KIDNEY DISEASE

PROGRAM ANALYSIS

A REPORT TO THE SURGEON GENERAL

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Prepared Under

Direction of Office of

Program Planning and Evaluation

Office of the Surgeon General

14 DEC 67

The Public Health Service has a continuing responsibility to examine the framework for effective decision-making required in the determination of health priorities and in the delineation of the most effective and efficient methods of approaching the solution of the health problems that face us. Therefore, in the spring of 1967 I convened a number of health program analysis groups to study and analyze critically the subject and program content in several specific areas of public health importance. Each of these groups was to examine present and potential goals and objectives, describe and discuss the current relevant state of knowledge and current operating programs, and to develop and analyze to the best of its ability alternative courses of action directed toward the achievement of these goals.

The analysis group responsible for this report on kidney disease was under the direction of Benjamin T. Burton, Ph.D., Associate Director for Program Analysis and Scientific Communication, NIAMD, who was assisted ably by staff from the various bureaus of the Public Health Service. Analyses of this kind are hampered by large data gaps which limit the breadth and precision with which specific program alternatives and effectiveness models can be developed. These limitations, however, do not invalidate the basic concepts contained or the alternative courses of action considered. In addition, the determination of the precise areas of insufficient knowledge emphatically underscores our need for additional research and development. Thus, although program analyses in the health field are still in the very early stages of development, it nevertheless is important that we continue and improve upon previous efforts using this analytic technique.

Dr. Burton, his staff, and members of the analysis group, are to be commended for their efforts to comply with my request in such a short span of time and for the quality of the report itself. There can be no question that this initial effort will be of value to me and my staff in considering not only Public Health Service Programs directed toward kidney disease, but also in the development of the methods and procedures required for subsequent analyses in the future.

William H. Stewart
Surgeon General

July 28, 1967

William H. Stewart, M.D.
Surgeon General
U. S. Public Health Service

Dear Dr. Stewart:

In the spring of 1967, pursuant to your memoranda of February 27 and
March 15, you established a Kidney Disease Program Analysis Group
and charged it with responsibility for an analytical study of kidney
disease in the light of present and future Public Health Service
goals and objectives.

This study, by a group of staff members from the various Bureaus of
the Service with competences relevant to the specific task, was
pursued actively until now. This group was comprised of Dr. R. van Hoek
of the Bureau of Health Services, Dr. G. H. Escovitz of the Bureau of
Health Manpower, Mr. J. O'S. Francis, Dr. R. B. Freeman, and Dr. N. A.
Hilmar of the Bureau of Disease Prevention and Environmental Control,
Mr. W. Anderson of your office, and Dr. W. R. DeCesare, Mr. E. Glaser,
Dr. W. H. Goldwater, Dr. D. E. Kayhoe, Dr. K. N. Gershengorn and myself
of the National Institutes of Health. Valuable quantitative analytic
competence was obtained through a contract with the Research Triangle
Institute,

The demands of this undertaking were high both in terms of the magni-
tude and diversity of the disease area involved and in terms of the
very brief time available for the study. Nevertheless, I believe I
am expressing the consensus of the group when I say that the individual
members feel rewarded by the new knowledge and insights which they have
gained during this study.

We have now completed our task and are pleased to present to you our
report. Please be assured of our continued interest and desire to
cooperate.

Respectfully submitted,

Benjamin T. Burton, Ph.D.
Chairman
Kidney Disease Program Analysis Group

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PREFACE

This kidney disease program analysis, one of several similar
efforts being conducted at the present time, was originally conceived
as an integral part of the planning and analytic effort required in
the implementation of the Planning, Programming, Budgeting System
throughout the United States Public Health Service. It is being
published and distributed at this time with a two-fold purpose. First,
to inform biomedical scientists and health professionals of some of the
current thinking of the Public Health Service on approaches to combating
illness, disability, and death, due to kidney disease. Secondly, to
elicit comment and criticism on the assumptions, methodologies, and
general character of the analysis in order to assist the Public Health
Service in efforts to improve upon this and subsequent studies related
to planning and evaluation of health programs. It should be clearly
stated that in both regards it is recognized by members of the Public
Health Service and the analysis group itself that parts of the analysis
are totally dependent upon assumptions in areas in which there is very
rigorous scientific dispute, i.e., the etiology and subsequent patho-
genesis of certain kidney diseases, as well as assumptions regarding the
ease or practicability of the delivery of preventive health services.
Nonetheless, the significance of these diseases in terms of human suffer-
ing and death challenges us to develop programs which will have the
maximum impact on human well being in relation to the resources that will
be available for these efforts.

The importance of planning and evaluation in any large scale
enterprise has gained increasing attention and emphasis during recent
years and has resulted in the establishment of a Planning, Programming,
Budgeting System through the Executive Branch of the Federal Government.
Although sometimes narrowly conceived as a limited management tool, its
broader effect of supporting more informed and therefore better decision-
making was clearly emphasized in the original memoranda transmitting the
Presidential decision to effect its wide-spread implementation. The
approach emphasizes (1) clear articulation of goals and objectives, and
(2) alternative approaches to attaining these objectives.

Numerous authorities on the Planning, Programming, Budgeting
System have emphasized the two major components of this approach as
"systems analysis" and "program budgeting." Systems analysis requires
a multidisciplinary approach by analytically oriented people skilled
in the use of quantitative techniques. Program budgeting requires
thinking of the budget in terms of program objectives, i.e., purposes
realized rather than objects of expenditure, i.e., facilities, equipment,
and the like. The unifying theme of program analysis is one of attempting
to relate program costs to program effectiveness. That some problems
have been encountered in attempting to implement this budgetary system
is understandable.

Charles J. Hitch, who directed the implementation of the Planning,
Programming, Budgeting System in the Department of Defense beginning in
1961, has repeatedly cautioned others on the need for adequate preparatory
work and development of the analytic competencies necessary to carry out
this activity. It is noted by Mr. Hitch in the Nuffield Lecture delivered
last year,

"In Defense we had several hundred analysts at the RAND

Corporation and elsewhere developing programming and

systems analysis techniques for a decade before the

Department attempted any large scale general application.

No remotely similar preparatory effort has gone into any

other governmental area and the number of trained and

skilled people is so limited that they are inevitably

spread far thinner in other departments of government

than they were and are in Defense."

