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BENEFIT EVALUATION OF SPACE PROCESSING OF BIOLOGICAL MATERIALS

FINAL REPORT
BENEFIT EVALUATION OF SPACE PROCESSING
OF BIOLOGICAL MATERIALS

CONTRACT NAS-9-15338

FINAL REPORT

December 1977
NOTE OF TRANSMITTAL

This study of the potential economic and social benefits of the space processing of three biological substances was performed for the Lyndon B. Johnson Space Center, National Aeronautics and Space Administration, under Contract NAS-9-15338. The NASA Technical Officer for this study was Mr. Herbert Greider.

The ECON study team consisted of Ms. Celia Drumheller, Mr. Keith Lietzke, Mr. B. P. Miller, Mr. Jay Perrine and Dr. Mark Thompson. Ms. Drumheller and Mr. Lietzke performed the study of Beta cells, Mr. Perrine performed the study of lymphocytes and urokinase-producing cells and Dr. Thompson examined the methodologies used for the evaluation of the economic and social impacts of biomedical research. Mr. B. P. Miller was Project Manager for this study.

B. P. Miller
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SUMMARY AND RECOMMENDATIONS
OBJECTIVES OF STUDY

The objectives of this study are to evaluate and select methodologies for use in estimating the potential economic and social benefits of applications of the NASA space bioprocessing program. The selected methodologies are then to be used to estimate the potential benefits that could result from the successful research and clinical application of three candidate space bioprocessing substances.

The central questions to be answered in this study are:

1. What are the accepted methodologies for the evaluation of the benefits of medical research?

2. What are the estimated potential benefits that could result from a successful research and clinical application program for specified candidate substances for space bioprocessing?
OBJECTIVES OF STUDY

- SURVEY METHODOLOGIES USED TO ESTIMATE BENEFITS OF MEDICAL RESEARCH. RECOMMEND ACCEPTABLE METHODOLOGIES FOR THE EVALUATION OF THE ECONOMIC AND SOCIAL BENEFITS OF CANDIDATE SUBSTANCES FOR NASA SPACE BIOPROCESSING PROGRAM.

- ESTIMATE THE POTENTIAL BENEFITS OF SUCCESSFUL RESEARCH AND CLINICAL APPLICATION OF THREE SUBSTANCES THAT ARE CANDIDATES FOR SPACE BIO­PROCESSING. THE THREE CANDIDATE SUBSTANCES ARE:

  + SEPARATION AND CLASSIFICATION OF LYMPHOCYTE SUBGROUPS
  + SEPARATION OF UROKINASE-PRODUCING CELLS
  + SEPARATION OF BETA CELLS.
CANDIDATE SUBSTANCES AND APPLICATIONS STUDIED

The purpose of the work described in this report is to provide a rational analytical basis for the evaluation of the potential benefits of the processing of biological materials in space. These quantitative evaluations could then be used by decision makers, in conjunction with other information, as a basis for the selection of candidate projects. In the work performed to date, a preliminary evaluation has been made of the potential benefits of three candidate space processed biological materials. The three materials investigated are human lymphocytes, urokinase and Beta cells. In the case of human lymphocytes, electrophoresis is to be used to separate and classify lymphocyte subgroups in order to improve the matching of donors and recipients for kidney transplantation. It is believed that lymphocytes play an important role in immune functions, and that the results of the proposed research, if successful, could lead to improved kidney transplant acceptance. Urokinase is a drug which appears to be able to dissolve blood clots, and may be useful in the treatment of thromboembolic diseases. Urokinase can either be extracted from human urine or from kidney cells. Urokinase produced from human urine is not used in the United States because of purity problems with fever-producing precursors which are difficult to remove from the urine. The alternative technique for the production of urokinase is to separate urokinase-producing cells from all other kidney cells. It has been theorized that using electrophoretic separation in space, kidney cells could be separated with respect to cell function, and returned to earth in a viable condition. Then, the urokinase-producing cells would be propagated in earth-based facilities.

Beta cells found in the human pancreas could provide a highly effective means for the treatment of juvenile-onset diabetes. As in the case of lymphocytes and urokinase, it is believed that electrophoretic separation in space could be used to extract Beta cells which could then be injected into a diabetic patient. If successfully accomplished, the use of Beta cells could eliminate many of the complications that arise from the use of bovine and porcine insulin for the treatment of diabetes.
<table>
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<th>SUBSTANCE</th>
<th>SPACE PROCESS</th>
<th>MECHANISM</th>
<th>CLINICAL APPLICATION</th>
<th>CLINICAL IMPACT</th>
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<td>BETA CELLS</td>
<td>SEPARATE BETA CELLS FROM OTHER PANCREATIC CELLS</td>
<td>ELECTROPHORESIS</td>
<td>INSULIN-DEPENDENT DIABETICS</td>
<td>REDUCE INCIDENCE AND SEVERITY OF COMPLICATIONS OF DIABETES</td>
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<td>LYMHPOCYTES</td>
<td>SEPARATE AND CLASSIFY LYMPHOCYTE SUBGROUPS</td>
<td>ELECTROPHORESIS</td>
<td>KIDNEY TRANSPLANTS IN END-STATE RENAL DISEASE PATIENTS</td>
<td>IMPROVE SUCCESS RATE OF TRANSPLANTS</td>
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<tr>
<td>UROKINASE</td>
<td>SEPARATE UROKINASE-PRODUCING CELLS FROM OTHER KIDNEY CELLS</td>
<td>ELECTROPHORESIS</td>
<td>THROMBOEMBOLIC DISEASES, SPECIFICALLY, PULMONARY EMBOLISMS</td>
<td>LYSE (DISSOLVE) BLOOD CLOTS</td>
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STUDY APPROACH

The approach used in this study is delineated in the opposite chart.

An extensive review of the literature of the economics of medical research was performed to identify the techniques used for the estimation of benefits of medical research. This study of methodologies identified the fact that it is necessary to consider both the economic and social benefits of medical research. The economic (or direct benefit) results from the reduced cost of a disease treatment which would yield an equal or greater productive life expectancy when compared to present treatments of the same disease. The social (or indirect benefit) stems from the possible extension of life and increased productivity from improved health resulting from the new disease treatment. Using available statistics on the current methods of treatment and expert estimates on the new methods of treatment, the benefits of the proposed research are calculated as the differences between the costs and productive life expectancies associated with existing treatment systems, and similar characteristics associated with the new treatment systems that could result from the processing of biological materials in space.
STUDY APPROACH

- Review literature on methodologies for estimation of economic and social benefits of medical research
- Select methodologies for evaluation of economic and social benefits that are widely used and generally accepted
- Select clinical applications for the three candidate substances for space bioprocessing
- Obtain mortality, morbidity and cost statistics for current treatment of selected clinical applications
- Obtain estimates of impact of candidate substances on morbidity, mortality and cost of treatment
- Estimate the potential economic and social benefits of the three candidate substances using the selected methodologies
SUMMARY OF RESULTS

This study has shown that several methodologies are used in the fields of health care economics, insurance and systems analysis to evaluate the benefits of improved disease treatment systems. ECON has selected a transitional probability (Markovian) methodology to model the disease treatment and to provide insight into the impact of new treatment system on morbidity, mortality, as well as the duration and cost of treatment. Using the model of the disease treatment system, the results are quantified as changes in the cost of treatment of the disease and its complications and as increased income as a result of an extended productive lifetime.

The techniques used in this analysis (transitional probability modeling and present value of future earnings) are well established and widely accepted in the health care economics community.
SUMMARY OF RESULTS

- STUDY HAS IDENTIFIED ACCEPTABILITY OF TRANSITIONAL PROBABILITY METHODOLOGY AND VALUE OF HUMAN CAPITAL APPROACH TO ESTIMATION OF ECONOMIC AND SOCIAL BENEFITS OF IMPROVED DISEASE TREATMENT

- DEVELOPED OR IMPROVED OPERATING BENEFIT MODELS FOR THREE CANDIDATE SUBSTANCES AND CLINICAL APPLICATIONS:
  + END STAGE RENAL DISEASE (LYMPHOCYTE SUBGROUP SEPARATION)
  + PULMONARY EMBOLISMS (SEPARATION OF UROKINASE PRODUCING CELLS)
  + HUMAN DIABETES (SEPARATION OF BETA CELLS)

- ESTIMATED THE POTENTIAL ECONOMIC AND SOCIAL BENEFITS OF SPACE BIOPROCESSING IN EACH OF THE ABOVE DISEASE TREATMENTS
SUMMARY OF BENEFITS

This figure summarizes the quantified economic and social benefits for the three candidate substances and clinical applications studied. For the purpose of this study, it was assumed that the new treatment systems would be available for initial use in 1985. It should be noted that the total benefits are given for the lifetime of the initial patient population that begins treatment in 1985, and that additional benefits could be realized as the new treatment systems are used for additional patients in each successive year.

Annual benefits for each year of treatment from disease onset to patient death have been discounted by 6 percent per year to the initial year to reflect the time value of money. Aggregate benefits are expressed in 1985 dollars since this is the assumed first year of operation. A 6 percent inflation rate was used. The use of 6 percent for both discount and inflation rates is purely coincidental.
### SUMMARY OF BENEFITS

*(ALL DOLLAR VALUES ARE 1985$ AT 6% DISCOUNT AND INFLATION RATES)*

<table>
<thead>
<tr>
<th>DISEASE TREATMENT</th>
<th>CANDIDATE SUBSTANCE</th>
<th>NUMBER OF PATIENTS PER YEAR BECOMING AFFLICTED</th>
<th>BENEFIT PER PERSON FROM TIME OF DISEASE ONSET*</th>
<th>YEARS OF LIFE EXTENDED BY THE SPACE-BASED ENDEAVOR</th>
<th>AVERAGE PER PERSON PRIVATE BENEFIT FROM REDUCED TREATMENT COSTS</th>
<th>AVERAGE PER PERSON PRIVATE BENEFIT FROM EXTENDED LIFE (EARNINGS)</th>
<th>ESTIMATED TOTAL BENEFIT FOR LIFETIME OF INITIAL TREATMENT POPULATION</th>
<th>ARE OTHER DISEASE TREATMENTS POTENTIALLY IMPACTED BY THIS SPACE-PROCESSING SPECIMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>END STAGE RENAL DISEASE</strong></td>
<td>LYMPHOCYTE SEPARATION</td>
<td>10,000</td>
<td>$124,222</td>
<td>3.39</td>
<td>$11,667</td>
<td>$22,670</td>
<td>$1,200,000,000</td>
<td>YES, OTHER TRANSPLANTS AND POSSIBLY CANCER</td>
</tr>
<tr>
<td><strong>PULMONARY EMBOLISM</strong></td>
<td>UROKINASE</td>
<td>750,000</td>
<td>$4,052</td>
<td>1.56</td>
<td>$ - 85</td>
<td>$4,137</td>
<td>$3,000,000,000</td>
<td>YES, OTHER THROMBO-EMBOLIC DISEASE</td>
</tr>
<tr>
<td><strong>DIABETES</strong></td>
<td>BETA CELLS</td>
<td>1,240,000***</td>
<td>$23,000</td>
<td>5.2</td>
<td>$11,040****</td>
<td>$12,860</td>
<td>$29,600,000,000</td>
<td>NO</td>
</tr>
</tbody>
</table>

* Includes private and public sector benefits for ESRD. There are no public sector benefits for pulmonary embolism and diabetes.

** Assumes beta cell transplant.

*** This is the number of diabetics who could constitute the treatment population in the first year. The population in successive years would be increased by the incremental number of new juvenile-onset diabetics diagnosed in that year.

**** Includes diabetic treatment and diabetic complications cost benefits.
RECOMMENDATIONS

The results of this study conclusively demonstrate that it is possible to use analytical techniques to quantify the potential economic and social benefits of new treatment systems that could be developed as a result of successful space bioprocessing experimentation. The specific benefit estimates are highly sensitive to the cost, morbidity and mortality input data used in the models. For this reason, it is recommended that the benefit estimates be considered to be preliminary until further work can be done to improve the quality of the input data.

Several other substances are also candidates for space bioprocessing experiments. It is recommended that this benefit study be continued to examine the potential benefits of additional candidate substances, thus providing a basis for comparing experiments that could compete for limited resources.

As the reader of this report will note, this is not a benefit/cost study. The costs of the space research, ground research and clinical trials leading to an approved pharmaceutical product have not been considered in this study. Moreover, the benefits assume that the space research and subsequent clinical trials will be fully successful. In order to rate the candidate substances, it is recommended that the additional dimensions of cost and probable outcomes of the research and development programs be considered in further studies of the candidate substances.
RECOMMENDATIONS

- CONTINUE STUDIES TO REFINE COSTS AND PROBABILITIES OF SUCCESS OF THE CANDIDATE SPACE BIOPROCESSING PROJECTS AND OTHER COMPETITIVE METHODS OF ACHIEVING THE SAME TREATMENT OBJECTIVES

- MODEL DISEASE TREATMENTS AND ESTIMATE BENEFITS FOR OTHER SEPARATION CANDIDATES AND CLINICAL APPLICATIONS SUCH AS:
  + STEM CELLS - ESTABLISHMENT OF IMMUNE SYSTEM FOR SUBSEQUENT ORGAN TRANSPLANT
  + GRANULOCYTES - TRANSFUSION FOLLOWING CHEMOTHERAPY AND/OR IRRADIATION FOR ACUTE MYELOBLASTIC LEUKEMIA
  + MEGAKARYOCYTES - TRANSFUSION FOLLOWING CHEMOTHERAPY AND/OR IRRADIATION TREATMENT FOR TUMOR CANCERS
  + PEPTIDE HORMONES - POST STEROID THERAPY
OBJECTIVES: CONTRACT NAS-9-15338

In a previous study for NASA Headquarters, ECON developed and applied a methodology for the evaluation of the potential benefits of space-based research in lymphocyte subgroup separation, and the separation of urokinase-producing cells.

The present study has three objectives. The first is to evaluate the acceptance of the methodology used for the estimation of economic benefits in our earlier study within the community of economists and public policy analysts who work on the evaluation of biomedical research. A second objective is to reassess the economic benefits and to evaluate the social benefits of lymphocyte subgroup separation and the separation of urokinase-producing cells. The third objective is to evaluate the economic and social benefits of the separation of Beta cells.
OBJECTIVES: CONTRACT NAS-9-15338

1. EVALUATE THE ACCEPTABILITY WITHIN THE MEDICAL RESEARCH ECONOMICS COMMUNITY OF THE METHODOLOGY FOR BENEFIT EVALUATION PREVIOUSLY DEVELOPED AND APPLIED BY ECON TO SPACE BIOPROCESSING PROBLEMS UNDER CONTRACT TO NASA HEADQUARTERS.


