major costs of both success and failure for transplant occur during the first year, while cost savings generally accrue in later years. Limited short-term cost savings, therefore, may divert policy attention away from choices that should be taken now if long-term savings are to be captured.

Nevertheless, the effects are in the appropriate direction: a significant improvement in quality of life accompanied by treatment cost savings.
V. CONCLUDING OBSERVATIONS

Several observations merit reiteration here, the most important one being the following: If a major advance in transplantation results in significant improvement in transplantation outcomes, as measured by cadaver graft survival, genuine cost savings will be realized relative to the present situation.

One major source of cost savings will derive from doing transplantation better; this means not only reducing the cost of successful transplantation, but more important, reducing the costs of transplant failure. Indeed, the beneficial cost effects of improved transplantation can be expected to appear here initially, since they are within the domain of the existing transplantation system and do not depend on cooperation by others.

The second major source of cost savings from improved transplantation will derive from shifting ESRD patients away from dialysis to transplantation. The magnitude of the savings, of course, will depend on the magnitude of the shift. The shift, in turn, will depend primarily upon the availability of donor kidneys and secondarily upon referrals of dialysis patients for transplantation, a process dominated, if not controlled, by nephrologists.

Our second conclusion is that beneficial cost effects will be realized gradually, not abruptly. Too many factors influence changes in the rate and cost of transplantation to permit a facile projection of how rapidly cost savings can be expected to accrue. Even though we posit a sharp improvement in transplantation outcomes and rates for analytical purposes, the initial rate of adoption of improved techniques is more likely to be gradual and continuous, not abrupt and marked by discontinuity.

As a third conclusion, we observe that other cost savings, in addition to those from Medicare, will be realized that are usually hidden from view. These will come from:

- Reduced costs to other government programs: Medicaid cost savings for both federal and state governments will be realized and disability benefits will be lower.
- Higher economic contributions of individuals: Employment of transplant recipients will increase and exceed that of dialysis patients; earnings will be higher; and taxes paid will be higher.
Several other studies support the argument that "hidden savings" will result from successful transplant. Krakauer [27] estimates that a successful transplant recipient has average earnings of $11,000 per year, based on the KTHS experience. Evans et al. [26], though not directly addressing this issue, provide data on rehabilitation benefits of transplants showing that successful transplant patients are more likely to be fully employed than failed transplant recipients or patients on home hemodialysis, in-center hemodialysis, or continuous ambulatory peritoneal dialysis (CAPD), and that fewer successful transplant patients are disabled and unable to work because of poor health.

Finally, in a conservative vein, we note that the system for treating chronic kidney failure will be limited in its capacity to respond to major improvements in transplantation outcomes by two related concurrent developments. First, the introduction of diagnostic related groupings (DRGs) as the basis for prospective reimbursement for Medicare in-patient services will affect the transplantation community in the months ahead. Whether DRGs facilitate or hinder the system's ability to take advantage of transplant improvements will depend on the complexity of the implementing regulations and on the precise incentives embodied in them. Already, kidney acquisition costs have been excluded from the new system and are to be billed directly to Medicare.

The second concurrent development that will strain the capacity of the ESRD treatment system to respond to transplant advances is the issuance of new regulations covering the reimbursement of outpatient dialysis treatment. These regulations will precipitate movement among hospital-based, free-standing, and home-dialysis treatment sites, and between hemodialysis CAPD treatment modes. If nothing else, the dialysis system will experience an overload associated with new reimbursement procedures in the immediate future. The new regulations will also place pressure on nephrologists' incomes and perhaps diminish the economic incentive to refer patients for transplantation.

In summary, then, if genuine progress in transplantation outcomes occurs, as now appears likely, there will be medical, social, and fiscal benefits, including cost savings to the Medicare program. Government policy should then support increased transplantation, and especially efforts to increase the procurement of kidneys. Even so, the ESRD program will remain primarily a dialysis program. Improved transplantation will reduce program costs in an important way but will hardly eliminate the need for continued federal government support of dialysis.
REFERENCES