There has not been a comparable "preparatory effort" in the health

field devoted to the development of appropriate techniques and

methodology. Moreover, more time is usually required than that avail-

able in the budgetary cycle to carry out cost effectiveness studies

that attempt to consider all costs, not just those that are readily

apparent and quantifiable. Thus tremendous demands are placed on

individuals attempting to carry out suitable program analysis in the

health problem areas. Nonetheless, it is important that a beginning be

made and that a body of experience be developed, critiqued, assessed,

and improved upon.

In this analysis of kidney disease a priority was placed on

attempting to obtain a synergistic interrelation between analytically

oriented individuals with substantive knowledge of kidney disease and

qualified analysts. The former were represented by selected staff

members of the Public Health Service serving on a task force. The

quantitative analytic competency was obtained through a contract with

the Research Triangle Institute. Great credit is due to all individuals

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involved who tried to grapple with the objectives of kidney disease programs and alternative program approaches for meeting them. It is hoped that through their efforts, as well as through comment and criticism that may be forthcoming from others, that we will be able to improve sequentially the process and the product in future analyses.

The Office of Program Planning and Evaluation, Office of the Surgeon General, is charged with the responsibility to define, develop, and implement analytic techniques of this kind. Any assistance, criticism, or comments from professional groups, the academic community, or interested individuals will be welcome and greatly appreciated.

<u>Kidney Disease Program Analysis Group</u>

Chairman: Benjamin T. Burton, Ph.D.
                             Associate Director for Program Analysis
                               and Scientific Communication
                                         and
                             Chief, Artificial Kidney Program
                             National Institute of Arthritis
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          WITH CHRONIC KIDNEY FAILURE

Chapter 1

INTRODUCTION AND SUMMARY

OF THE

KIDNEY DISEASE PROGRAM ANALYSIS

I. INTRODUCTION

A. Objectives and Goals of the Report

In the spring of 1967 the Surgeon General of the U. S. Public Health

Service established, among others, a health program analysis group to under-

take studies and analyses in the area of kidney disease. Members of the

group were chosen from among senior staff of the National Institutes of

Health and other bureaus of the Public Health Service, who were responsible

for ongoing kidney disease-related programs or whose competence lay in the

areas of program planning and analysis. In his charge to the group, the

Surgeon General directed it to describe and discuss the nation's kidney

disease problem, to outline the current state of knowledge and ongoing programs

in the area of kidney diseases, to consider advanced states of knowledge

and desirable programs, to develop goals and objectives for effective amelio-

ration of the problem, and to explore alternative approaches to the attainment

of these objectives.

An important part of the group's work was to be a logical analysis of

programs leading to a solution or amelioration of the problem of kidney disease,

including:

1) A thorough discussion of goals and objectives and ways of measuring them;

2) A description of alternative approaches which could lead toward the same objectives;

3) An analysis of the cost of reaching various points on the continuum of objectives by means of alternative approaches; and

4) A discussion of the basic assumptions upon which conclusions depend, of uncertainties which affect the estimates used, and of the issues which cannot be resolved at this time.

The work of the kidney disease program analysis group is intended to guide the Office of the Surgeon General and, ultimately, the Office of the Secretary, Health, Education, and Welfare, in the development of future progi long range financial plans and budgets, and legislative proposals.

B. **Background**

During the last five years, diseases of the kidney have steadily gained in significance as an area of social importance for both Federal and non-Federal research and service efforts. Much of the impetus for this increasing interest in kidney diseases has come from the development of two dramatic but expensive therapeutic approaches to end-stage disease—chronic hemodialysis and kidney transplantation. The successes of both techniques—coupled with other research advances leading to a better understanding of kidney diseases—have led to a proliferation of activities directed toward reducing the morbidity and mortality these cause in the population.

There are a number of mechanisms, or program components, that are traditionally brought to bear on a disease problem such as this. These are:

1) Expanded use of existing preventive techniques.

2) Expanded use of existing diagnostic techniques.

3) Expanded use of existing treatments, including chronic dialysis, kidney transplantation and conservative management (drugs, diets, etc.).

4) Laboratory and clinical research to produce new preventive, diagnostic, therapeutic and rehabilitative methods.

5) Increased specialized scientific medical and paramedical training to provide the manpower needed for the research and treatment attack on the kidney disease problem. This also includes continued postgraduate education to train practicing physicians in the use of the latest diagnostic and treatment modalities.

6) Increased public education to alert potential victims of kidney disease to seek medical help at the earliest possible emergence of warning signs.

7) Provision of specialized facilities not currently in existence which are essential for the execution of any of the above programs.

It must be understood from the outset that these program components are interdependent in most cases. For example, preventive techniques exist that need further research to make them maximally effective for braod application. New treatment methods are useless if existing diagnostic techniques are not being applied in medical practice. Because of

the present inadequacies of existing treatments, be they dialysis, trans-
plantation, or conservative management, a considerable research effort
is called for to increase their efficacy and economy to make them more
broadly useful.

C. Consideration of Program Approaches

It is unlikely that a single program component would lead to a major
reduction in the national kidney disease problem; therefore, a mixture
of approaches will have to be employed by the Federal Government to
reduce the morbidity and mortality due to kidney disease. The total
funding level and the respective proportions for each approach in the
overall effort will determine, to a large extent, the benefits attain-
able in each successive year from this effort. Advances in the state of
knowledge will affect the nature of this "mix" and will shift the emphasis
from certain program components to others if we are to continue to derive
maximum benefits from the total expenditure of funds in this area.

Another important consideration in making choices for the funding of
specific program approaches is the effect of the expenditure of such
Federal funds on the overall national expenditure of funds in this area
including money spent by state and local governments, voluntary agencies,
universities and foundations, and the large segment of private expenditures
for medical diagnosis and treatment. Here, the precise choice of direction
of the placement of Federal funds can determine to a large degree whether:

1) The resulting fruits of research or increased case findings at
    an early stage of the disease will stimulate an expanded use
    of nongovernmental money for earlier and more effective treatment--

with an overall beneficial effect on the state of kidney disease
in the nation; or

2) Whether certain choices for the expenditure of Federal funds
would serve to diminish the participation of the nongovernmental
sector in efforts against kidney disease by making it financially
more attractive to "let Sam do it."

It is obvious therefore, that under a given set of conditions where
unlimited Federal funds are not available for the solution of a single
national disease problem, such as kidney disease, a rational balance must
be struck between the various relevant program approaches--investigative,
preventive, therapeutic and educational--so as to derive maximum benefits
from any current or possibly extended future Federal efforts.