3. ESTIMATE THE ECONOMIC AND SOCIAL BENEFITS FOR SEPARATION OF BETA CELLS IN SPACE FOR APPLICATION TO TREATMENT OF DIABETES.
BACKGROUND

In our previously referenced study for NASA Headquarters\(^1\), two promising candidate substances for space bioprocessing were selected for benefit evaluation. These two substances were lymphocytes and urokinase. In the case of lymphocytes, ground-based research has led to the classification of two subgroups, and the objective of the space-based research is to further separate and extend the classification process within the two presently identified subgroups. At the present time, using ground-based techniques, urokinase-producing cells cannot be separated from other kidney cells. In both instances, electrophoretic separation in space has been proposed as the mechanism to effect separation. The clinical application selected for study in connection with lymphocyte subgroup classification, is the matching of donors and recipients for kidney transplantation; while the application selected for urokinase is the reduction of blood clots associated with pulmonary embolisms. While other possible applications exist for these two substances, these two applications represent areas where immediate progress could be made if the space-based research is successful.

This preliminary study concluded that very large economic benefits could result from successful lymphocyte subgroup separation. During this earlier study, it was also determined that it is possible that urokinase production costs could be reduced as a result of the successful separation of urokinase-producing cells, thus leading to increased availability and widespread use of urokinase in the treatment of thromboembolic diseases. This, in turn, could lead to a reduction in the number of deaths from pulmonary embolisms, and could possibly reduce the need for some surgical procedures and thus reduce the length of hospital stay.

\(^1\)Preliminary Benefit Analysis of Biological Space Processing, ECON, Inc., 1 September 1976.
BACKGROUND

- Previous study of lymphocyte subgroup separation and separation of urokinase-produing cells used transitional probability techniques to estimate economic benefits.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Lymphocytes</th>
<th>Urokinase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Space Process</td>
<td>Separate and classify subgroups</td>
<td>Separate and concentrate urokinase-producing cells</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Electrophoresis</td>
<td>Electrophoresis</td>
</tr>
<tr>
<td>Clinical Application</td>
<td>Kidney transplantation</td>
<td>Thromboembolic diseases</td>
</tr>
<tr>
<td>Clinical Impact</td>
<td>Improve transplant acceptance</td>
<td>Lyse blood clots</td>
</tr>
</tbody>
</table>
THE NEED FOR QUANTIFIED ESTIMATES OF BENEFITS

The common starting point for analysts of biomedical research is the need to quantify estimates of benefit. This need is apparent in decision making. In annual budget processes, research projects compete against each other and with other social priorities for limited resources. Whenever one project is funded in preference to another of equal cost, it is implicitly rated higher on the scale of anticipated benefits. To date, that scale has primarily reflected scientific merit, although recent years have seen efforts to bring encompassing societal priorities to bear.

As conceptual difficulties, data deficiencies, and individual resistance have hampered explicit quantification of the rationale behind funding decisions, they continue to be made on an ad hoc basis. For so long as the obstacles to quantification endure, opportunities for inconsistency persist. Quantifying the expected benefits forces decision makers to adopt a consistent comprehensible scale (1) for explaining and justifying their actions, (2) for enabling systematic adherence to relevant priorities and thereby avoiding suspicions of unfairness, and (3) for relating resource commitments to anticipated return.
THE NEED FOR QUANTIFIED ESTIMATES OF BENEFITS

- COMPETITION FOR LIMITED RESOURCES

- DECISIONS BASED UPON SCIENTIFIC MERIT AND SOCIETAL PRIORITIES

- ENCOURAGES DECISION MAKERS TO ADOPT A CONSISTENT AND UNDERSTANDABLE SCALE FOR
  + EXPLAINING ACTIONS
  + MAINTAINING ADHERENCE TO PRIORITIES
  + RELATING RESOURCE COMMITMENTS TO EXPECTED RESULTS
DEFINITION OF ECONOMIC AND SOCIAL BENEFITS

Two classes of benefits must be considered when the benefits of a proposed new method of disease treatment are to be evaluated. For the purpose of this study, these two classes of benefits are considered to be the economic (or direct) benefits and social (or indirect) benefits. The economic benefits are defined as those benefits that occur in the private and public sector from the changes in the cost of treatment of the disease and its complications. Social benefits are defined as those benefits that result from decreases in mortality and/or morbidity as a result of the new treatment process. For example, prior to the use of penicillin, many bacterial infections required hospitalization and long periods of convalescence. With the use of penicillin, an economic benefit results as the cost of treatment of bacterial infection has been decreased. Further, a social benefit also results as the use of penicillin has reduced the incidence of death and periods of disability from bacterial infection.

The purpose of a benefit evaluation study is to express these benefits in measurable quantities such as dollars and years of life extension.
DEFINITION OF ECONOMIC AND SOCIAL BENEFITS

- TWO BENEFIT COMPONENTS
  + ECONOMIC - COST OF DISEASE TREATMENT
  + SOCIAL - DECREASED MORTALITY AND/OR INCREASED PRODUCTIVITY

- PURPOSE OF BENEFIT EVALUATION IS TO CONVERT ABOVE TO SCALAR QUANTITIES
  + DOLLARS
  + YEARS
SOCIAL BENEFITS

An improved state of health is a social benefit which can be measured in several ways. The number of persons who avoid a premature death can be counted and a value placed on their lives. Death can be postponed for some period of time which can be measured. Regardless of whether life is extended there is often increased productivity from improved health, that is, people who might otherwise be debilitated could return to work. Most of these improvements can then be quantified in dollars or some scalar quantity such as average number of years of life extension. When these benefits are compared to other candidate substance benefits, a ranking is possible.
SOCIAL BENEFITS

- DECREASED MORTALITY
  + AVOID DEATH FROM SERIOUS ILLNESS
  + POSTPONE DEATH FOR N NUMBER OF YEARS IN SEMIHEALTHY STATE

- INCREASED PRODUCTIVITY
  + IMPROVED HEALTH
  + SHORTENED MEDICAL TREATMENT

- CONVERT ABOVE TO SCALAR QUANTITIES
KEY QUESTION

The key question to be addressed in the evaluation of social benefits is: What is the benefit of extending the life of a person who is afflicted with some specific disease? This question can be rephrased as: What is the benefit of extending the average life expectancy of a group of persons all afflicted with the same disease?
KEY QUESTION

WHAT IS THE BENEFIT OF EXTENDING A PERSON'S LIFE (OR GROUP OF PERSONS AFFLICTED WITH THE SAME DISEASE) N YEARS?
VALUING HUMAN LIVES

The concept of placing an economic value on reductions in mortality and morbidity is common

to several professions. The techniques used in these professions were reviewed in order to select
techniques for use in this study that have broad acceptance.
VALUING HUMAN LIVES

INVESTIGATED TECHNIQUES USED TO VALUE HUMAN LIVES FROM SEVERAL PROFESSIONAL PERSPECTIVES

- LAW
- INSURANCE
- ECONOMICS, ESPECIALLY HEALTH ECONOMICS
- SYSTEMS ANALYSIS OF MEDICAL RESEARCH BENEFITS
INSURANCE INDUSTRY APPROACH

The insurance industry was one of the first to place a value on a human life in order to sell insurance on the value obtained. The approach utilized is to sum all future earnings from the present until age 65, first subtracting costs for one's own consumption, and then discounting that amount to the present using a risk-free interest rate (about 4 percent). The concept is that a person, particularly a family breadwinner, should insure his life for an amount equal to the capitalized value obtained so that in the event of his death the family would obtain an income equal to that of the deceased if he had survived. This technique is called the capitalized human value method, or human capital technique.
INSURANCE INDUSTRY APPROACH

SUM ALL FUTURE EARNINGS TO AGE 65 (OR 62), SUBTRACT ONE'S OWN CONSUMPTION, AND THEN OBTAIN PRESENT VALUE OF THE NET USING A SUITABLE RISK-FREE INTEREST RATE.

(ONE SHOULD THEN OBTAIN INSURANCE EQUAL TO THIS AMOUNT TO PROVIDE THE SAME INCOME AS WOULD BE EXPECTED HAD THE INDIVIDUAL LIVED.)
LIFE VALUES FROM LEGAL JUDGMENTS

The courts have long been called upon to determine the value of a human who has been killed in a manner where fault can be proven, such as in a plane crash or auto accident. After the determination of guilt by legal methods, the decision has to be made on a pecuniary value in the wrongful death case. The award is generally made after expert testimony by an actuary or economist who in some manner calculates the present value (discounted) of expected future earnings and, depending on state laws, adds additional sums for such family losses as training of children. These awards are entirely dependent on the exact situation of the person at the time of death (age, income, family size, dependents, age of dependents, etc.).
LIFE VALUES FROM LEGAL JUDGMENTS

IN WRONGFUL DEATH CASES THE AWARD IS USUALLY DETERMINED BY:

• EXPERT TESTIMONY ON THE PRESENT VALUE OF EXPECTED FUTURE EARNINGS (FOR A CHILD, THE PROBABLE EARNINGS MINUS SUPPORT COSTS TO RAISE CHILD TO ADULTHOOD)

• PECUNIARY LOSS OF PRESENT AND PROBABLE FUTURE BENEFITS
  + TRAINING, GUIDANCE AND ADVICE (ESPECIALLY OF CHILDREN)
  + SOCIETY AND COMPANIONSHIP

• TOTAL AWARD QUITE DEPENDENT ON CONDITIONS AT TIME OF DEATH (INCOME, AGE, DEPENDENTS, ETC.)
ECONOMICS AND SYSTEMS ANALYSIS APPROACHES

Medical economics and systems analysis studies have utilized the four techniques listed on the opposite page. These techniques will be discussed on the following pages.
ECONOMICS AND SYSTEMS ANALYSIS APPROACHES

IN GOVERNMENT BENEFIT-COST AND MEDICAL RESEARCH FUNDING STUDIES, FOUR TECHNIQUES HAVE BEEN EMPLOYED:

1. HUMAN CAPITAL TECHNIQUE
2. IMPLICIT VALUE TECHNIQUE
3. LIFE-VALUE TECHNIQUE
4. WILLINGNESS-TO-PAY TECHNIQUE
HUMAN CAPITAL TECHNIQUE

The human capital technique, in which future earnings are discounted to obtain present values, is widely utilized. Tables are generated from government-supplied employment and income statistics so that all members of society are represented. This technique has by far the widest utilization. Medical studies generally make use of tables generated by Dorothy P. Rice, who is now the director of the National Center for Health Statistics. The criticisms against the use of this technique are that women, the elderly and minorities are unfairly valued and that income, in general, is no indicator of worth. This technique, in its many variations, is probably the most widely used.
HUMAN CAPITAL TECHNIQUE

PRESENT VALUE OF FUTURE EARNINGS, SOMETIMES SUBTRACTING PERSONAL CONSUMPTION

- MOST WIDELY USED TECHNIQUE
  + MANY MEDICAL STUDIES UTILIZE TABLES AND TECHNIQUE ESTABLISHED BY D. P. RICE

- DATA WIDELY AVAILABLE
- UNEQUITABLE FOR WOMEN, MINORITIES, ELDERLY AND UNEMPLOYED
IMPLICIT VALUE TECHNIQUE

This technique obtains the value of human lives implicitly. This circular argument assumes that if each life saved by a new road intersection project was valued at $15,000, then the value of human lives must, in fact be $15,000. If an ejector seat for a military plane costs the equivalent of $1 million per expected life saved, do we use that value or the value implicit in the highway project? Were the values determined in 1970 good guidelines for 1985?
IMPLICIT VALUE TECHNIQUE

OBTAIN VALUE OF HUMAN LIVES IMPLICIT IN PREVIOUS GOVERNMENT PROJECTS

- CIRCULAR ARGUMENT
- WHICH PROJECTS?
+ VALUES MAY RANGE FROM 10,000 TO 1,000,000
- ARE PAST DECISIONS GUIDELINES FOR PRESENT EFFORTS?
LIFE-VALUE TECHNIQUE

The life-value technique utilizes life insurance purchases and/or court awards as the basis for valuing human life. If a person purchases only $15,000 of insurance, does that establish his/her life value? In like manner, which court cases should be chosen, the ones where the jury was liberal or very restrained? Little use is made of this technique.
LIFE-VALUE TECHNIQUE

UTILIZE INSURANCE PURCHASE OR COURT AWAPD DECISIONS AS BASIS FOR VALUE OF HUMAN LIFE

- INSURANCE PURCHASED IS NOT AN INDICATION OF SELF-WORTH

- ACCEPTANCE OF $100,000 FOR AN ASSIGNMENT WITH ONE CHANCE IN FIVE OF DEATH CANNOT MEAN ACCEPTANCE OF CERTAIN DEATH FOR $500,000!

- WHICH COURT CASES SHOULD BE UTILIZED?

- LITTLE USE MADE OF THIS TECHNIQUE
WILLINGNESS-TO-PAY TECHNIQUE

Considerable interest is given this approach in economic literature. The drawback is that many surveys need to be conducted to establish this as an acceptable technique, a procedure too costly for most research projects needing this information. The one survey conducted produced values closely resembling the human capital approach. This technique has been only selectively utilized.
WILLINGNESS-TO-PAY TECHNIQUE

CONDUCT A SURVEY TO DETERMINE WHAT PRICE PEOPLE WOULD PAY TO CONDUCT RESEARCH TO ELIMINATE A SPECIFIC DISEASE AND EXTRAPOLATE LIFE VALUES

- ANSWERS FROM ONE SURVEY RESEMBLED HUMAN CAPITAL APPROACH

- TOO LITTLE EMPIRICAL EVIDENCE AVAILABLE TO SUPPORT THE TECHNIQUE

- NO INCENTIVE ON PART OF THE RESPONDENT TO PROVIDE TRUE PREFERENCES
PROCEDURES AND ASSUMPTIONS FOR ESTIMATION OF THE VALUE OF HUMAN CAPITAL
VALUE OF HUMAN CAPITAL

This chart illustrates typical human capital curves as developed over a decade ago by Dorothy P. Rice and recently updated to reflect current experience. The value obtained from these curves for any particular year of an average person's life represents the discounted value. Thus, if that sum were invested in an interest-bearing savings account, withdrawals equal to the average salary could be made for the years which the deceased would have lived. The total money thus withdrawn from the account would yield far more than the amount deposited (the amount of the value at the age on the curve).
VALUE OF HUMAN CAPITAL

$ (thousands)

Age (years)

WM - white males
WF - white females
AOM - all other males
AOF - all other females
SAMPLE CALCULATION FOR VALUE OF HUMAN CAPITAL

In order to better understand the present value of future earnings, this simplified example is provided. The example assumes a white male, age 40 is earning $10,000 per year until age 65 and then his value would be $1,000 per year keeping house. We assume here that he suddenly loses his life and we want to plot his potential future earnings if he had not died. The cumulative and the discounted value of those earnings is shown. The discounted value assumes a six percent discount rate and the earnings are discounted back to age 40. The cumulative discounted value at the end of the curve (age 90) would be one point (at age 40 - white male) on the discounted life earnings curve if actual income figures had been used in this example.
SAMPLE CALCULATIONS FOR VALUE OF HUMAN CAPITAL

ASSUMED: WHITE MALE, AGED 40, INCOME $10,000/yr UNTIL AGE 65, THEN $1000/yr (HOUSEKEEPING VALUE)*

Note that the incomes used in this sample calculation are illustrative. For this reason, the numerical results obtained differ slightly from the actual figures in the Value of Human Capital Curve.

*This value represents one entry on the Value of a Human Capital Curve.
MODIFIED VALUE OF HUMAN CAPITAL

ECON has selected the Value of Human Capital technique for the purpose of quantifying social benefits. This choice was made based on the wide acceptance by the medical economic community and the availability of well-documented data to produce such tables and life-value curves. To modify the curves we have obtained average-earnings data from the Department of Labor, and we have made minor modifications to remove some sex and race bias. In all other respects the technique remains intact.
MODIFIED VALUE OF HUMAN CAPITAL

TO QUANTIFY SOCIAL BENEFITS THE VALUE OF HUMAN CAPITAL
TECHNIQUE HAS BEEN SLIGHTLY MODIFIED TO REDUCE SEX AND RACE BIAS

- WIDELY UTILIZED
- PROVIDES GOOD BASELINE
- DATA AVAILABLE AND WELL DOCUMENTED
PRESENT VALUE OF HUMAN CAPITAL (1976)

This slide represents the life-value curves developed by ECON utilizing the Value of Human Capital approach. This technique will be utilized to compute the value of extending life for a specified period. The procedures and assumptions used to prepare these revised curves are described in Appendix A.
PRESENT VALUE OF HUMAN CAPITAL (1976)

- WH - WHITE MALES
- AOM - ALL OTHER MALES
- WF - WHITE FEMALES
- AOF - ALL OTHER FEMALES
SAMPLE CALCULATION FOR THE BENEFIT OF EXTENDING LIFE TWO YEARS

The example on page 48 illustrates the technique utilized to determine the present value of future earnings out to age 90. Now let us take an example that is more similar to the situation encountered in this study, namely the benefit of postponing death for N years. In the example, we have the same white male earning $10,000 per year and afflicted with a disease at age 40. With present treatment, his average life expectancy is 10 years but with the new treatment his life-expectancy is increased to 12 years. This technique is used in this study for determining the value of extending lives, but a 6 percent discount factor is utilized and actual earnings data from the Department of Labor. In the example the social benefit is calculated as the discounted value of the two additional years of earnings ($10,238). This method has been used in this study in order to quantify the social benefit of life extension. Actual earnings data from the Department of Labor and a 6 percent rate of discount have been used in this study.
SAMPLE CALCULATION FOR THE BENEFIT OF EXTENDING LIFE TWO YEARS

DISEASE ONSET ASSUMED AT AGE 40,
DISCOUNT RATE OF 6 PERCENT

EARNINGS IS $10,238
BENEFITS OF LYMPHOCYTE SUBGROUP SEPARATION AND CLASSIFICATION
FOR TREATMENT OF END STAGE RENAL DISEASE
AND
BENEFITS OF THE SEPARATION OF UROKINASE PRODUCING CELLS
FOR TREATMENT OF PULMONARY EMBOLISMS
BACKGROUND

In a previous study for NASA Headquarters, two promising candidate substances for space bioprocessing were selected for benefit evaluations. These two substances were lymphocytes and urokinase. In the case of lymphocytes, ground-based research has led to the classification of two subgroups, and the objective of the space-based research is to further separate and extend the classification process within the two presently identified subgroups. At the present time, using ground-based techniques, urokinase-producing cells cannot be separated from other kidney cells. In both instances, electrophoretic separation in space has been proposed as the mechanism to effect separation. The clinical application selected for study in connection with lymphocyte subgroup classification, is the matching of donors and recipients for kidney transplantation; while the application selected for urokinase is the reduction of blood clots associated with thromboembolic diseases, specifically pulmonary embolisms. The referenced previous study contains a complete description of these two diseases and treatment systems, which is not repeated in this report for the sake of brevity. While other possible applications exist for these two substances, these two applications represent areas where immediate progress could be made if the space-based research is successful.

This previous study concluded that very large economic benefits could result from successful lymphocyte subgroup separation. During this study, it was also determined that it is possible that urokinase production costs could be reduced as a result of the successful separation of urokinase-producing cells, thus leading to increased availability and widespread use of urokinase in the treatment of thromboembolic diseases. This, in turn, could lead to a reduction in the number of deaths from pulmonary embolisms, and could possibly reduce the need for some surgical procedures and thus reduce the length of hospital stay.

In the present study the disease therapy system models for these two applications were reviewed, and the results extended to include both economic and social benefits.

1 Preliminary Benefit Analysis of Biological Space Processing. ECON, Inc, 1 September 1976.
PREVIOUS STUDY OF LYMPHOCYTE SUBGROUP SEPARATION AND SEPARATION OF UROKINASE-PRODUCING CELLS USED A TRANSITIONAL PROBABILITY TECHNIQUE TO ESTIMATE ECONOMIC BENEFITS

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>LYMPHOCYTES</th>
<th>UROKINASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPACE PROCESS</td>
<td>SEPARATE AND CLASSIFY SUBGROUPS</td>
<td>SEPARATE AND CONCENTRATE UROKINASE-PRODUCING</td>
</tr>
<tr>
<td>MECHANISM</td>
<td>ELECTROPHORISIS</td>
<td>ELECTROPHORISIS</td>
</tr>
<tr>
<td>CLINICAL APPLICATION</td>
<td>KIDNEY TRANSPLANTATION</td>
<td>THROMBOEMBOLIC DISEASES</td>
</tr>
<tr>
<td>CLINICAL IMPACT</td>
<td>IMPROVE TRANSPLANT ACCEPTANCE</td>
<td>LYSE BLOOD CLOTS</td>
</tr>
</tbody>
</table>
MORE DEFINITIVE DATA COLLECTED

To improve the reliability and accuracy of the model results in this study, additional data were collected about the treatment, costs and mortality rates of end stage renal disease (impacted by lymphocyte separation) and pulmonary embolisms (impacted by urokinase).
MORE DEFINITIVE DATA COLLECTED

TO IMPROVE THE BENEFIT ESTIMATION, DATA WAS COLLECTED RELATIVE TO:

- END STAGE RENAL DISEASE (ESRD)
  + TREATMENT
  + COSTS
  + MORTALITY

- PULMONARY EMBOLISM
  + TREATMENT
  + COSTS
  + MORTALITY
END STAGE RENAL DISEASE
MODEL OF KIDNEY DISEASE

The treatments for end stage renal disease (ESRD) known today are dialysis and transplant. It is believed that through lymphocyte separation in space, a better understanding of the body's immunological systems will come about, resulting in better tissue matching and hence, a greater success rate in transplant operations.

Eight states are defined in the model of kidney disease. Note that all five states encircled are reached after contraction of ESRD. These five states were singled out for the model thereby ignoring healthy people and those who had kidney disease, but not ESRD. We defined a discrete Markov Process for these five states, dictating that each year a transition would occur. The transition could result in movement from one state to the next or possibly in no movement at all.

Statistics were collected to enable the estimation of the potential benefits of space processing of lymphocyte separation. Three cases were defined with which to exercise the model: (1) current status, (2) partial improvement due to space processing, and (3) optimistic improvement due to space processing.

Among the statistics we collected for each case were:

1. How long did the patient live after contracting ESRD?
2. How many years after contracting ESRD did the patient enter each state?
3. How many years did the patient "reside" in each state?
5. Cost to private sector.
MODEL OF KIDNEY DISEASE

GENERAL POPULATION

KIDNEY DISEASE

E.S.R.D.

DIALYSIS

TRANSPLANT

CONT DIALYSIS

POST TRANSPLANT

DEATH
ESRD DATA COLLECTION

Recent data was obtained enumerating the number of patients undergoing dialysis and the number receiving transplants. The data indicate that ECON had properly modeled the treatment regimes for ESRD in our previous study for NASA Headquarters. Additionally, only minor modification was necessary to the cost data. The cost data used in this study for treatment of ESRD is shown in Appendix B.

Preliminary Benefit Analysis of Biological Space Processing. ECON, Inc., 1 September 1976.
ESRD DATA COLLECTION

- LATEST KIDNEY TRANSPLANT STATISTICS OBTAINED
- MOST RECENT COUNT OF ESRD PATIENTS ON DIALYSIS OBTAINED
- COST DATA PREVIOUSLY OBTAINED APPEARS ADEQUATE
- ARTICLE REGARDING LONG-TERM TRANSPLANTATION CALCULATIONS LOCATED
TRANSITIONAL PROBABILITIES FOR END STAGE RENAL DISEASE

Transitional probabilities can be conveniently represented through the use of a matrix. The matrix is arranged with the present states listed vertically on the left of the matrix and the states which can be entered horizontally across the top. Thus, by following the column across the matrix the probabilities can be seen for entering any other state. There are certain transitions that are not possible and those transition boxes are darkened on the matrix in the figures (or given a value of zero).

The transition probabilities for the treatment of ESRD were estimated through consultation with experts in kidney disease and kidney transplantation, and by literature review. The probabilities were estimated for two cases: a baseline case and an improvement case. The baseline case represents the present state-of-the-art for treatment of ESRD. The improvement case represents the expected improvement brought about by the use of space processing to separate and classify lymphocyte subgroups.
## Transition Probabilities for End Stage Renal Disease

### Probability Matrix for Baseline Case

<table>
<thead>
<tr>
<th></th>
<th>1ST YEAR DIALYSIS</th>
<th>CONT' DIALYSIS</th>
<th>TRANSPLANT</th>
<th>POST TRANSPLANT</th>
<th>DEATH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1ST YEAR DIALYSIS</td>
<td>.7</td>
<td>.2</td>
<td>.1</td>
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<tr>
<td>CONT' DIALYSIS</td>
<td>.92</td>
<td>.02</td>
<td>.06</td>
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<td>TRANSPLANT</td>
<td>.45</td>
<td>.03</td>
<td>.02</td>
<td>.025</td>
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</tr>
<tr>
<td>POST TRANSPLANT</td>
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<td></td>
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</tr>
<tr>
<td>DEATH</td>
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<td></td>
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<td></td>
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</tbody>
</table>

### Probability Matrix for Improvement Case

<table>
<thead>
<tr>
<th></th>
<th>1ST YEAR DIALYSIS</th>
<th>CONT' DIALYSIS</th>
<th>TRANSPLANT</th>
<th>POST TRANSPLANT</th>
<th>DEATH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1ST YEAR DIALYSIS</td>
<td>.45</td>
<td>.45</td>
<td>.06</td>
<td></td>
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</tr>
<tr>
<td>CONT' DIALYSIS</td>
<td>.79</td>
<td>.15</td>
<td>.02</td>
<td>.77</td>
<td>.05</td>
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<tr>
<td>TRANSPLANT</td>
<td>.16</td>
<td>.02</td>
<td>.91</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>POST TRANSPLANT</td>
<td>.05</td>
<td>.02</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEATH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
</tbody>
</table>

### Source:

Probability transitions determined from analyzing the statistics on the number of persons contracting ESRD annually, the number receiving dialysis, the number receiving transplants and the estimate of the percent dying the first year of ESRD. Sources include:

- House of Representatives, Hearings before the House Subcommittee on Oversight on Medicare's End Stage Renal Disease Program. G.P.O., June 24 - July 10, 1975.
- National Dialysis Registry, National Institute of Arthritis and Metabolic Diseases, N.I.H., Bethesda, Maryland, October 1, 1975
RESULTS OF ESRD TREATMENT SIMULATION

One thousand iterations were run for the probability transition matrices for ESRD utilizing a Monte Carlo simulation. The results of the simulation are shown in the opposite chart.

As the transplant rejection rate and the death rate decrease, the life expectancy of the average patient increases. The assumption was made that as the kidney transplant rejection rate decreases, more patients will elect that form of treatment and thus the probability of transitioning to the transplant state was increased in the improvement case. Through a reduced mortality for transplant patients, and an increase in the number of patients choosing that treatment, the expected patient life after contracting ESRD was extended by more than three years in the improvement case. Because the costs to both the government and the individual are both less for the post-transplant state a reduced cost situation is encountered, even with the extended period of life.
### RESULTS OF ESPD TREATMENT SIMULATION

<table>
<thead>
<tr>
<th></th>
<th>MEAN</th>
<th>MEAN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&quot;AGE&quot; (A) AT DEATH</strong></td>
<td>13.72</td>
<td>17.11</td>
</tr>
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<td><strong>NUMBER OF YEARS IN:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CONTINUING DIALYSIS</td>
<td>10.64</td>
<td>3.60</td>
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<td>TRANSPLANT</td>
<td>0.55</td>
<td>1.55</td>
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<td>POST-TRANSPLANT</td>
<td>1.14</td>
<td>10.20</td>
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<td><strong>COST TO PUBLIC SECTOR PER INDIVIDUAL OVER INDIVIDUAL'S LIFE (1985 DOLLARS)</strong></td>
<td></td>
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</tr>
<tr>
<td>UNDISCOUNTED</td>
<td>403,969</td>
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<td>DISCOUNTED AT 6%</td>
<td>195,690</td>
<td>106,804</td>
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<tr>
<td><strong>COST TO PRIVATE SECTOR PER INDIVIDUAL (1985 DOLLARS)</strong></td>
<td></td>
<td></td>
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<tr>
<td>UNDISCOUNTED</td>
<td>226,807</td>
<td>201,801</td>
</tr>
<tr>
<td>DISCOUNTED AT 6%</td>
<td>110,046</td>
<td>98,379</td>
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</table>

(A) Throughout, "AGE" is meant to be years after contracting ESPD.
THROMBOEMBOLIC DISEASES
MODEL OF PULMONARY EMBOLISM

The current treatments of thromboembolic diseases, specifically pulmonary embolisms, are heparin therapy and surgery. Additionally, it is believed that the use of the drug urokinase will become an effective treatment regime once it receives FDA approval for use in the United States and is commercially available. It is anticipated that not only will urokinase lyse, or dissolve, clots of the lungs, but also have the same effect on clots in other parts of the body.

Ten states were defined for the treatment of pulmonary embolisms as shown in the opposite figure. For the simulation, all states were utilized except the state representing the general population.

Statistics were collected to enable a comparison of the costs of treatment of pulmonary embolisms pre and post introduction of urokinase. Two cases were defined: baseline and improvement. The baseline case represents the current state-of-the-art of treatment of pulmonary embolisms (without urokinase), while the improvement case represents the anticipated state-of-the-art after the introduction of urokinase as a therapy system.