D. **Program Analysis for Decision Making**

The future of Federal programs in the field of kidney diseases, be
it for research, disease prevention, improvement of treatment methods
including hemodialysis and transplantation, or manpower training needs
decisions based upon a thorough, dispassionate and logical analysis.
With the aid of such analysis, public officials responsible for health
programs who face the problem of allocation of limited financial resources
in the struggle against kidney disease could make such decisions on the
basis of logical priorities. These priorities would be based on the
present state of knowledge and on needs based on present morbidities
and mortalities, as well as on the basis of anticipated developments
in the future state of the art and the pertinent changes which they
are likely to introduce into the overall kidney disease picture. The
fundamental intent of such an analysis and its raison d'etre is to
provide maximum benefits in terms of prolonged, rewarding lives and reduced

morbidity for those afflicted with kidney disorders and for those in the population who will be stricken by it in the future, from the application of Federal funds to research, disease prevention, treatment, and manpower training, directed against kidney disease.

E. The Analysis

Faced with the fact that its study and explorations could perforce not be infinitely exhaustive it was decided that, for the sake of practicability and feasibility, the heterogenous field of kidney disease be divided into four major groups as follows:

 I. Infectious Diseases of the Urinary Tract,

 II. Hypersensitivity Diseases of the Kidney,

 III. Kidney Diseases Associated with Hypertension, and

 IV. End-Stage Kidney Disease.

The first three groups encompass in toto about 75 percent of kidney morbidity and mortality; the fourth group, end-stage kidney disease, exemplifies progressive and ultimately fatal kidney failure from all possible causes.

Each of these groups accounts for a major percentage of overall kidney morbidity and since each group of diseases was based on one major distinct causative principle it was felt that it is possible to discuss logically each group individually in terms of the common overall mechanisms involved and in terms of the application of the various possible program elements— research, prevention, treatment, professional training and lay education— to the solution of the problem which it represents.

In addition to the first groups, there remains a miscellaneous group of renal diseases of variable and distinct etiologies:

a) Diseases of development (polycystic disease, hypoplastic

   kidneys, anomalies of position or structure, etc.);

b) Renal involvement in metabolic diseases (diabetes, gout, amy-

   loidosis, oxaluria, etc.);

c) Kidney damage due to obstruction (benign prostatic hypertrophy

   of the aged, kidney stones, etc.);

d) Cancer of the kidney, both of primary or secondary origin; and

e) Mechanical injury.

2. Limitations

Programs and approaches for solution or amelioration of problems

associated with this latter mixed group of renal diseases are discussed

in the text of the report but were not subjected to individual cost-

effectiveness or benefit-cost analyses. This decision was made to

avoid an unwieldy, and in many cases, impractical fragmentation of the

report. Moreover, each one of these disorders may be the end result

of a primary disease for which there exist other, independent research

and preventive and/or curative efforts which, hopefully, would affect

beneficially the existing prevalence of the disease.

For example, research advances of the last seven years in the area

of gout, once they are rigorously applied in the everyday practice of

medicine, will decrease considerably the prevalence of kidney damage due

to neglected or long standing chronic gout. Similar considerations were

applied to other disorders belonging to the residual mixed group of mis-

cellaneous diseases impinging on the functional integrity of the kidney.

It was also decided to exclude neoplasms of the kidney from the

program analysis. Inclusion of this category in the present analysis

was felt to be undesirable because other extensive research and public
health programs affect the state of the art in cancer; moreover, in a
large percentage of patients afflicted with primary or secondary cancer
of the kidney, kidney function per se does not deteriorate until the
extent of the lesion becomes overwhelming--at which point the life of
the patient is usually threatened by the neoplasm and its metastases
more than by the attendant renal failure.

The present analysis was limited to kidney diseases which are pre-
dominantly chronic or to mechanisms which though they may precipitate
acute kidney disease, play a major role in eventual or potential chronicity
of the disorder. Thus, acute renal poisoning due to accidental causes
or suicide attempts, and nephrotoxic drug reactions were not included
in the analyses or program projections.

3. Appendices

In the course of discussing possible programs and their specific
impacts, new ideas were developed which seemed of sufficient interest
and potential benefit to be included in the report. Subsequently, the
overall principles involved were fitted into the logical mainstream of
the report. For the sake of brevity and continuity, however, the more
detailed projections or applications of such future programs were
included in appendices to the report, whenever they appeared of interest.

4. Recommendations

In projecting future programs and in analyzing their possible impact
on the mortality and morbidity due to each major sub-group of kidney
diseases, the committee attempted to avoid implied or overt recommendations.

It was felt that in each case the analysis and its logical extrapolations spoke for themselves.

II. SUMMARY

The following summary presents the committee's most significant generalized findings and a discussion thereof, and is not intended to include all observations made. These will be found in detail in the body of the report.

As a first step in its analysis in depth of kidney disease as a national health problem, the committee studied each of the many diseases of diverse etiologies which are encompassed in the general term 'kidney disease'. (Please see Chapter 2, Kidney Disease--Current Status) In each case the current state of scientific knowledge for each disease was determined including its underlying etiology, mechanisms of pathogenesis, symptomatology, prognosis, severity and duration, methods of diagnosis, and treatment. Where applicable, consideration was given to existing gaps in knowledge, additional research needs, possible prevention, diagnosis, and treatment under the conditions of present or future states of the art, and interrelationships with other diseases. Up-to-date statistical data were collected, such as prevalence in the population, mortality, morbidity in terms of days of restricted activity, average cost of treatment, and other relevant costs.

Since the subject matter embraces a vast number of diseases with highly divergent pathogenic mechanisms and nature, the committee made decisions-in-principle concerning which of these would serve best as a

basis for a rational analysis under the limitations of the present study (please see INTRODUCTION, E.,1., Organization of the Subject Matter). The three main groups of primary kidney diseases and end-stage kidney disease common to them were utilized in the statistical analyses in this report. This group encompasses the overwhelming majority of kidney mortality and morbidity. The remaining primary and secondary kidney diseases of statistically lesser import were discussed in the text of the report but were not included in the present program analysis.

Subsequently a thorough study was made (Chapter 3, Current Kidney Disease Control Programs) of the current governmental kidney disease programs and relevant public and private expenditures for the nationwide treatment of kidney disease. The latter includes cost of physician care, hospital care, nursing home care, and other professional services for diagnosis and therapy of kidney diseases, as well as the cost of drugs and net insurance costs. In addition, the cost was estimated for ongoing research efforts, for demonstration, screening and detection programs, for education and training efforts and for that portion of the cost of construction of hospital and medical facilities which can be prorated to the use of patients with kidney disease.