Among the statistics collected for each case were:

1. How long did the patient live after contracting pulmonary embolism?
2. How long did the patient "reside" in each state, particularly the post-treatment state which represents surgery?
3. Costs to the individual.
MODEL OF PULMONARY EMBOLISM

GENERAL POPULATION

PULMONARY EMBOLISM

NO DIAGNOSIS WITH TREATMENT

NO DIAGNOSIS AND NO TREATMENT

POST P.E. WITH NO PROPHYLAXIS

POST P.E. WITH PROPHYLAXIS

SURGERY

HEPARIN

UROKINASE AND HEPARIN

DEATH

Area within dotted line indicates modelled area
THROMBOEMBOLIC DISEASES DATA COLLECTION

The data-gathering effort provided a more refined and reliable estimate of life extension possible from the new health treatments made possible through space processing.
THROMBOEMBOLIC DISEASES DATA COLLECTION

• DATA ON THROMBOEMBOLIC DISEASES BESIDES PULMONARY EMBOLISM OBTAINED
• BETTER DATA ON MORTALITY FROM PULMONARY EMBOLISM OBTAINED
• SOME DATA ON DOCTOR VISITS AND HOSPITAL STAYS OBTAINED
• IMPROVED DATA INPUTS WILL ALLOW MODEL TO GENERATE MORE ACCURATE ESTIMATES OF:
  + YEARS OF LIFE EXTENDED
  + REDUCED MORBIDITY
Transition probabilities for the treatment of pulmonary embolisms through consulting with experts familiar with urokinase efficacy and by analyzing the literature on pulmonary embolisms. The sources of the transitional probabilities and the costs for treatment of pulmonary embolisms are shown in Appendix C. The transition probability matrices are given for the two cases as shown on the opposite page.

Cost estimates are based on actual experience in the case of a surgeon's fees, and on an approximation based on costs in other countries in the case of urokinase. The degree of severity of an embolism determines costs and the range is great. One patient may need surgery followed by intensive care while another patient may be treated medically, only to have to undergo surgery later.
### Transition Probabilities for Treatment of Pulmonary Embolisms

#### Baseline Pulmonary Embolism Case

<table>
<thead>
<tr>
<th>Pulmonary Embolism</th>
<th>No Diagnosis With Treatment</th>
<th>No Diagnosis and No Treatment</th>
<th>Post P.E. With Prophylaxis</th>
<th>Heparin Treatment</th>
<th>Urokinase With Heparin Treatment</th>
<th>Surgery</th>
<th>Post P.E. With Prophylaxis</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary Embolism</td>
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<td></td>
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<td></td>
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<td>.00</td>
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#### Improvement Pulmonary Embolism Case

<table>
<thead>
<tr>
<th>Pulmonary Embolism</th>
<th>No Diagnosis With Treatment</th>
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<th>Post P.E. With Prophylaxis</th>
<th>Heparin Treatment</th>
<th>Urokinase With Heparin Treatment</th>
<th>Surgery</th>
<th>Post P.E. With Prophylaxis</th>
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<td>No Diagnosis and No Treatment</td>
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<td>Urokinase With Heparin Treatment</td>
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<td>.01</td>
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</tr>
</tbody>
</table>

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RESULTS OF PULMONARY EMBOLISM TREATMENT SIMULATION

The probability matrices for pulmonary embolism were run utilizing a Monte Carlo simulation technique. The results of the runs are shown in the opposite chart.

The small increase in age at death of 1.56 years between the baseline and improvement cases is attributable to the fact that 11% of the pulmonary embolism cases result in immediate death, and that a very significant number of pulmonary embolisms are not diagnosed and do not receive treatment.1

# RESULTS OF PULMONARY EMBOLISM TREATMENT SIMULATION

<table>
<thead>
<tr>
<th>MEASURE</th>
<th>BASELINE CASE</th>
<th>IMPROVEMENT CASE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&quot;AGE&quot; (A) AT DEATH</strong></td>
<td>20.33</td>
<td>21.89</td>
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<td><strong>NUMBER OF YEARS IN</strong></td>
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<td></td>
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<tr>
<td>POST P.E. W/OUT PROPHYLAXIS</td>
<td>10.57</td>
<td>11.25</td>
</tr>
<tr>
<td>POST P.E. WITH PROPHYLAXIS</td>
<td>6.45</td>
<td>7.24</td>
</tr>
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<td><strong>COST TO PRIVATE SECTOR PER INDIVIDUAL OVER INDIVIDUAL'S LIFESPAN ($)</strong></td>
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<td></td>
</tr>
<tr>
<td>UNDISCOUNTED</td>
<td>18,332</td>
<td>19,255</td>
</tr>
<tr>
<td>DISCOUNTED AT 6%</td>
<td>9,095</td>
<td>9,180</td>
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(A) Throughout "AGE" is meant to be years after contracting P.E.
SUMMARY OF BENEFITS FOR TREATMENT OF
END STAGE RENAL DISEASE AND PULMONARY EMBOLISMS
SUMMARY OF BENEFITS OF TREATMENT FOR END STATE RENAL DISEASE AND PULMONARY EMBOLISMS

The ECON-developed medical treatment simulation model computes the expected life span of a patient contracting the disease in question and the expected costs to one average patient. It is estimated that there are 10,000 new ESRD patients each year and 750,000 cases of pulmonary embolism occur each year (whether diagnosed or not). The opposite table shows the benefits accruing to the group entering the disease state in one year. If no new treatment technique comes along, these benefits would accrue to those contracting the particular disease each successive year.

The computer program listing for the model of ESRD and pulmonary embolism treatment is given in Appendix D.
### SUMMARY OF BENEFITS FOR TREATMENT OF END STAGE RENAL DISEASE AND PULMONARY EMBOLISMS

<table>
<thead>
<tr>
<th>TYPE OF BENEFIT</th>
<th>BENEFITS TO DISEASE AS A RESULT OF NEW TREATMENT TECHNIQUES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PULMONARY EMBOLISM</td>
</tr>
<tr>
<td>ECONOMIC (DECREASED COST FOR EQUAL CAPABILITY)</td>
<td>-$112.9 MILLION (OVER A 22 YEAR PERIOD) TO PEOPLE CONTRACTING P.E. DURING ONE YEAR (THIS COST COULD ALSO ACCRUE TO PEOPLE ENTERING THE SYSTEM EACH SUCCESSIVE YEAR)*</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>SOCIAL (EXTENDED MEAN LIFE EXPECTANCY ONCE DISEASE IS CONTRACTED)</td>
<td>AVERAGE CAPITALIZED VALUE OF EARNINGS FOR 1.56 YEARS FOR 750,000 PEOPLE IS $3.103 BILLION</td>
</tr>
</tbody>
</table>

*COST OF TREATMENT WITH UROKINASE EXCEEDS COST OF PRESENT TREATMENT*
BENEFITS OF THE SEPARATION OF BETA CELLS FOR THE TREATMENT OF DIABETES
TYPES OF DIABETES MELLITUS

Generally speaking, there are two types of diabetes mellitus: adult-onset and juvenile-onset. Adult-onset diabetes is frequently and increasingly being controlled by diet manipulation and oral hypoglycemic techniques; these diabetics are typically not insulin-dependent. Juvenile-onset diabetics, on the other hand, typically are insulin-dependent and would benefit from any technologies which could improve insulin therapy, either the process of introduction of insulin into the body or the quality of the insulin itself.
TYPES OF DIABETES MELLITUS

• ADULT ONSET (INSULIN-INDEPENDENT)
  + ONSET USUALLY AFTER 40
  + GENERALLY CONTROLLED BY DIET AND/OR ORAL HYPOGLYCEMIC AGENTs
  + HIGH INCIDENCE OF CORONARY COMPLICATIONS

• JUVENILE ONSET (INSULIN-DEPENDENT)
  + ONSET USUALLY BEFORE 25 (90%)
  + REQUIRES USE OF INSULIN
  + HIGH INCIDENCE OF KIDNEY AND EYE COMPLICATIONS
DIABETIC PATIENT POPULATION OF THE UNITED STATES

Of the 1.24 million insulin-dependent diabetics in the United States today 85 percent are thought to have had diabetes onset between 0 and 19 years of age, 5 percent between 20 and 39 years, 5 percent between 40 and 59 and 5 percent at age 60 or more.

Further, the population is:

33.0% White Male
52.2% White Female
5.7% All Other Male
9.1% All Other Female.

Source: Medical advisors and major statistical sources, see page 119.
DIABETIC PATIENT POPULATION OF THE UNITED STATES

1.24 MILLION INSULIN-DEPENDENT
1.25 MILLION ORAL MEDICATION
3.50 MILLION DIET CONTROLLED
4 MILLION ESTIMATED UNDIAGNOSED
CAUSES OF DIABETIC DEATHS: 1897-1968

The rapid growth of insulin therapy in the early part of this century greatly decreased the incidence of diabetic coma. The problem of survival of the diabetic became not one of immediate complications (that is, coma), but of long-term complications. Juvenile-onset diabetics could be expected to function normally in society up to the point where the long-term complications, such as kidney, ocular and cardio-vascular, started to evidence later in life.
CAUSES OF DIABETIC DEATHS: 1897-1968

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1897-1914</td>
<td>326</td>
</tr>
<tr>
<td>1914-1922</td>
<td>836</td>
</tr>
<tr>
<td>1922-1932</td>
<td>4,157</td>
</tr>
<tr>
<td>1937-1943</td>
<td>3,639</td>
</tr>
<tr>
<td>1944-1949</td>
<td>4,148</td>
</tr>
<tr>
<td>1950-1959</td>
<td>9,851</td>
</tr>
<tr>
<td>1960-1968</td>
<td>5,009</td>
</tr>
</tbody>
</table>
MAJOR COMPLICATIONS OF DIABETES

All of the major, known complications of diabetes were considered in this study. Several of these--neuropathy, ketosis, allergy and visual impairments other than diabetic retinopathy--were not explicitly modeled because their effects were not sufficiently significant, because not enough was known about the complication, or because it was felt that the improvements being studied would not impact the complication. The major complications--diabetic retinopathy, nephropathy, cardiovascular, peripheral vascular and insulin resistance--are all modeled in this study.
MAJOR COMPLICATIONS OF DIABETES

1. DIABETIC RETINOPATHY - MODELED
2. OTHER VISUAL (GLAUCOMA, CATARACTS) - EFFECTS NOT SIGNIFICANT
3. NEPHROPATHY - MODELED
4. CARDIOVASCULAR - MODELED
5. NEUROPATHY - INSUFFICIENT DATA
6. PERIPHERAL VASCULAR - MODELED
7. KETOSIS - NOT IMPACTABLE
8. ALLERGIC REACTION - EFFECTS NOT SIGNIFICANT
9. INSULIN RESISTANCE - MODELED
HYPOTHESES ABOUT DEVELOPMENT OF COMPLICATIONS IN DIABETICS

After consulting with medical contacts and reviewing relevant medical literature, it was assumed for the modeling effort that 50 percent of all complications arose from imperfect control of blood sugar levels, 25 percent were due to antibody build up to foreign insulin and 25 percent to other unknown factors. These estimates reflect the degree of agreement among the expert medical community. That is, while virtually all physicians agree that complications arise from poor control of diabetes, fewer believe that antibody production or other unknown factors are significant causes. In most cases this lack of agreement takes the form of uncertainty rather than disagreement.

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See page 119 for list of medical advisors and major statistical sources.
HYPOTHESES ABOUT DEVELOPMENT OF COMPLICATIONS IN DIABETICS

1. IMPERFECT CONTROL

2. ANTIBODIES OF FOREIGN (PORCINE, BOVINE) INSULIN

3. UNKNOWN FACTORS
ANIMAL INSULIN: EXPECTED CHANGES IN SUPPLY AND DEMAND

The supply of animal insulin is expected to become more expensive in the future. This is due to the fact that the removal of the pancreas from cattle and hog carcasses is labor intensive and meat packers are resisting the performance of this function. On the other hand, the incidence of diabetes in the United States is increasing at about 6 percent per year, thus creating greater demand pressures on the existing supply.
ANIMAL INSULIN: EXPECTED CHANGES IN SUPPLY AND DEMAND

- **SUPPLY:**
  + INCREASED COST OR REDUCTION IN PRODUCTION EXPECTED

- **DEMAND**
  + INCREASED DEMAND EXPECTED DUE TO RISE IN INCIDENCE OF DIABETES BY 6% PER YEAR
POSSIBLE TREATMENTS OF DIABETES

ECON modeled several possible treatments of diabetes, including the most commonly used now: injection of foreign insulin. The problem of build-up of antibodies could be overcome by the use of "human" insulin, taken directly from human pancreas, cultured from Beta cells extracted from human pancreas, synthesized, or produced from E. coli bacteria. Space bioprocessing can assist the extraction of insulin or Beta cells from the human pancreas by providing a superior environment for electrophoresis. Either foreign or human insulin can be used in combination with an implanted device known as an artificial pancreas which monitors the insulin level in the body and secretes insulin as necessary on a continual basis. The extraction of Beta cells from the human pancreas offers the possibility that these cells can be injected into and accepted by a diabetic patient. If successfully accomplished, this could eliminate the problem of diabetes. In extreme cases, pancreas transplants may be warranted; this would not be a primary form of treatment, however, because the survival rate of such transplant patients is extremely low. Other forms of treatment, such as hormone control, were not modeled either due to insufficient information or because they were not directly pertinent to the subject of this study.
POSSIBLE TREATMENTS OF DIABETES

CONVENTIONAL
*HUMAN INSULIN - INJECTION OF FOREIGN (BOVINE, PORCINE) INSULIN
- FROM CULTURED BETA CELLS
- SYNTHESIS OR E. COLI

ARTIFICIAL PANCREAS - MONITORING AND SECRETING FOREIGN INSULIN
*ARTIFICIAL PANCREAS - MONITORING AND SECRETING HUMAN INSULIN
*BETA-CELL TRANSPLANT - TRANSPLANT OF SEPARATED INSULIN-PRODUCING CELLS
PANCREAS TRANSPLANT - DUE TO COMPLEXITY AND LIMITED SUCCESS MODELED
- ONLY AS A TREATMENT FOR MULTIPLE COMPLICATIONS

OTHER HORMONE CONTROL - NOT MODELED DUE TO INSUFFICIENT INFORMATION

* POTENTIALLY IMPACTABLE BY SPACE BIOPROCESSING
TIME TO ASSESS SUCCESS OF TREATMENT

Even if human insulin and artificial pancreas techniques are developed, the actual proof of their success will require many years of evaluation. This is because we are dealing with long-run complications. The effects of treatment begun now on a juvenile diabetic cannot be assessed on average for at least twenty years.
TIME TO ASSESS SUCCESS OF TREATMENT

- HUMAN INSULIN—MINIMUM OF 10 TO 20 YEARS REQUIRED
- BETA CELL TRANSPLANT OR ARTIFICIAL PANCREAS MAY REQUIRE LESS TIME
As a simplified illustration of the model, a healthy person can be found to have insulin-dependent diabetes. He then acquires some form of treatment and stays with that treatment (unless he has a successful Beta cell transplant in which case he is "cured") until he either dies or develops some complication. The complication persists (generally diabetic complications are not curable) until the patient dies or enters a state of severe, or life-threatening, complications. At this point a pancreas transplant is considered if it is deemed likely that the patient's life can be extended. The terminal state is, of course, death. Although not shown, the patient continues with the same diabetic therapy throughout his life (unless he has a successful Beta-cell transplant). Our model assumes steady state conditions, dealing with new patient population. Because of the steady state nature of the model we assume that once a patient enters a given treatment regime that he remains in that regime for the remainder of his life. The best available treatment at the time of onset will always be selected.

The model is employed to assess how a form of treatment, if available, compares to the other available treatments.
BETA CELLS ISLETS OF THE LANGERHANS--SIMPLIFIED ILLUSTRATION OF THE DISEASE THERAPY MODEL
DIABETES TRANSITIONAL PROBABILITY MODEL

The transitional probability model performs as follows: an insulin-dependent patient is selected from among the four age-of-onset classes shown. A treatment is selected and the individual's progression through life is simulated. At any point in time (time is incremented in five-year steps) the individual has a specified probability of contracting any of the complications modeled, or of dying. Any or all complications can be contracted before death. If the individual has several complications, yet is young enough to warrant a pancreas transplant this is an additional possible state before death. The model works iteratively, selecting many patients from each age-of-onset class.

The program listing for this model is contained in Appendix E.
DIABETES TRANSITIONAL PROBABILITY MODEL

AGE AT ONSET (INPUT)
- 0 - 19
- 20 - 39
- 40 - 59
- 60 +

TREATMENT (INPUT)
- CONVENTIONAL
- HUMAN INSULIN
- ARTIFICIAL PANCREAS
- FOREIGN INSULIN
- ARTIFICIAL PANCREAS
- HUMAN INSULIN
- BETA-CELL TRANSPLANT

COMPLICATIONS
- RETINOPATHY
- CARDIOVASCULAR DISEASE
- PERIPHERAL VASCULAR DISEASE
- NEPHRPATHY
- INSULIN RESISTANCE

ADDITIONAL STATES
- PANCREAS TRANSPLANT
- DEATH
PREVALENCE OF CARDIOVASCULAR COMPLICATIONS AMONG DIABETICS AND GENERAL POPULATION

Improvements due to superior therapy reduce the incidence of any particular complication among the diabetic population. Improvements beyond the typical, nondiabetic individual are not considered. The difference in the prevalence of any complication between the diabetic under conventional treatment and the nondiabetic is shown as \( \Delta \) in the opposite figure. This distance is assumed to be reduced by different amounts (by 25 percent for the dashed line shown) according to the treatment type and the complication involved.
PREVALENCE OF CARDIOVASCULAR COMPLICATIONS AMONG DIABETICS AND GENERAL POPULATION

DIABETIC INDIVIDUAL (AGE AT ONSET: 10 YEARS)

HYPOTHETICAL DIABETIC USING HUMAN INSULIN

NONDIABETIC INDIVIDUAL

REDUCTION IN Δ RESULTING FROM NEW TREATMENT

PREVALENCE, %

AGE, YEARS
ASSUMED IMPROVEMENTS DUE TO IMPROVED TREATMENTS IN PREVALENCE OF DIABETIC COMPLICATIONS

The introduction of the treatment of diabetes with human insulin will reduce the complications of diabetes by alleviating the problem of the production of antibodies to foreign insulin and perhaps by providing better control of blood sugar levels. The chart presented here shows the expected reduction of prevalence of complications in the diabetic population relative to the normal population, the Δ from the previous figure. This is not the same as reducing the absolute prevalence of complications by the given percent in that the complicating diseases do occur in the general population and it is not expected that through the use of human insulin or any other treatment of diabetes, diabetic prevalence could be reduced below the level encountered in the general population. Because of the uncertainty in the medical profession as to the cause of diabetic complications, two estimates of the possible reductions, "optimistic" and more "realistic" reductions, have been assigned for human insulin treatment.

The treatment of diabetes with a Beta cell transplant is assumed to reduce the prevalence of complicating diseases to the level observed in the normal population.

In either case, since insulin resistance is seen to be totally the result to antibody binding with the use of foreign insulin, this complication would be eliminated.
**DIABETIC RETINOPATHY**
- Optimistic: 25%
- Realistic: 17.5%
- Reduction: 50%
- Optimistic: 75
- Realistic: 62.5
- Beta Cell: 100

**CARDIOVASCULAR**
- Optimistic: 25%
- Realistic: 12.5%
- Reduction: 50%
- Optimistic: 75
- Realistic: 62.5
- Beta Cell: 100

**NEPHROPATHY**
- Optimistic: 50%
- Realistic: 25%
- Reduction: 25%
- Optimistic: 75
- Realistic: 50
- Beta Cell: 100

**PERIPHERAL VASCULAR**
- Optimistic: 25%
- Realistic: 12.5%
- Reduction: 50%
- Optimistic: 75
- Realistic: 62.5
- Beta Cell: 100

**INSULIN RESISTANCE**
- Optimistic: 100%
- Realistic: 100%
- Reduction: 0%
- Optimistic: 100
- Realistic: 100
- Beta Cell: 100
DIABETES MODEL

The age at onset of the individual as well as the best available treatment are selected and input into the model. The model contains probabilities of moving from any state to another as a function of time. Costs of treatment and costs of complications (direct and indirect) are calculated as the individual progresses. The costs of death based on the amount of productive lifetime foregone are also included. For each patient the total costs are calculated and averaged across individuals and age-of-onset classes to obtain an estimate of the costs of diabetes associated with each type of treatment.
DIABETES MODEL

• INPUT REQUIREMENTS
  
  + AGE OF PATIENT AT ONSET OF DIABETES
  + TREATMENT TYPE

• INCORPORATED IN MODEL
  
  + INCIDENCE OF COMPLICATIONS BY AGE AT ONSET AND DURATION OF DIABETES
  + COSTS OF TREATMENT BY TYPE
  + DIRECT AND INDIRECT COST OF TREATING DIABETES AND ITS COMPLICATIONS
  + MORTALITY RATES BY COMPLICATION AND ASSOCIATED COSTS
  + EXPECTED IMPROVEMENT IN MORTALITY AND MORBIDITY DUE TO TREATMENT TYPES
THE ASSUMPTIONS

The important assumptions embedded in the transitional probability model are listed here.
THE ASSUMPTIONS

• THERE IS NO POSSIBILITY OF CHANGING FROM ONE TYPE OF TREATMENT TO ANOTHER; IT IS ASSumed THAT ONCE A TREATMENT IS SELECTED, THE PATIENT WILL FOLLOW THE SAME TREATMENT UNTIL DEATH

• THE HUMAN CAPITAL APPROACH TO THE VALUE OF EXTENDING PRODUCTIVE LIFE IS ASSUMED

• COSTS, BOTH DIRECT AND INDIRECT, ARE DISCOUNTED AT 6 PERCENT TO OBTAIN PRESENT VALUE

• BENEFITS ARE INFLATED AT A CONSTANT RATE OF 6 PERCENT TO 1985, THE ASSUMED FIRST YEAR OF TREATMENT BENEFITS

• 50 PERCENT OF COMPLICATIONS ARISE DUE TO IMPERFECT CONTROL OF BLOOD SUGAR LEVELS, 25 PERCENT TO ANTIBODY BUILD-UP AGAINST FOREIGN INSULIN, AND 25 PERCENT TO OTHER UNKNOWN FACTORS

• COSTS OF TREATMENTS AND COMPLICATIONS ARE SHOWN IN APPENDICES F AND G

• 25 PERCENT OF THOSE PATIENTS WITH THREE COMPLICATIONS UNDER 60 YEARS OF AGE RECEIVE PANCREAS TRANSPLANT, 35 PERCENT OF THOSE UNDER 60 YEARS WITH FOUR OR MORE COMPLICATIONS RECEIVE PANCREAS TRANSPLANT

• 70 PERCENT OF THOSE RECEIVING A PANCREAS TRANSPLANT DIE WITHIN THE FIRST FIVE-YEAR PERIOD, THE REMAINDER DIE IN THE NEXT FIVE-YEAR PERIOD
MAJOR DATA SOURCES

The major sources of information for the model formulation and description of the diabetic population are listed here.
MAJOR DATA SOURCES

• INFORMATION SOURCES
  C.J. VAN OSS - STATE UNIVERSITY OF NEW YORK
  M. MACGILLIVRAY - BUFFALO CHILDRENS HOSPITAL
  W. CHICK - JOSLIN CLINIC
  D. MARTIN - MASSACHUSETTS GENERAL HOSPITAL
  J.S. NAJARIAN - UNIVERSITY OF MINNESOTA

• STATISTICAL SOURCES
  REPORT OF THE NATIONAL COMMISSION ON DIABETES TO THE CONGRESS OF THE UNITED STATES,
  NATIONAL INSTITUTES OF HEALTH
  DIABETES MELLITUS, NATIONAL INSTITUTES OF HEALTH
  DIABETES SOURCE BOOK, U.S. PUBLIC HEALTH SERVICE
  MORBIDITY AND MORTALITY IN DIABETICS IN THE FARMINGTON POPULATION SIXTEEN YEAR
  FOLLOW-UP STUDY, GARCIA, ET. AL.
  JOSLIN'S DIABETES MELLITUS, MARBLE, ET AL.
  CHANGES IN THE COSTS OF TREATMENT OF SELECTED ILLNESSES, SCITOVSKY AND MCCALL
  THE ECONOMIC COST OF ILLNESS REVISITED, COOPER AND RICE
TRANSITION PROBABILITY TABLE FOR CONVENTIONAL TREATMENT FOR RETINOPATHY

For each complication, the probability of incidence, $P_1(T)$, (assuming that the complication was not present in the last time interval) is specified as a function of age onset and duration of diabetes. A separate probability transition table exists for each type of treatment, as well as each complication. The probability of dying, $P_2(T)$, is similarly modeled as a function of the number of complications present as well.
## Transition Probability Table for Conventional Treatment for Retinopathy

<table>
<thead>
<tr>
<th>Age at Onset</th>
<th>Duration of Diabetes (Years)</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25+</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-19</td>
<td></td>
<td>0.00</td>
<td>0.07</td>
<td>0.16</td>
<td>0.21</td>
<td>0.47</td>
</tr>
<tr>
<td>20-39</td>
<td></td>
<td>0.03</td>
<td>0.07</td>
<td>0.22</td>
<td>0.36</td>
<td>0.07</td>
</tr>
<tr>
<td>40-59</td>
<td></td>
<td>0.04</td>
<td>0.22</td>
<td>0.13</td>
<td>0.23</td>
<td>0.24</td>
</tr>
<tr>
<td>60+</td>
<td></td>
<td>0.11</td>
<td>0.15</td>
<td>0.07</td>
<td>0.06</td>
<td>0.10</td>
</tr>
</tbody>
</table>

![Transition Diagram](image)

- $P_1(t)$: Probability of Treatment for Retinopathy
- $P_2(t)$: Probability of Death
STATISTICAL DATA SOURCES FOR TRANSITIONAL PROBABILITY MATRICES OF CONVENTIONAL TREATMENT

The literature on diabetic complications was thoroughly searched in order to obtain data for the transition probability tables. A list of the primary data sources is presented.
STATISTICAL DATA SOURCES FOR TRANSITIONAL PROBABILITY MATRICES OF CONVENTIONAL TREATMENT

Retinopathy


Proteinuria (Nephropathy)


Coronary Artery Disease (Cardiovascular)

Diabetes and Its Management, Oakley et al.


Peripheral Vascular

EXAMPLE OF THE OPERATION OF THE DIABETES TRANSITIONAL PROBABILITY MODEL

Consider some individual patient from one of the classes of age-of-onset. During each period of time, he has a specified chance of contracting each of the complications—unless he already has the complication, in which case he keeps it until death. The costs of treatment as well as the morbidity costs (e.g., absence from work or inability to work) are calculated period by period. At some point the individual dies, at which time a mortality cost, which is the income foregone for the remainder of the expected lifetime of the non-diabetic individual, is added. All costs are appropriately discounted (6 percent is used as the discount rate) and summed to obtain a present value cost associated with that patient.

The sample patient shown opposite incurs no complications in the first five-year period, but is afflicted with nephropathy in the second five-year interval. In the next interval, no new complication evidences although nephropathy persists. In the fourth period, the sample patient is afflicted with both retinopathy and peripheral vascular complications. All complications incurred persist and in the sixth period a pancreas transplant is performed. The patient dies in the following period.
EXAMPLE OF THE OPERATION OF THE DIABETES TRANSITIONAL PROBABILITY MODEL

TREATMENT AND MORBIDITY COST — MORTALITY COST

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COST OF DIABETES TREATMENT

Costs of treatment in 1976 dollars are presented for the initial five years after onset and for each five-year period following. Three cost levels (#1, #2, #3) are given for the costs of obtaining human insulin since more specific information is not available at this time. Appendix F presents these costs in considerable detail. The distinction between the "optimistic" and "realistic" cases refers not to cost distinctions but to the improvement in complications believed possible as discussed on page 112 of this report.
## Cost of Diabetes Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>First 5-Year Period ($/Patient)</th>
<th>Additional 5-Year Periods ($/Patient)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. CONVENTIONAL</td>
<td>3080</td>
<td>2665</td>
</tr>
<tr>
<td>2. HUMAN INSULIN #1 OPTIMISTIC**</td>
<td>3080</td>
<td>2665</td>
</tr>
<tr>
<td>3. HUMAN INSULIN #1 REALISTIC</td>
<td>3080</td>
<td>3765</td>
</tr>
<tr>
<td>4. HUMAN INSULIN #2 OPTIMISTIC**</td>
<td>3630</td>
<td>3765</td>
</tr>
<tr>
<td>5. HUMAN INSULIN #2 REALISTIC</td>
<td>3630</td>
<td>5140</td>
</tr>
<tr>
<td>6. HUMAN INSULIN #3 OPTIMISTIC**</td>
<td>4318</td>
<td>5140</td>
</tr>
<tr>
<td>7. HUMAN INSULIN #3 REALISTIC</td>
<td>4318</td>
<td>11075</td>
</tr>
<tr>
<td>8. ARTIFICIAL PANCREAS/FOREIGN</td>
<td>22695</td>
<td>11075</td>
</tr>
<tr>
<td>9. ARTIFICIAL PANCREAS/HUMAN #1** OPTIMISTIC</td>
<td>22695</td>
<td>11075</td>
</tr>
<tr>
<td>10. ARTIFICIAL PANCREAS/HUMAN #1 REALISTIC</td>
<td>22695</td>
<td>11075</td>
</tr>
<tr>
<td>11. ARTIFICIAL PANCREAS/HUMAN #2** OPTIMISTIC</td>
<td>23355</td>
<td>12175</td>
</tr>
<tr>
<td>12. ARTIFICIAL PANCREAS/HUMAN #2 REALISTIC</td>
<td>23355</td>
<td>12175</td>
</tr>
<tr>
<td>13. ARTIFICIAL PANCREAS/HUMAN #3** OPTIMISTIC</td>
<td>24380</td>
<td>13550</td>
</tr>
<tr>
<td>14. ARTIFICIAL PANCREAS/HUMAN #3 REALISTIC</td>
<td>24380</td>
<td>13550</td>
</tr>
<tr>
<td>15. BETACELL TRANSPLANT</td>
<td>7092</td>
<td>618</td>
</tr>
<tr>
<td>PANCREAS TRANSPLANT</td>
<td>30098</td>
<td>25500</td>
</tr>
</tbody>
</table>

*Cost of Diabetic Treatment

**See Appendix F for variations in cost of human insulin, cost levels #1, 2 and 3
COST OF DIABETIC COMPLICATIONS

Similarly, the costs of each complication are presented. More detail is available in Appendix G.
### COST OF DIABETIC COMPLICATIONS*

<table>
<thead>
<tr>
<th>COMPLICATION</th>
<th>FIRST 5-YEAR PERIOD** ($/PATIENT)</th>
<th>ADDITIONAL 5-YEAR PERIODS** ($/PATIENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RETINOPATHY</td>
<td>$625</td>
<td>$1,250</td>
</tr>
<tr>
<td>CARDIOVASCULAR DISEASE</td>
<td>9,940</td>
<td>11,665</td>
</tr>
<tr>
<td>PERIPHERAL VASCULAR DISEASE</td>
<td>20,500</td>
<td>35,000</td>
</tr>
<tr>
<td>NEPHROPATHY</td>
<td>2,500</td>
<td>5,000</td>
</tr>
<tr>
<td>INSULIN RESISTANCE</td>
<td>14,433</td>
<td>12,685</td>
</tr>
</tbody>
</table>

*See Appendix G for cost breakdown and sources.