Program Analysis Models

Based on the substantive information obtained and statistical and economic data collected, the committee analysed the benefits to be gained by different approaches to the solution or amelioration of the overall national kidney disease problem at different expenditure levels of HEW funds. Models were devised after experimentation with various statistical mechanisms and indices.

They are based on a benefit-cost analysis for the four disease groups studied, i.e., infectious diseases of the urinary tract, kidney diseases related to hypersensitivity phenomena, kidney diseases related to hypertensive vascular diseases, and end-stage kidney disease. Four specific programs are considered for each disease group. These programs which are delineated by time, funding level, and state of the art comprise the following:

1) Hypothetical Program at the Current HEW Expenditure Level, Based on the Current State of the Art;

2) Hypothetical Program at an Intermediate HEW Expenditure Level, Based on the Current State of the Art;

3) Hypothetical Program at an Accelerated HEW Expenditure Level, Based on the Current State of the Art; and

4) Hypothetical Program for Fiscal Year 1975, at an Accelerated HEW Expenditure Level, Based on the Expected Advanced State of the Art in 1975.

Each program consisted of a hypothetical situation where a specific level of HEW program funding was divided among a rational mix of program components (screening, diagnosis and treatment, research, training, etc.) based on the particular characteristics of the specific disease group involved, and was applied to specifically involved or particularly vulnerable groups or, as the case may be, to the entire population. The benefits accruable from these programs were then estimated and stated in terms of overall reduction of mortality, prevalence, and morbidity due to kidney disease. Wherever the making of assumptions was unavoidable, the resulting estimates were based on the best scientific evidence and available data and were held within conservative limits.

Benefit indices were quantified in terms of the reduction in annual
mortality, the reduction in annual morbidity (number of sick days per year)
and in terms of the disease prevalence in the total population due to the
specific type of kidney disorder analyzed, which would accrue thanks to the
impact of the various program components—such as research advances, disease
prevention and improved treatment. It was felt that these specific benefit
indices were more appropriate for the purposes of this study than other
potential indices such as "loss of productivity," loss of gross national
product due to the death of individuals, or loss to the Federal Government of
tax revenue due to death or inactivity of individuals. Moreover, it was felt
that it would be more desirable to quantify the benefits which could accrue
from HEW-supported programs aimed at the kidney disease problem in terms
related directly to the human beings who are to benefit from such expenditure,
rather than in terms of a highly impersonal inert commodity—dollars. The fact
that mortality and morbidity figures could be manipulated statistically just
as well as dollars, but could be used without introducing too many estimates
and assumptions ("What is the price of a human life?", "How much money is lost,
and to whom, when a sick person does not report to work?") induced the committee
to choose these indices for its benefit-cost analyses.

A detailed explanation of the various postulated programs and the analysis
of their potential benefits will be found in Chapter 4, Research Methodology,
and Chapter 5, Program Analysis. The nature of these programs, and the benefits
and costs associated with each of the four programs in each disease group are
summarized and discussed below.

Summary of Alternative Programs for Individual Disease Groups

1. Infectious Diseases of the Urinary Tract

   a. Hypothetical Program at Current HEW
      Expenditure Level, Based on the Current State of the Art

   A major component of this program is the screening of the
following specific high-risk groups: patients in hospitals and
nursing homes, non-hospitalized pregnant females, and non-
hospitalized diabetic patients. This would be followed by the
establishment of definitive diagnoses and vigorous treatment of
any kidney infections discovered. A second major projected
program component is laboratory and clinical research directly
relevant to infections of the kidney. Other program components
are concerned with the education of medical personnel and the
specific training of additional manpower. The cost to HEW is
estimated at $9,203,000.

   Short-term benefits of this program (discernible when the
program reaches full operation), would be represented by an annual
reduction in mortality of 70, a reduction in prevalence of
3,231,260 cases and a reduction of 15,962,420 morbid days in the
involved vulnerable group. Long-term benefits (to be seen many
years after the program becomes fully operational) are represented
by the avoidance of irreversible, fatal uremia in 1,750 individuals
per year.

   b. Hypothetical Program at an Intermediate HEW Expenditure Level,
      Based on the Current State of the Art

   At the intermediate program level, HEW expenditures are about
two times greater than in the preceding program. Again a major
component of this program is the screening, diagnosis and treatment

of urinary tract infections. An additional high-risk group has
been added: females 6 to 9 years of age. The cost to HEW is
estimated at $20,179,000.

Short-term benefits attributable to this program are quantita-
tively greater (percentage reductions do not change), due to the
addition of another high-risk group. A reduction in short-term
mortality of 70 is again expected due to the very low mortality
from infections of the urinary tract in the added vulnerable group.
Prevalence is reduced by 3,243,860 and morbid days by 16,273,640.
A yearly reduction of fatal end-stage kidney disease by 1,770 is
expected.

Expansion of the proposed basic program (see previous model)
to a level which is two times larger, in an effort to include an
additional vulnerable group, did not result in a near-proportionate
increase in benefits. Once a new potentially vulnerable group
was included in which the percentage of individuals harboring
urinary tract infections was much lower than in the previous hypo-
thetical situation, the point of rapidly diminishing returns was
reached. Thus an indication was received of the possible limits
of effectiveness for a screening-diagnosis-treatment program for
infectious diseases of the kidney in the general, non-morbid
population under conditions of the current state of knowledge.

c. Hypothetical Program at an Accelerated HEW Expenditure Level,
    Based on the Current State of the Art

In this projected situation, the HEW expenditure level is about
two and one-half times greater than the current level. Again, a
major component of this program is the screening, diagnosis and

treatment of infections of the urinary tract. The high-risk group

at which the program is aimed has been expanded to include all

females under 21 years of age.

The short-term benefits attributable to this program include

a similar percentage reduction in mortality and morbid days as

before, but since a larger vulnerable population was involved,

quantitative benefits are greater. The cost to HEW is $27,394,000.

Short-term benefits include an annual reduction of 70 deaths,

3,292,860 cases, and 17,483,880 morbid days.

Long-term benefits are represented by the elimination of

irreversible, fatal uremia in 1,870 individuals per year.

The same comments made on the less-than proportionate increase

in benefits in the intermediate program apply, even more strongly,

to this hypothetical situation. It is obvious that under the

conditions of the present state of the art the limits of effective-

ness for this approach have been reached at the previous level

of expenditure, in the intermediate program.

d. Hypothetical Program, for Fiscal Year 1975 at an Accelerated
   HEW Expenditure Level, Based on an Advanced State of the Art

In this projected situation, the HEW expenditure is about

three and one-half times greater than the original program. Funds

for research have been increased considerably. Screening, diagnosis

and treatment still remain a major program component.