**Cost of treatment and morbidity
PRESENT VALUE OF ECONOMIC AND SOCIAL COSTS BY TREATMENT
FOR PRESENT DIABETIC POPULATION

If one were to consider the present diabetic population, one could use the model discussed herein
to estimate the total costs attributable to diabetes in its present state. This is done in standard
Monte Carlo fashion by running through the model many patients in each age-of-onset class and then
averaging to find an average cost per patient for each class. This average is then multiplied by the
number of patients in each class in the current patient population. These costs, summed across
classes, are presented here for each treatment type. Economic costs are direct expenditures for
treatment, both for diabetes and complications, while social costs refer to work days lost and
reduced productive lifetime.

The dollar value represents 1985 dollars which are calculated from 1976 dollars using a 6 percent
rate of inflation.
## Present Value of Economic and Social Costs by Treatment for Present Diabetic Population

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Conventional</td>
<td>34466.9</td>
<td>59112.3</td>
<td>93579.2</td>
</tr>
<tr>
<td>2. Human Insulin #1 Optimistic</td>
<td>28974.1</td>
<td>53605.1</td>
<td>82579.2</td>
</tr>
<tr>
<td>3. Human Insulin #1 Realistic</td>
<td>32724.7</td>
<td>55156.3</td>
<td>87881.0</td>
</tr>
<tr>
<td>4. Human Insulin #2 Optimistic</td>
<td>34255.7</td>
<td>52939.7</td>
<td>87195.4</td>
</tr>
<tr>
<td>5. Human Insulin #2 Realistic</td>
<td>38270.9</td>
<td>54810.8</td>
<td>93081.7</td>
</tr>
<tr>
<td>6. Human Insulin #3 Optimistic</td>
<td>41011.4</td>
<td>52613.8</td>
<td>91936.4</td>
</tr>
<tr>
<td>7. Human Insulin #3 Realistic</td>
<td>43689.4</td>
<td>57035.5</td>
<td>100724.9</td>
</tr>
<tr>
<td>8. Artificial Pancreas/Foreign</td>
<td>99425.8</td>
<td>49346.1</td>
<td>148772.0</td>
</tr>
<tr>
<td>9. Art. Pan./Human #1 Optimistic</td>
<td>94477.4</td>
<td>47178.7</td>
<td>141656.1</td>
</tr>
<tr>
<td>10. Art. Pan./Human #1 Realistic</td>
<td>95741.4</td>
<td>51745.9</td>
<td>147487.1</td>
</tr>
<tr>
<td>11. Art. Pan./Human #2 Optimistic</td>
<td>100152.8</td>
<td>46815.1</td>
<td>146967.9</td>
</tr>
<tr>
<td>12. Art. Pan./Human #2 Realistic</td>
<td>102367.6</td>
<td>47580.3</td>
<td>149947.8</td>
</tr>
<tr>
<td>13. Art. Pan./Human #3 Optimistic</td>
<td>107634.9</td>
<td>48069.6</td>
<td>155705.4</td>
</tr>
<tr>
<td>14. Art. Pan./Human #3 Realistic</td>
<td>108166.5</td>
<td>47695.2</td>
<td>155861.7</td>
</tr>
<tr>
<td>15. Beta-Cell Transplant</td>
<td>20778.2</td>
<td>43211.5</td>
<td>63989.7</td>
</tr>
</tbody>
</table>

*Cost assumed equal to present kidney transplant costs

**Assumes 50 percent reduction of treatment costs
PRESENT VALUE OF BENEFITS OF TREATMENT IN COMPARISON TO CONVENTIONAL TREATMENT FOR PRESENT U.S. DIABETIC POPULATION

Some, but not all, of the alternative treatments modeled compare favorably with the current, conventional treatment. Direct injection of human insulin can provide a present value benefit of up to $11 billion (1985 dollars) or a disbenefit of $7.1 billion, depending upon the assumptions employed. The advantages of the artificial pancreas appear to be substantially outweighed by its cost; given our estimated inputs to the model, the artificial pancreas is clearly not economic. Beta cell transplants, if available at the reasonable costs assumed (see Appendix F), are extremely beneficial; this treatment, if successful, effectively eliminates the problem of diabetes for the patient.

Of course, space bioprocessing is only one possible means of obtaining these benefits. Laboratory synthesized human insulin, for example, may result even without space bioprocessing.

Thus, the benefits shown are really the benefits of the improved treatment and are independent of the technology that leads to the improvement.
PRESENT VALUE OF BENEFITS OF TREATMENT IN COMPARISON TO
CONVENTIONAL TREATMENT FOR PRESENT U.S. DIABETIC POPULATION

<table>
<thead>
<tr>
<th>Description</th>
<th>Present Value</th>
<th>Total Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(1985$, billions)</td>
<td></td>
</tr>
<tr>
<td>1. CONVENTIONAL (BOVINE/PROCINE INSULIN)</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>2. HUMAN INSULIN #1 OPTIMISTIC</td>
<td>11.0</td>
<td></td>
</tr>
<tr>
<td>3. HUMAN INSULIN #1 REALISTIC</td>
<td>5.7</td>
<td></td>
</tr>
<tr>
<td>4. HUMAN INSULIN #2 OPTIMISTIC</td>
<td>6.4</td>
<td></td>
</tr>
<tr>
<td>5. HUMAN INSULIN #2 REALISTIC</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>6. HUMAN INSULIN #3 OPTIMISTIC</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td>7. HUMAN INSULIN #3 REALISTIC</td>
<td>-7.1</td>
<td></td>
</tr>
<tr>
<td>8. ARTIFICIAL PANCREAS/FOREIGN</td>
<td>-55.2</td>
<td>-33.3</td>
</tr>
<tr>
<td>9. ART. PAN./HUMAN #1 OPTIMISTIC</td>
<td>48.2</td>
<td>-26.0</td>
</tr>
<tr>
<td>10. ART. PAN./HUMAN #1 REALISTIC</td>
<td>-53.9</td>
<td>-30.6</td>
</tr>
<tr>
<td>11. ART. PAN./HUMAN #2 OPTIMISTIC</td>
<td>-53.4</td>
<td>-29.1</td>
</tr>
<tr>
<td>12. ART. PAN./HUMAN #2 REALISTIC</td>
<td>-56.3</td>
<td>-32.1</td>
</tr>
<tr>
<td>13. ART. PAN./HUMAN #3 OPTIMISTIC</td>
<td>-62.2</td>
<td>-35.1</td>
</tr>
<tr>
<td>14. ART. PAN./HUMAN #3 REALISTIC</td>
<td>-62.3</td>
<td>-35.3</td>
</tr>
<tr>
<td>15. BETA-CELL TRANSPLANT</td>
<td>29.6</td>
<td></td>
</tr>
</tbody>
</table>

*COST ASSUMED EQUAL TO PRESENT KIDNEY TRANSPLANT COSTS

**ASSUMES 50 PERCENT REDUCTION OF TREATMENT COSTS
BENEFITS OVER CONVENTIONAL TREATMENT
DIRECT AND INDIRECT COSTS

The opposite figure plots the expected benefits of each of the treatments considered relative to the conventional treatment (bovine/porcine insulin).
PRESENT VALUE
OF BENEFITS
(1985$ BILLIONS)

HUMAN INSULIN

ARTIFICIAL PANCREAS

BETA CELL TRANSPLANT

CONVENTIONAL TREATMENT

IMPACTABLE BY SPACE
BIOPROCESSING

NOT IMPACTABLE BY SPACE
BIOPROCESSING
SUMMARY OF BENEFITS OF BETA CELL TRANSPLANTS

Presented here are more detailed results from the Beta cell treatment case. The number of diabetics in each age-of-onset class is listed as well as average age at death and the benefits of the treatment when compared with the conventional. As can be seen, the patients' lifetimes always increase. The largest benefit, of course, comes from the youngest age-of-onset class, primarily because of the large population size of that class, but also because theirs is a longer diabetic lifetime to be affected by the improved treatment.
### SUMMARY OF BENEFITS OF BETA CELL TRANSPLANTS

<table>
<thead>
<tr>
<th>AGE AT DIABETES ONSET (YEARS OF AGE)</th>
<th>NUMBER IN U.S. POPULATION (MILLIONS OF PERSONS)</th>
<th>AVERAGE AGE AT DEATH**</th>
<th>BENEFITS TO TREATMENT COSTS (MILLIONS OF DOLLARS)**</th>
<th>BENEFITS TO COMPLICATION COSTS (MILLIONS OF DOLLARS)**</th>
<th>BENEFITS TO MORTALITY COSTS (MILLIONS OF DOLLARS)**</th>
<th>TOTAL BENEFIT (MILLIONS OF DOLLARS)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 19</td>
<td>1.06</td>
<td>47.7 (41.9)</td>
<td>6667</td>
<td>4967</td>
<td>15031</td>
<td>26665</td>
</tr>
<tr>
<td>20 - 39</td>
<td>.06</td>
<td>64.6 (60.3)</td>
<td>365</td>
<td>329</td>
<td>559</td>
<td>1255</td>
</tr>
<tr>
<td>40 - 59</td>
<td>.06</td>
<td>73.6 (71.2)</td>
<td>282</td>
<td>485</td>
<td>335</td>
<td>1102</td>
</tr>
<tr>
<td>60+</td>
<td>.06</td>
<td>76.0 (75.9)</td>
<td>220</td>
<td>367</td>
<td>19</td>
<td>568</td>
</tr>
<tr>
<td>TOTAL***</td>
<td>1.24</td>
<td>51.1 (45.9)</td>
<td>7542</td>
<td>6148</td>
<td>15944</td>
<td>29633</td>
</tr>
</tbody>
</table>

*Average at death, beta cell transplant (average age at death, conventional treatment)

**Present value in 1985 dollars

***Differences between column totals and total row are due to rounding errors
PRELIMINARY FINDINGS

Our preliminary results show that there may be substantial benefit from the production of human insulin or the separation of Beta cells for transplantation. These benefits could be in the range of $11 billion (1985 dollars) to $29.6 billion (1985 dollars). Considerably more information on the costs of human insulin production or Beta cell separation must be obtained, however, before we can have confidence in the size of the ultimate benefit. Hopefully more information and consensus on the effects of insulin-antibody build-up in the body will also be forthcoming from medical researchers.

Both treatments clearly show the potential for substantial benefits and research in both should continue.
PRELIMINARY FINDINGS

- PRODUCTION OF HUMAN INSULIN
  + POTENTIAL ECONOMIC AND SOCIAL BENEFITS MAY BE LARGE
  + IMPROVED ESTIMATES OF COST OF PRODUCTION OF INSULIN AND IMPACT OF HUMAN INSULIN ON DIABETIC COMPLICATIONS REQUIRED TO REDUCE UNCERTAINTY IN BENEFIT ESTIMATES

- BETA-CELL TRANSPLANT
  + LARGER POTENTIAL ECONOMIC AND SOCIAL BENEFITS
  + SHORTER TIME REQUIRED TO ASSESSE BENEFITS
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New York Times, Harold M. Schmeck, Jr., U.S. Panel Rates Diabetes as Third-Highest Cause of Death; Long-Range Plan Urged to Fight Disease, Thursday, December 11, 1975


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SELECTED BIBLIOGRAPHY - DIABETES MELLITUS (CONTINUED)

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APPENDIX A

HUMAN CAPITAL PROCEDURES/ASSUMPTIONS
HUMAN CAPITAL PROCEDURES/ASSUMPTIONS

- Mean earnings of full-time, year round employees obtained from Department of Labor, *Monthly Labor Review*, June 1976

<table>
<thead>
<tr>
<th>Group</th>
<th>Earnings</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Men</td>
<td>$14,286</td>
</tr>
<tr>
<td>All Other Men</td>
<td>10,538</td>
</tr>
<tr>
<td>White Women</td>
<td>8,055</td>
</tr>
<tr>
<td>All Other Women</td>
<td>7,633</td>
</tr>
</tbody>
</table>

- Full-time employees represent the following percentage of all persons with work experience:

<table>
<thead>
<tr>
<th>Group</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Men</td>
<td>64.7%</td>
</tr>
<tr>
<td>All Other Men</td>
<td>56.5%</td>
</tr>
<tr>
<td>White Women</td>
<td>41.0%</td>
</tr>
<tr>
<td>All Other Women</td>
<td>43.6%</td>
</tr>
</tbody>
</table>

  Thus, this percentage was multiplied times the respective earnings.

- Mean earnings figures are then adjusted upward to account for wage supplements (employer contributions for social insurance, private pension and welfare funds). The uniform factor is 1.0776.