Under an advanced state of the art it is assumed that the

extensive research efforts have made possible:

1) More effective antimicrobial therapy,

2) Better understanding of the pathophysiology of urinary

   tract infections, and

3) Better understanding of the natural history of

pyelonephritis.

The cost to HEW is estimated at $31,228,000.

Short-term benefits now include an annual reduction of 80

deaths, 5,630,780 cases, and 26,064,430 morbid days. Long-term

benefits are represented by the elimination of irreversible,

fatal uremia in 4,125 individuals per year.

2. Hypersensitivity Diseases of the Kidney

a. Hypothetical Program at the Current HEW Expenditure Level,
    Based on the Current State of the Art

It was concluded that present knowledge of hypersensitivity

diseases of the kidney is insufficient to justify a special program

of case finding, diagnosis and treatment since it is doubtful

whether it could make an effective impact on current morbidity

and mortality figures due to these diseases. The most important

projected program component is laboratory and clinical research

relevant to immunology and hypersensitivity diseases of the kidney.

An additional component is postgraduate physician education,

research training, and expansion of research facilities. The

cost to HEW is estimated at $7,480,000.

Short-term benefits expected are a reduction of 610 in

immediate mortality, primarily due to the postgraduate physician

education and consequent improved medical practice. No immediate

benefits are expected from the research effort undertaken.

A 1% reduction in mortality, a 50% reduction in prevalence

and a 65% reduction in morbid days is anticipated over a future

ten-year period as a result of this program primarily due to
anticipated research advances, and secondarily due to a higher
quality of medical care (see anticipated benefits for 1975).
This was one of the most uncertain estimates made; it was based
on the research advances of the last 10 years and on the arbitrary
assumption that the rate of new developments will remain the
same.

b. **Hypothetical Program at an Intermediate HEW Expenditure Level,
Based on the Current State of the Art**

In this situation, the program components have not changed
essentially, but the HEW expenditure level has been increased.
The most important program component is, again, research. The
cost to HEW is estimated at $20,000,000.

Short-term benefits would remain similar to those described
at the previous, lower expenditure level (see above).

Long-term benefits will only be increased significantly over
the previous program if the funds for research in the latter had
been a limiting factor for productive research.

c. **Hypothetical Program at an Accelerated HEW Expenditure Level,
Based on the Current State of the Art**

In this situation, the program components have not changed
essentially, but the original HEW expenditure level has been
tripled. The most important program component is, again, research.
The cost to HEW is estimated at $23,875,000.

Short-term benefits would remain similar to those described
at a non-accelerated HEW level (see above).

Here again, long-term benefits will only be increased
significantly over the previous program if the funds for
research in the latter had been a limiting factor for productive
research.

d. Hypothetical Program at an Accelerated HEW Expenditure Level,
    Based on an Advanced State of the Art (1975)

Under an advanced state of the art, it is assumed that the
preceding research has resulted in the development of effective
means of preventing hypersensitivity diseases of the kidney, or
of treating them. Possible examples are:

1) An effective anti-streptococcal vaccine;

2) Failing that, discovery of a means for early detection of
    streptococcal infections and for the interruption of the
    immunological mechanisms that lead to acute glomerulonephritis
    and/or

3) Increased understanding of the meaning of proteinuria and
    means for identification and treatment of individuals in
    whom it heralds eventual chronic renal disease.

A program based on the use of an anti-streptococcal vaccine in
a majority of the population and on early detection and treatment
of persistent proteinuria would yield the following short-term
benefits: an annual reduction in mortality of 770, a reduction in
prevalence by 62,250 cases and a reduction of 2,610,000 morbid days
in those affected.

Long-term benefits would be represented by a decrease of 8,610
individuals per year who would otherwise reach end-stage kidney
failure in the future. The cost to HEW has been estimated at
$77,320,000.

It is important to note that any of the program approaches involving the advances mentioned above would have a profound impact on the prevention and treatment of hypersensitivity diseases in general, such as rheumatic fever, rheumatic heart disease, and others.

8. Kidney Diseases Associated with Hypertension

   a. Hypothetical Program at the Current HEW Expenditure Level, Based on the Current State of the Art

   The projected program consists of three major components:

   1) Screening, diagnosis and treatment of individuals 17 years of age and over with curable (non-essential) hypertension and non-curable hypertension;

   2) Postgraduate education of practicing physicians and education of the population relevant to early recognition and treatment of the disease; and

   3) Laboratory and clinical research.

A relatively minor component for research training of physicians and allied personnel is also included. HEW costs are estimated at $9,180,000.

Estimated annual short-term benefits include a decrease in mortality by 7,830, a reduction in prevalence of 54,000 cases, and a reduction of 5,959,000 in morbid days due to hypertensive disease. It has been assumed that approximately 30% of the benefited individuals with hypertension have renal involvement. Thus the figures for benefits accruing to patients with renal disease associated with hypertension are 2,190, 27,000, and 1,802,000, respectively.

A reduction of 4,330 per year in the number of individuals dying from irreversible uremia is expected as a long-term benefit.

b. **Hypothetical Program at an Intermediate HEW Expenditure Level, Based on the Current State of the Art**

The projected program is similar to the preceding one except that under an increased funding level (about two and one-half times greater than before) an additional population group is subjected to screening, diagnosis and treatment. Reference is to persons 17 years of age and over who have had no care from a physician during the preceding year. The program affecting the additional group is expected to cover a six-year cycle. Estimated costs for HEW are $21,207,000.

Estimated annual short-term benefits for patients with renal involvement are now increased to 2,270 avoided deaths, a reduction in prevalence of 34,880 cases and a reduction in morbid days of 2,056,820. Expected long-term benefits are estimated to include an annual reduction in fatal end-stage uremia of 4,820 cases.

c. **Hypothetical Program at an Accelerated HEW Expenditure Level, Based on the Current State of the Art**

This program is similar to the one postulated for an intermediate level of expenditure except that the program affecting the additional high-risk group of previously unscreened individuals has been accelerated to cover a three-year cycle rather than six years. The estimated cost to HEW is $28,639,000 (about three times the original level of expenditure).

Estimated annual short-term benefits for patients with renal involvement now include 2,380 avoided deaths, a reduction in prevalence of 42,750 cases, and a reduction in morbid days of

2,311,340. Expected long-term benefits are estimated at an

annual reduction in end-stage uremia of 4,820 cases.