- Seventy percent of $4,000 was added to all women's earnings for housekeeping services: $400 was added for all males. $4,000 was imputed as housekeeper earnings for all retired females and $1,000 for men.

- A 6 percent discount rate was utilized.
HUMAN CAPITAL PROCEDURES/ASSUMPTIONS (Continued)

- The present value of future earnings of a person at age $a$ is defined by the following formula:

$$V_a = \sum_{n=a}^{85 \text{ & over}} \frac{X_n \cdot W_n \cdot P_n}{(1+i)^{n-a}}$$

where:

- $a$ is the midyear age for the given cohort of persons;
- $X_n$ is the annual mean earnings for all persons in the category with earnings in an age group where the midpoint is age $n$;
- $i$ is the discount rate;
- $W_n \cdot P_n$ is defined as the number of labor force years per person in an age group.
APPENDIX B

COST DATA FOR TREATMENT OF END STAGE RENAL DISEASE
PUBLIC SECTOR COSTS

DIALYSIS

1. FIRST YEAR
   - 80% of hospital costs after 3 months: $13,500.00
   - 80% of doctors' fees: 1,700.00
   - 20% of patients on welfare: 1,000.00
   - Total: $16,200.00

2. SUBSEQUENT YEARS
   - 80% of hospital costs: $18,000.00
   - 80% of doctors' fees: 2,300.00
   - 20% of patients on welfare: 1,000.00
   - Total: $21,300.00

TRANSPLANT

3. FIRST YEAR
   - 80% of transplant operation
     (see transplant cost breakdown): $13,000.00

4. SUBSEQUENT YEARS
   - Total: 0

DEATHS

5. Total: 0
PRIVATE SECTOR COSTS

DIALYSIS

1. FIRST YEAR
   CENTER DIALYSIS COST: $17,000 (70%) = $11,900
   (SEE CENTER DIALYSIS COST BREAKDOWN)
   HOME DIALYSIS: $18,450 (30%) = 5,535
   AVERAGE $17,435

2. SUBSEQUENT YEARS
   CENTER DIALYSIS COST $11,850 x 70% = $8,295
   HOME DIALYSIS COST $8,450 x 30% = 2,535
   $10,830

TRANSPLANT

3. FIRST YEAR
   20% OF AVERAGE OPERATION COST PLUS
   OTHER INCURRED COSTS $9,250

4. SUBSEQUENT YEARS
   COSTS $5,100

DEATH

5. DEATH -0-
<table>
<thead>
<tr>
<th>Item</th>
<th>1st Year</th>
<th>2nd Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery for connection</td>
<td>500</td>
<td>0</td>
</tr>
<tr>
<td>Counseling (50% assuming $1500/year)</td>
<td>750</td>
<td>150</td>
</tr>
<tr>
<td>Changes in diet</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Job loss</td>
<td>4800</td>
<td>3000</td>
</tr>
<tr>
<td>Retraining</td>
<td>500</td>
<td>0</td>
</tr>
<tr>
<td>Tutoring</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Diet supplements</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>Moving expenses</td>
<td>1000</td>
<td>750</td>
</tr>
<tr>
<td>Spouse or family job loss or reduction</td>
<td>750</td>
<td>750</td>
</tr>
<tr>
<td>Transportation costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dialysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3-Month Initial Period</strong></td>
<td>1300</td>
<td>6000</td>
</tr>
<tr>
<td>Medicare coverage (80%)</td>
<td>4500</td>
<td></td>
</tr>
<tr>
<td>M.D.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>3-Month Initial Period</strong></td>
<td>750</td>
<td>-</td>
</tr>
<tr>
<td>Medicare coverage (80%)</td>
<td>430</td>
<td>600</td>
</tr>
<tr>
<td></td>
<td>17,000</td>
<td>11,850</td>
</tr>
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</table>
## HOME DIALYSIS COST BREAKDOWN ($)

<table>
<thead>
<tr>
<th>Item</th>
<th>1st Year</th>
<th>Subsequent Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOSS OF SPOUSE WORK</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>CHAIR</td>
<td>250</td>
<td>-</td>
</tr>
<tr>
<td>PLUMBING</td>
<td>400</td>
<td>-</td>
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<tr>
<td>WATER</td>
<td>600</td>
<td>600</td>
</tr>
<tr>
<td>UTILITIES</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>TRAINING</td>
<td>4000</td>
<td>-</td>
</tr>
<tr>
<td>M.D.</td>
<td>800</td>
<td>-</td>
</tr>
<tr>
<td>MACHINE</td>
<td>4000</td>
<td>-</td>
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<tr>
<td>MAINTENANCE</td>
<td>300</td>
<td>300</td>
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<tr>
<td>LAB</td>
<td>350</td>
<td>350</td>
</tr>
<tr>
<td>HOSPITAL BACKUP</td>
<td>3000</td>
<td>3000</td>
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<tr>
<td>COUNSELING</td>
<td>500</td>
<td>350</td>
</tr>
<tr>
<td>DIET CHANGES</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>JOB LOSS</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>RETRAINING</td>
<td>500</td>
<td>-</td>
</tr>
<tr>
<td>TUTORING</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>DIET SUPPLEMENTS</td>
<td>250</td>
<td>250</td>
</tr>
<tr>
<td>SPOUSE OR FAMILY JOB LOSS</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>M.D.</td>
<td>600</td>
<td>600</td>
</tr>
</tbody>
</table>

TOTAL                           | 18,450   | 8,450            |
## Transplant Cost Breakdown

<table>
<thead>
<tr>
<th>Category</th>
<th>1st Year</th>
<th>Post Transplant Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>FROM LIVING PERSON (30% of Total X $14,000)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FROM CADAVER (70% of Total X $12,800)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVERAGE COST OF OPERATION TO PATIENT (20% of Total Cost)</td>
<td>2600</td>
<td>-</td>
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<tr>
<td>WORK LOSS</td>
<td>1800</td>
<td>-</td>
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<tr>
<td>DONOR WORK LOSS</td>
<td>1300</td>
<td>-</td>
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<tr>
<td>MEDICATION AND M.O.'S</td>
<td>1500</td>
<td>3500</td>
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<tr>
<td>DIET CHANGES</td>
<td>200</td>
<td>200</td>
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<tr>
<td>COUNSELING</td>
<td>500</td>
<td>300</td>
</tr>
<tr>
<td>TUTORING</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>DIET SUPPLEMENTS</td>
<td>250</td>
<td>-</td>
</tr>
<tr>
<td>JOB DECREASE (TOO WEAK, CANNOT CONTINUE OLD SKILL)</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>Total</td>
<td>9,250</td>
<td>5,100</td>
</tr>
</tbody>
</table>

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APPENDIX C

COST DATA FOR TREATMENT OF PULMONARY EMBOLISM
TRANSITION PROBABILITIES

SOURCES


ASSUMPTIONS

- THE PROBABILITY OF DEATH FOR THOSE PATIENTS BEING TREATED WITH UROKINASE WILL DECREASE FROM .09 TO .04.

- 80% OF PATIENTS WITH A DIAGNOSED PULMONARY EMBOLISM WILL BE TREATED WITH UROKINASE.

- A TREATMENT CONSISTING OF A PRECAUTIONARY INJECTION OF UROKINASE WILL BE GIVEN TO 30% OF UNDIAGNOSED PATIENTS. THIS INJECTION WOULD BE GIVEN BY MEDICS OR EMERGENCY ROOM PERSONNEL AS STANDARD PROCEDURE BUT NO DIAGNOSIS OF THE EMBOLISM WOULD TAKE PLACE (AS OFTEN OCCURS!).
COST ASSUMPTIONS FOR PULMONARY EMBOLISM

• NO EARNINGS ARE TABULATED, ONLY COSTS, BUT LOST EARNINGS ARE CONSIDERED A COST.

• EARNINGS (FOR LOST WAGES) WERE OBTAINED FROM THE DEPARTMENT OF LABOR.

• AVERAGE DAILY IN-PATIENT HOSPITAL COSTS FOR 1976 WERE OBTAINED FROM THE AMERICAN HOSPITAL ASSOCIATION.

• A 10 TO 1 COST REDUCTION FOR THE PRODUCTION OF UROKINASE WAS ASSUMED, BRINGING THE COST OF ONE DOSE DOWN TO $200.00.
COST BREAKDOWN BY TREATMENT STATE

1. PULMONARY EMBOLISM -
   NONE, BY DEFINITION

2. NO DIAGNOSIS WITH TREATMENT
   1 MONTH LOST EARNINGS $913.75
   HOSPITAL COSTS
   4 DAYS @ $158.39 633.56
   UROKINASE 200.00
   TOTAL $1747.31
   (ROUNDED $1750.)

3. NO DIAGNOSIS AND NO TREATMENT
   1 MONTH LOST EARNINGS $913.75
   HOSPITAL COSTS
   5 DAYS @ $158.39 791.95
   TOTAL $1705.70
   (ROUNDED $1700.)

4. POST PULMONARY EMBOLISM, NO PROPHYLAXIS
   NONE

5. HEPARIN TREATMENT
   M.D. $1000.00
   HOSPITAL COST
   5 DAYS INTENSIVE CARE
   @ $400/DAY 2000.00
   9 MEDIUM CARE @ $158.39 1425.50
   HEPARIN 20.00
   LUNG SCAN 913.75
   LOST WAGES (1 MONTH) 600.00
   TOTAL $5939.25
   (ROUNDED $5940.)
COST BREAKDOWN BY TREATMENT STATE (CONTINUED)

6. UROKINASE AND HEPARIN

M.D. $1000.00

HOSPITAL COSTS
3 DAYS INTENSIVE CARE @ $400. 1200.00
9 DAYS MEDIUM CARE @ $158.39 1425.50
LOST WAGES 913.75
LUNG SCAN 600.00
UROKINASE 200.00

(ROUNDED $5340.) $5339.25

7. SURGERY

HOSPITAL COSTS
4 DAYS INTENSIVE CARE @ $400. $1600.00
12 DAYS MEDIUM CARE @ $158.39 1900.88
HEPARIN 20.00
SURGEON 1900.00
INTERNIST 500.00
LUNG SCAN 600.00
LOST WAGES (2 MONTHS) 1827.50

(ROUNDED $8350.) $8348.18

8. POST PULMONARY EMBOLISM WITH PROPHYLAXIS

M.D. $300.00
HEPARIN 20.00
LUNG SCAN 600.00

$920.00

9. DEATH
APPENDIX D

COMPUTER PROGRAM LISTING FOR THE MODEL OF ESRD AND PULMONARY EMBOLISM
FILEDEF P DSK A1 DATA
FILEDEF G DSK A1 OUTPUT LPECL 132
RNL BIG WEST
FILEDEF * CLEAR

ORIGINIAL PAGE IN
OF POOR QUALITY
ORIGINAL PAGE IS OF POOR QUALITY

1:00 3:10
1:10
1:20
1:30
1:40
1:50
2:00
2:10
2:20
2:30
2:40
2:50
3:00
3:10
3:20
3:30
3:40
3:50
4:00
4:10
4:20
4:30
4:40
4:50
5:00
5:10
6:00
6:10
7:00
8:00
9:00
10:00
11:00
12:00
1:00
DO 20 I=1,NS
A(I) = AXY + 1
Y(I) = 0
T(I) = 0
20 CONTINUE

* = 1
Z(I) = 1
CS = 1

I = MAT(YPS, YP, YS)
X = FAX(1,35713)
CSP = FCPPS(1) + CS*Y + YS
A(CSP) = "Y"(A(CSP)) + 1
IF(CCPPS(I) = 1) GO TO 155
Y(CSP) = Y(Y(CSP)) + 1
IF(CCS + ECSPS) Z(CSP) = Z(CSP) + 1
CC() = C(CSP)
DC() = D(CSP)
CODE = C(CSP)*BICCC(-1)**(-1)
DEC = D(CSP)*BIDS(-1)**(-1)
TCC = TCC + CC(T)
STCC = TCC + CEC(1)
TDC = TDC + DC(T)
CC = CC + TCC + STCC(T)
A = A + 1
CS = CS
IF(A = W) GO TO 13
CS = :1
155 FL = A = ":
ACCS = "
CS = CS + I = 1 + S
IF(A = 0) GO TO 19
IF(A + 1) = A(I) = A(I) + 1
IF(A + 2) = Z(I) = Z(I)
150 IF(A + 1) = A(I) + 1) LIT(I) = .ITC(I) + 1
133 CS = TOS + TSC
AVETCC = AVETCC + TCC
STCC = STCC + TCC
AVETCS = AVETCS + TCC
STDC = STDC + TSC
AVALE = AVALE + ALPA
SL = SL + ALPA
AVET = AVET + STCC
SYCC = SYCC + STCC
AVCDD = AVCDD + LDD
SDTO = SDTO + STCC
CO 156 FL = "
AVEC(I) = AVEC(I) + A(I)
SCB(I) = SCB(I) + A(I) + 1
AVEZ(I) = AVEZ(I) + Z(I)
L(I) = L(I) + Z(I)
L(I) = L(I) + 1
L(I) = L(I) + Y(I)
S = Y(I) = Y(I) + Y(I)
1.7 CONTINUE
CO 170 I = 1 + W
AVECC(I) = AVECC(I) + OCC(I)
STUFF ERROR
FILEDEF 6 USK 61 DATA
FILEDEF 9 USK BIOSORT DATA LRFCL 1.0
FILEDEF 6 USK BICOLT DATA LRFCL 132
LOAD BIO MAT NEWS
CERLGS
FILEDEF 4 CLEAR
FUNCTION  REAL, CS
RES  13, 15, 15
Z = 0
DO 10 J = 1, CS
Z = Z + F(I*CS0)
IF(2.3T, Y) GO TO 20
10 CONTINUE
STOP 456
20 GESC = J
JETJK
END