In this case, further expansion of the program above the

intermediate level did not appear warranted by the resulting increase

in benefits, which was very far from proportional. Here again,

an indication was received of the possible limits of effective-

ness for a screening-diagnosis-treatment program for kidney

diseases associated with hypertension in the non-symptomatic

population ("individuals who have not seen a physician during

the preceding year"), under conditions of the _current_ state of

knowledge.

d. Hypothetical Program at an Accelerated HEW Expenditure Level,
   Based on an Advanced State of the Art (1975)

Under an advanced state of the art it is assumed that the

preceding extensive research efforts have resulted in the following:

1) Advances in understanding of the underlying cause(s) of

   hypertension;

2) Improved diagnostic tests for detecting hypertension;

3) Specific effective therapy(ies) directed toward the various

   underlying causes; and,

4) Advances in surgical methodology for the types of hypertension

   amenable to such treatment.

Screening, diagnosis and treatment still remain the major program

components in this projected situation. The target population is

the same as in the preceding programs. HEW costs are estimated at

$35,832,000.

Estimated annual short-term benefits for patients with renal

involvement include a 9,300 decrease in mortality, a reduction of

289,700 in prevalence and a reduction in morbid days of 5,579,000.

Long-term benefits are expected to result in an estimated
annual avoidance of fatal end-stage kidney disease in 9,480
individuals.

4. **End-Stage Kidney Disease**

End-stage kidney disease as indicated earlier exemplifies
progressive and ultimately fatal kidney failure from all causes.
Because of the unique and costly treatment methods currently available
this group was studied not only from the standpoint of the four program
alternatives (used for the three primary disease groups) but also from
the standpoint of a program which attempts to treat all patients with
chronic kidney failure.

    a. **Hypothetical Program at Current HEW Expenditure Level Based
       on the Current State of the Art**

The major component in this program consists of treatment of
patients in end-stage renal failure by dialysis and/or kidney
transplantation. A second program component is laboratory and
clinical research relevant to both treatment modalities, develop-
mental research for dialysis hardware improvement, and development
of organ preservation technology and facilities. A third program
component, considerably smaller, involves training of relevant
manpower and provision of needed facilities. The estimated HEW
cost is $21,000,000.

The benefits in this program are measured in terms of mortality
avoided in the total group of patients in irreversible renal failure
whose lives are in jeopardy. Under the circumstances of this
particular program, 600 patients will be maintained through

chronic dialysis and 90 lives yearly will be saved through successful transplantation.

This program of dialysis and transplantation, at current HEW expenditure levels, provides life-saving care for about 1.5% of the number of patients threatened by death during that particular year because of end-stage kidney disease.

b. **Hypothetical Program at an Intermediate HEW Expenditure Level, Based on the Current State of the Art**

In this projected situation the level of HEW funding has been increased appreciably to reflect the immediate urgency posed by the threatened lives of patients in irreversible renal failure. Treatment expenditures have been increased by a factor of 5 over the previous level, research expenditures by a factor of 1.5 and training and facilities by a factor of 5.

Under the circumstances of this particular program, about 1,150 patients would be maintained by chronic dialysis and about 420 individuals would be cured by transplantation.

This program which involves about $56,000,000 of HEW funds will provide life sustaining treatment for about 3% of the annual number of persons who have end-stage kidney disease during the first year of the program. During the second year of such a program, however, because of the carry-over of about 80% of the patients dialyzed during the preceding year, the same sum of money will provide treatment for considerably less than 3% of the uremic patients threatened by death during the second year. Because of the increasing carryover load of dialysis patients

from previous years, this limiting effect will increase with each successive year of such a program. Unless the budget, manpower, and facilities are increased considerably during each succeeding year over the respective previous levels, only a small proportion of the total group threatened with death due to end-stage kidney disease each year will actually be saved in such a program. This problem is discussed in greater detail later in this summary chapter and particularly in Chapter 6, The Cost of Treating All Patients with Chronic Kidney Failure.

c. Hypothetical Program at an Accelerated HEW Expenditure Level, Based on the Current State of the Art

In this projected situation, the level of HEW funding has been increased tenfold to reflect the immediate urgency posed by the threatened lives of patients in irreversible renal failure. Although the overall funding is increased tenfold in an effort to extend treatment to as many patients as possible, research funds have only been doubled over the current level, since this was felt to be the limit of research and development which could possibly be productive at this point in time. Training and facility expenditures have also increased tenfold because of the immensely increased patient load.

Under the circumstances of this particular hypothetic program 4,100 lives will be maintained through chronic dialysis and 3,575 lives will be saved yearly through successful transplantation.

This program, which utilizes $210,000,000 of HEW money (about $170,000,000 of which are expended for patient care), provides

treatment for about 15% of the overall number of patients
threatened by death because of end-stage kidney disease and
available during the first year of the program. The same
problem of buildup of carry-over patients in future years exists
under this program and interferes with the achievement of its
goals unless the level of expenditure is raised appreciably
during each succeeding year.

d. Hypothetical Program at an Accelerated HEW Expenditure
   Level, Based on an Advanced State of the Art in 1975

Under an advanced state of the art, it is assumed that the
preceding extensive research efforts have resulted in the
following advances:

1) Dialysis treatment can be carried out by the patient
   essentially independently of treatment facilities
   (except for periodic medical checkups), and the debili-
   tating complications seen in patients on dialysis
   therapy have been eliminated;

2) A highly developed program for organ matching and
   preservation is in existence, immunosuppressive techniques
   are highly effective, transplantation survival is vastly
   increased, and the procedure can now be carried out in
   most of the general hospitals in the United States; and

3) In the case of both treatment modalities the cost has
   been reduced appreciably.

In this projected situation, the total HEW expenditure is
smaller than the accelerated budget level assuming current state
of the art (see above). The expenditures for research have been

decreased considerably because of the research and development

achievements of previous years. Training and facility expendi-

tures have remained on the same accelerated level because of

the large patient population which is being treated. The major

program element is treatment of all suitable patients by

transplantation, since this is a one-time treatment. This

permanent treatment is, of course, preceded by supportive

dialysis and patients in whom the procedure is unsuccessful

are also maintained by dialysis pending a second attempt at

transplantation. About 12,000 of the remaining patients in

renal failure who are not suitable surgery candidates are placed

on life-long dialysis.

Under the circumstances of this highly idealized program,

about 16,000 lives will be saved annually through transplantation

in the vulnerable group. In addition, about 11,400 individuals

will be maintained through chronic dialysis; most of these will

be carry-over patients from previous years.

This hypothetical program which utilizes $150,000,000 of

HEW funds, most of which are devoted to patient treatment, provides

treatment for about 55% of the number of patients threatened by

death because of end-stage kidney disease during the first year

of its operation (1975). It is important to note that advanced

age and concurrent disorders prevent the successful application

of transplantation and/or chronic dialysis to every one of the

approximately 50,000 patients who present themselves each year

with end-stage kidney disease.

A comparison summary of the results of the three hypothetical situations with regard to end-stage kidney disease shows that an immediate tenfold increase of HEW expenditures primarily for patient treatment under conditions of the present state of the art would, at best, approach a solution for 15% of the patient population threatened by fatal kidney failure in the first year; thereafter, a progressingly smaller percentage of the vulnerable group could be helped. (This situation is, of course, wholly hypothetical, since there does not exist sufficient medical man-power either qualified or willing to participate in such a program). Advances in the state of the art which can be expected through a judicious doubling of HEW support for research and passage of sufficient time to permit the unfolding of research achievements would make it possible to save the lives of about 55% of the threatened patient population in the first year of such a program with a smaller expenditure of funds for patient care than was postulated for the previously described accelerated level program under the current state of the art, which only starts to take care of 15% of those in need of treatment.

e. Hypothetical Program Attempting Treatment of All Patients with Chronic Kidney Failure

1) Introduction

Whenever consideration is given to the problem of ultimately fatal chronic renal failure, the question is frequently raised of what it would cost to make an attempt at treating all patients threatened by a

uremic death--either with the aid of lifelong chronic dialysis or through attempts at kidney transplantation whenever donor kidneys may be available. This question is usually raised by well-meaning individuals for humanitarian reasons.

Approximately three-fourths of the 50,000 patients who present themselves each year with fatal end-stage kidney disease are known to be above the age of 60. This fact together with the many concurrent other disorders afflicting most of these patients (and the rather stringent requirement for emotional suitability for chronic dialysis) make it extremely unlikely that a large-scale application of either transplantation or chronic dialysis to all or practically all of these 50,000 individuals would be successful. A further discussion of practical restraints in terms of requirements for specialized manpower and facilities is found in Chapter 6 (The Cost of Treating All Patients with Chronic Kidney Failure), Section V. Nevertheless, although the original mission of the Kidney Disease Analysis Group did not include the preparation of an answer to this question concerning the cost of a hypothetical "total push" program, it was felt that an analysis of this cost would be a natural corollary to the preceding analyses of costs and benefits of optimal programs aimed at the major primary kidney diseases and at end-stage kidney disease. In any consideration of

possible programs for the amelioration of the kidney
disease problem, an attempt to treat _all_ patients threatened
with a uremic death regardless of the possible costs,
for humanitarian reasons, represents one extreme in a
broad spectrum of possible programs. The committee
therefore felt that this hypothetical cost should be
ascertained to serve as a maximal bench mark for any
intensive attempt at program analysis or planning.

The details of such a hypothetical total push program
and the necessary calculations are found in Chapter 6.

2) _Calculation of Costs_

It was obvious that the mere calculation of the cost
of the _first_ year of such a total push program would
leave a misleading impression as to the true long-term
expense involved if such an approach is chosen. Because
of the significant rate of survival from year to year
among the patients treated by chronic dialysis, the cost
of extending treatment to all those needing it in sub-
sequent years will increase considerably with the passage
of time. It was therefore decided to calculate the
actual cost of the treatment of _all_ individuals requiring
it (the new group of vulnerable uremic patients presenting
itself each year, the patients on lifelong dialysis who
are survivors from previous years, and the patients in
whom transplantation was unsuccessful and who must be
maintained with the aid of chronic dialysis) for as many

years as needed after the start of the program until a year was reached which could be considered characteristic of a "steady state." At this particular point in time the number of new patients included each year in this program would equal the number of patients dying in the same year, and in this situation a constant or near-constant yearly cost of the program would be reached.

Calculations showed that under the conditions of this program its yearly cost would increase greatly each year during the first 15 years, that the subsequent yearly increases in cost would be of a somewhat lesser magnitude but still highly significant, and that an asymptotic curve approach would show that the steady state would not yet be reached by the twenty-fifth year. Obviously one can expect research advances to occur well within the first 10 or 15 years which would modify greatly the respective efficacies of transplantation and hemodialysis and their costs. It was therefore decided that it would be unrealistic to report the cost of the hypothetical total push treatment program for end-stage kidney disease in terms of the eventual yearly cost of the steady state after 25 years. Rather, it was felt that it would be sufficiently indicative of the true costs to be expected to report the cost of the first year of such a program (the lowest yearly cost), the cost of

the fifth year (a realistically foreseeable sum which
is not likely to be influenced significantly by changes
in the state of the art), and the cost of the
fifteenth year (which is considerably higher than the
cost of the fifth year and begins to approach the
markedly higher eventual cost of the steady state year).

To obtain a realistic range of cost, the calculations
were done on the basis of two cost assumptions for each
treatment modality: A higher "present cost" figure
which reflects accurately today's costs of transplantation
and chronic dialysis, and a realistically reduced "future
cost" figure for these treatment modalities.

3) Results Obtained

First Year

Based on "present cost" figures, the cost of attempting
to treat 40,000 patients out of the total vulnerable
population of 50,000 during the first year of this
hypothetical program, by means of chronic dialysis or
kidney transplantation, would be $611,000,000.

(Note: If an attempt is made to treat all 50,000 vulner-
able patients, the cost of this program during the first
year will be $761,000,000.)

If the calculation for the first year is based on the
less likely "future cost" rate, the respective figures

would be $422,000,000 and $522,000,000.

Fifth Year

The cost of this program in the fifth year of its

existence will range between $1,043,600,000 (based on

the low, "future cost" figure) and $1,543,415,000

(based on the higher, "present cost" figure). In

this year, 102,161 patients would be treated under the

program by transplantation or chronic dialysis.

Fifteenth Year

The cost of this program in the 15th year of its existence

will range between $1,816,000,000 (based on the low

"future cost" figure) and $2,702,000,000 (based on the

higher "present cost" figure). In this year, 179,401

patients would be treated under this program, by trans-

plantation or chronic dialysis.

In view of the fact that it is anticipated that research

advances evolving during and after the first fifteen

years of the program would introduce considerable improve-

ments into both treatment modalities and would influence

true costs significantly, projected expenses for the

twentieth and twenty-fifth year of the program were calcu-

lated but not reported. It should be noted, however,

that the population which would require treatment during

each year of this program would continue to grow and thus

the yearly costs would increase, until a point beyond the

twenty-fifth year at which a steady state would be reached.