ORIGINAL PAGE IS
OF POOR QUALITY
APPENDIX E

DIABETES TRANSITIONAL PROBABILITY MODEL PROGRAM
COMPUTER LISTING
1010 DIM S(10), CL(20), H(10), X(20), U(10), W(10)
1020 DIM S(10), E(10), F(10), G(10), H(10), X(20), R(10), U(10), V(20)
1030 DIM L(20)
1040 L(1)=10
1050 L(2)=30
1060 L(3)=50
1070 L(4)=60
1080 FILES PROB, COST, MORT, COM, TREAT, WAGES
1090 MAT READ # 2: C
1100 MAT READ # 4: P
1110 MAT READ # 6: V
1120 DISP "ENTER NUMBER OF ITERATIONS":
1130 INPUT N
1140 FOR L=1 TO 4
1150 Q=L(L)
1160 FORMAT "THE NUMBER OF ITERATIONS IS", F6.0
1170 M=5
1180 DISP "ENTER AGE AT ONSET":
1190 REM INPUT Q
1200 FOR Q=1 TO 15
1210 PRINT LIN2; "******---------------------------------------------------------------", LIN1
1220 WRITE (2, 1160: M)
1230 FORMAT "TREATMENT COSTS", F10.2
1240 T8=INT(Q/5)
1250 T9=0
1260 IF Q >= 60 THEN 1260
1270 T9=INT((60-Q)/5)
1280 WRITE (2, 1230: Q)
1290 FORMAT "THE AGE AT ONSET IS", F6.0
1300 DISP "ENTER TREATMENT NUMBER":
1310 REM INPUT Q
1320 MAT READ # 5, 92: Y
1330 WRITE (2, 1350: Q2)
1340 WRITE (2, 1230: C[92, 1], C[92, 2])
1350 FORMAT "THE TREATMENT NUMBER IS", F6.0
1360 F9=INT(Q/20)+1
1370 IF F9<5 THEN 1370
1380 F9=4
1390 MAT READ # 1, (F9-1)*4+1; P
1400 FOR I=1 TO 10
1410 FOR j=1 TO 5
1420 P(I, j)=P(I, j)+U(I)
1430 NEXT J
1440 NEXT I
1450 FOR I=1 TO 10
1460 DI(I, 1)=PI(I, 1)
1470 FOR j=2 TO 5
1480 DI(I, j)=PI(I, j)-PI(I, j-1)
1490 NEXT J
1500 Z=P(I, 1)
1510 FOR J=2 TO 5
1520 PCI, J) = D[I, J]/(1 - Z)
1530 Z = Z + D[I, J]
1540 NEXT J
1550 FOR J = 6 TO 20
1560 PCI, J) = 0
1570 NEXT J
1580 NEXT I
1590 PRINT LIM1, "PROBABILITY TABLE"
1600 FOR I = 1 TO 5
1610 FOR J = 1 TO 5
1620 WRITE (2, 1630) PL[I, J]
1630 FORMAT F7.3
1640 NEXT J
1650 PRINT " "
1660 NEXT I
1670 MAT READ 3, (F9-1)*4+1; D
1680 MAT Y = ZER
1690 MAT A = ZER
1700 MAT B = ZER
1710 MAT E = ZER
1720 MAT F = ZER
1730 MAT G = ZER
1740 N = 0
1750 N = N + 1
1760 IF N > N9 THEN 2280
1770 DISP "ITER"N
1780 MAT S = ZER
1790 MAT H = ZER
1800 Y = 0
1810 Z = 1
1820 Y = Y + 1
1830 Z9 = Z
1850 S = S[OZ, 1]
1860 IF Y = 1 THEN 1880
1870 S = S[OZ, 2]
1880 FOR I = 1 TO M
1890 IF S[I] = 1 THEN 1930
1900 IF RND(Q) > P[I, Y] THEN 1990
1910 S = S + R[I, 1]
1920 SE[I] = 1
1930 E[I] = E[I] + 1
1940 F[I] = F[I] + Y
1950 H[I] = Y
1960 Z = Z + 1
1970 GOTO 1990
1980 S = S + R[I, 2]
1990 NEXT I
2000 IF Z < 3 OR Y > 9 THEN 2170
2010 IF S[6] = 1 THEN 2140
2020 T2 = 0.25
2030  IF Z=3 THEN 2050
2040  T2=.0 .35
2050  IF RNDQ>T2 THEN 2170
2060  Z=Z+1
2070  S[J]=1
2080  E[J]=E[J]+1
2090  H[J]=Y
2100  F[J]=F[J]+Y
2110  S=S+C[20,1]
2120  IF RNDQ>0.7 THEN 2170
2130  GOTO 2150
2140  S=S+C[20,2]
2150  X[J]=X[J]+S
2160  GOTO 2190
2170  X[J]=X[J]+S
2180  IF RNDQ>(D[Z,Y]+D[Z9,Y])*.5 THEN 1820
2190  B[Z]=B[Z]+1
2200  Y9=Y*0 .5
2210  FOR I=1 TO M+1
2220  IF H[I]=0 THEN 2240
2240  NEXT I
2250  IF H[5]=0 THEN 2270
2270  GOTO 1750
2280  S1=S2=S7=0
2300  FOR Y=1 TO 20
2310  IF A[Y]=0 THEN 2400
2320  T7=Y+T8
2330  D=A[Y]-A[Y+1]
2340  WRITE (2,2350)(Y-1)*5+1,Y*5,D*D*Y[T7]*X[Y]/A[Y]
2350  FORMAT F5.0,"-",F4.0,F12.0,2F14.0
2360  S1=S1*D*Y[T7]
2370  S2=S2+D*D*Y[T7]*V[T7]
2380  S7=S7+X[Y]
2390  NEXT Y
2400  S5=S6=0
2410  FOR Y=1 TO 20
2420  IF A[Y]=0 THEN 2460
2440  S6=S6+(A[Y]-A[Y+1])*Y*Y*25
2450  NEXT Y
2460  S5=S5/N9
2470  WRITE (2,2480)S1/N9
2480  FORMAT /,"AVE LOST WAGES",F12.0
2490  S8=1
2500  IF S5>=5 THEN 2520
2510  S8=S8/5
2520  S4=S8*C[Q2,1]+(S5-S8)*C[Q2,2]/5
2530  WRITE (2,2540)S4, (S7/N9-S4)
2540 FORMAT "TREATMENT COST", F12.0, "COMPLICATION COST", F9.0
2550 WRITE (2, 2560) S7/N9
2560 FORMAT "AVE TOTAL COST", F12.0
2570 S6=S6/N9
2580 V=(S6-S5*S5)**0.5
2590 WRITE (2, 2600) S5+0, V
2600 FORMAT "/", "AGE AT DEATH", F10.1
2610 PRINT
2620 S1=S1/N9
2630 S2=S2/N9
2640 S3=(S2-S1*S1)**0.5
2650 N9=N-1
2660 PRINT "PROB OF GETTING NUMBER OF COMPLICATIONS"
2670 FOR I=1 TO 7
2680 P=BE[I]/N9
2690 WRITE (2, 2700) (I-1), P*100, 100*(P*(1-P))**0.5
2700 FORMAT F8.0, 2F10.1
2710 NEXT I
2720 PRINT
2730 PRINT "PROB OF GETTING SPECIFIC COMPLICATION"
2740 FOR I=1 TO N+1
2750 P=EI[I]/N9
2760 WRITE (2, 2700) I, 100*P, 100*(P*(1-P))**0.5
2770 NEXT I
2780 PRINT
2790 PRINT "AGE GETTING COMPLICATION"
2800 FOR I=1 TO N+1
2810 S=0
2820 IF EI[I]=0 THEN 2860
2830 S=S+EI[I]/EI[I]+Q-2.5
2840 IF I=W THEN 2860
2850 S=S-2.5
2860 WRITE (2, 2700) I, S
2870 NEXT I
2880 PRINT
2890 PRINT "NUMBER OF YEARS WITH COMPLICATION"
2900 FOR I=1 TO N+1
2910 S=0
2920 IF EI[I]=0 THEN 2940
2930 S=GI[I]/EI[I]+5
2940 WRITE (2, 2700) I, S
2950 NEXT I
2960 NEXT Q2
2970 NEXT L
2980 END
APPENDIX F
COST OF DIABETES TREATMENT
COST PER PATIENT OF INITIAL DIABETES TREATMENT (TREATMENT AT ONSET)

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost</th>
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<tbody>
<tr>
<td>7 DAYS HOSPITAL</td>
<td>$1,225</td>
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<tr>
<td>DIABETES TREATMENT</td>
<td>215</td>
</tr>
<tr>
<td>WORK LOSS (14 DAYS)</td>
<td>308</td>
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</table>

**Total**: $1,748
ANNUAL COST PER PATIENT OF CONVENTIONAL TREATMENT

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>INSULIN AND MEDICAL SUPPLY</td>
<td>$115</td>
</tr>
<tr>
<td>2 CLINIC VISITS</td>
<td>96</td>
</tr>
<tr>
<td>WORK LOSS (ONE DAY)</td>
<td>22</td>
</tr>
<tr>
<td>DIET CHANGE</td>
<td>200</td>
</tr>
<tr>
<td>TUTORING</td>
<td>100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$533</strong></td>
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</tbody>
</table>
### Annual Per Patient Cost of Human Insulin

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost 1</th>
<th>Cost 2</th>
<th>Cost 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin &amp; Medical Supply</td>
<td>$115</td>
<td>$335</td>
<td>$610</td>
</tr>
<tr>
<td>2 Clinic Visits</td>
<td>96</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Work Loss (1 Day)</td>
<td>22</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Diet Change</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Tutoring</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$533</strong></td>
<td><strong>$753</strong></td>
<td><strong>$1,028</strong></td>
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## ANNUAL COST PER PATIENT OF ARTIFICIAL PANCREAS/FOREIGN INSULIN TREATMENT

<table>
<thead>
<tr>
<th>Item</th>
<th>FIRST YEAR</th>
<th>POST YEAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation and Device</td>
<td>$12,800</td>
<td>$ -</td>
</tr>
<tr>
<td>Work Loss</td>
<td>1,800</td>
<td>-</td>
</tr>
<tr>
<td>Medication (except insulin) and M.D.'s</td>
<td>1,500</td>
<td>500</td>
</tr>
<tr>
<td>Diet Changes</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Counseling</td>
<td>500</td>
<td>300</td>
</tr>
<tr>
<td>Tutoring</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Diet Supplements</td>
<td>250</td>
<td>-</td>
</tr>
<tr>
<td>Job Decrease</td>
<td>1,000</td>
<td>1,000</td>
</tr>
<tr>
<td>Insulin and Medical Supplies</td>
<td>115</td>
<td>115</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$18,265</strong></td>
<td><strong>$2,215</strong></td>
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## ANNUAL COST PER PATIENT OF BETA CELL TRANSPLANT

<table>
<thead>
<tr>
<th></th>
<th>FIRST YEAR</th>
<th>POST YEAR</th>
</tr>
</thead>
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<tr>
<td>OPERATION</td>
<td>$6000</td>
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</tr>
<tr>
<td>WORK LOSS</td>
<td>374</td>
<td></td>
</tr>
<tr>
<td>CLINIC VISITS (2)</td>
<td>96</td>
<td>$96</td>
</tr>
<tr>
<td>WORK LOSS (ONE DAY)</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>DIET AND TUTORING</td>
<td>600</td>
<td>500</td>
</tr>
<tr>
<td></td>
<td><strong>$7092</strong></td>
<td><strong>$618</strong></td>
</tr>
</tbody>
</table>
ANNUAL COST PER PATIENT OF ARTIFICIAL PANCREAS WITH HUMAN INSULIN

<table>
<thead>
<tr>
<th></th>
<th>FIRST YEAR HUMAN #1</th>
<th>FIRST YEAR HUMAN #2</th>
<th>FIRST YEAR HUMAN #3</th>
<th>POST YEAR HUMAN #1</th>
<th>POST YEAR HUMAN #2</th>
<th>POST YEAR HUMAN #3</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPERATION AND DEVICE</td>
<td>$12,800</td>
<td>$12,800</td>
<td>$12,800</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>WORK LOSS</td>
<td>1,800</td>
<td>1,800</td>
<td>1,800</td>
<td>-</td>
<td>-</td>
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<tr>
<td>MEDICATION (EXCEPT INSULIN) AND PHYSICIANS</td>
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<tr>
<td>TUTORING</td>
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<td>100</td>
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<tr>
<td>DIET SUPPLEMENTS</td>
<td>250</td>
<td>250</td>
<td>250</td>
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</tr>
<tr>
<td>JOB DECREASE</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
<td>1,000</td>
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<tr>
<td>INSULIN AND MEDICAL SUPPLIES</td>
<td>115</td>
<td>335</td>
<td>610</td>
<td>115</td>
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<td>TOTAL</td>
<td>$18,265</td>
<td>$18,485</td>
<td>$18,760</td>
<td>$2,215</td>
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COST PER PATIENT OF PANCREAS TRANSPLANT

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<tr>
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<th>First Year</th>
<th>Post Year</th>
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<tr>
<td>OPERATION (CADAVER)</td>
<td>$12,800</td>
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<td>WORK LOSS</td>
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<tr>
<td>TUTORING</td>
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<td>100</td>
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<tr>
<td>DIET SUPPLEMENTS</td>
<td>250</td>
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<tr>
<td>JOB DECREASE (UNABLE TO CONTINUE OLD SKILL)</td>
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<td>$18,150</td>
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APPENDIX G

COST OF DIABETIC COMPLICATION CARE
COST OF DIABETIC RETINOPATHY

COST PER PATIENT--DIRECT AND INDIRECT
$625 FIRST 5-YEAR PERIOD
$1250 SUBSEQUENT 5-YEAR PERIOD

COST OF CARDIOVASCULAR COMPLICATIONS

COST PER PATIENT—DIRECT AND INDIRECT

$9,940 FIRST 5-YEAR PERIOD

$11,665 SUBSEQUENT 5-YEAR PERIODS

• DIRECT COST, COST OF MYOCARDIAL INFARCTION, CHANGES IN THE COSTS OF TREATMENT OF SELECTED ILLNESSES, ANNE A. SCITOVSKY AND NELDA MCCALL, HEALTH POLICY PROGRAM, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, 1975

• INDIRECT COSTS 37.2 DAYS LOST INCOME FOR INITIAL TREATMENT

REDUCTION OF SUBSEQUENT INCOME BY ONE-THIRD
COST OF PERIPHERAL VASCULAR COMPLICATIONS

COST PER PATIENT--DIRECT AND INDIRECT

$20,500 FIRST 5-YEAR PERIOD
$35,000 SUBSEQUENT 5-YEAR PERIOD

- DIRECT COSTS OF FIRST YEAR TREATMENT $3000 (VERY OFTEN AMPUTATIONS)
- INDIRECT COSTS--LOSS OF AVERAGE EARNING CAPACITY
COST OF NEPHROPATHY TREATMENT

PER PATIENT COSTS DIRECT AND INDIRECT

$2,500 FIRST 5-YEAR PERIOD
$5,000 SUBSEQUENT 5-YEAR PERIODS


THE ECONOMIC COST OF ILLNESS REVISITED, BARBARA S. COOPER AND DOROTHY P. RICE, 1976, DHEW PUBLICATION NO. (SSA) 76-11703.
COST OF INSULIN RESISTANCE

COST PER PATIENT DIRECT AND INDIRECT
$14,433  FIRST 5-YEAR PERIOD
$12,685  SUBSEQUENT 5-YEAR PERIODS

BREAKDOWN:

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<tr>
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<tr>
<td>ADDITIONAL INSULIN (800 UNITS/DAY)</td>
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<td>ADDITIONAL CLINIC VISITS (4/YEAR)</td>
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<td>HOSPITAL STAY</td>
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<td>$4,285</td>
<td>$2,537</td>
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SOURCES:  MEDICAL ADVISORS
          JOSLIN CLINIC