B. A Total Program Aimed at Kidney Disease

1. Introduction

It is evident from the foregoing models that concentration in
future programs merely on the treatment of end-stage kidney disease
is not likely to solve the problem of annual deaths due to irreversible
uremia unless unlimited funds are available for an indefinite continua-
tion of such a program. Thus, steps must be taken to decrease the
number of people who enter the irreversible fatal stage each year by
a systematic prevention or treatment of the primary kidney diseases
which initiate their progressive downhill course. It is obvious
from the analyses in the three major kidney disease groups--infectious,
hypersensitive and hypertensive--that the otherwise inevitable annual
reservoir of patients with irreversible kidney failure can be
diminished considerably through vigorous programs activated to deal
with each of these groups. The application of relatively minor funds
in the group of infectious kidney diseases to stimulate systematic
screening of high-risk groups followed by diagnosis and treatment,
even within the current state of the art and without awaiting addi-
tional advances due to ongoing or future research, can bring about a
significant future reduction in the number of end-stage patients.
Continued and expanded research activities will be necessary to
increase the percentage of patients ultimately benefitted by this
approach.

In the area of hypersensitivity diseases involving the kidney
there appears to be no promising mode of attack in sight except for
the launching of a systematic research effort intended to increase

our knowledge of the disease mechanisms involved. Here, the sooner this effort is started the greater the likelihood of a reduction of the number of end-stage victims in the near future. The promise for benefits to be derived from this type of research effort is such that it should not be postponed—particularly since any new effective treatment or prevention modality would produce major benefits in the entire field of hypersensitivity diseases, such as rheumatic heart disease, rheumatoid arthritis and others.

In the group of hypertensive diseases of the kidney an immediate start, within the current state of the art, of screening, diagnosis and treatment can begin to diminish the number of patients who will eventually require end-stage treatment because of their progressive renal involvement. Simultaneous research efforts are likely to make this particular portion of the overall program more effective as time goes by, in the same fashion in which the new antihypertensive drugs developed during the last ten years have succeeded in decreasing by about 50 percent the mortality due to malignant hypertension.

Thus, a meaningful Federal program to reduce the annual mortality due to kidney disease and aimed at a general reduction of the prevalence of the various kidney diseases must perforce be a multifactorial one which brings into play all of the program components—research, prevention, treatment and education—available in our armamentarium. An optimally proportioned mix of these program components must be present to yield maximum benefits in overall number of lives saved. This last concept includes not only deaths avoided today but deaths to be prevented in the years to come. Needless to say, such a total program, to be meaningful and productive, must be aimed at all three

major primary kidney diseases, as well as at end-stage kidney failure.

2. Structure of Total Program Models

In order to arrive at the overall makeup of such a mixed attack on the problem of kidney disease, Tables I and II were prepared. These Tables outline the composition of four hypothetical overall programs-- three at different levels of expenditure and under the conditions of the present state of the art, and the fourth under the conditions of the expected advanced state of the art in 1975. Table III presents the benefits estimated for the four overall programs. Scanning this table horizontally provides an intercomparison of benefits in the four disease categories. A vertical scan of this table provides an indication of the sensitivity of the four kidney disease categories to changes in expenditure levels.

These projected total programs consist of a combination of the individual models of programs aimed at the various major primary kidney diseases and end-stage kidney failure which have been mentioned pre- viously and which are described in detail in Chapter 5. Thus, each hypothetical total program divides a specific level of HEW funding among a rational mix of program components the composition of which, in turn, is based on the conclusions from the previous analyses.

Figures 1 and 2 provide another illustration of the qualitative and quantitative makeup of the first three total programs postulated for the current state of the art in Tables I and II. These pie charts serve to illustrate very graphically the influence of the available level of funding on the relative composition of these hypothetical programs. Thus, under circumstances of small budgets the percentage of treatment funds tends to be small, and that of research tends to

Table I

HEW COST SUMMARY
($1,000)

Program Level	Kidney Disease Categories				Total	
	Infectious	Hypersensitivity	Hypertensive***	End-Stage	Cost	Percent
Current Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	3,803	1,500	4,000	——	9,303	19.92
Diagnosis and Treatment	——	——	——	7,240	7,240	15.50
Sub-Total	3,803	1,500	4,000	7,240	16,543	35.42
Research	4,000	5,250	3,800	12,100	25,150	53.85
Training	400	560	380	1,000	2,340	5.01
Facilities	1,000	170	1,000	500	2,670	5.72
TOTAL	9,203	7,480	9,180	20,840	46,703	100.00
Intermediate Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	5,929	3,000	8,057	——	16,986	14.47
Diagnosis and Treatment	——	——	——	30,000	30,000	25.56
Sub-Total	5,929	3,000	8,057	30,000	46,986	40.03
Research	5,500	8,250	4,650	18,000	36,400	31.01
Training	750	750	500	5,500	7,500	6.39
Facilities	8,000	8,000	8,000	2,500	26,500	22.57
TOTAL	20,179	20,000	21,207	56,000	117,386	100.00
Accelerated Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	9,919	3,000	10,114	——	23,033	7.94
Diagnosis and Treatment	——	——	——	171,000	171,000	58.98
Sub-Total	9,919	3,000	10,114	171,000	194,033	66.92
Research	6,500	10,125	5,500	24,000	46,125	15.91
Training	975	750	1,425	10,000	13,150	4.54
Facilities	10,000	10,000	11,600	5,000	36,600	12.63
TOTAL	27,394	23,875	28,639	210,000	289,908	100.00
Accelerated Expenditure Level--1975**						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	11,308	{43,000-Vaccine {13,000	11,732	——	76,040	25.94
Diagnosis and Treatment	——	——	——	132,225	132,225	45.11
Sub-Total	11,308	56,000	11,732	132,225	208,265	71.05
Research	7,410	12,450	9,500	1,500	30,860	10.53
Training	1,110	1,870	3,000	5,000	10,980	3.75
Facilities	11,400	10,000	11,600	10,000	43,000	14.67
TOTAL	31,228	77,320	35,832	148,725	293,105	100.00

*   Current State of the Art

**   Advanced State of the Art

***   Attributable to renal disease associated with hypertension.

Source: See Chapter 6.

Table II

TOTAL COST SUMMARY
($1,000)

Program Level	Kidney Disease Categories				Total	
	Infectious	Hypersensitivity	Hypertensive***	End-Stage	Cost	Percent
Current Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	11,687	2,000	5,330	—	19,017	7.88
Diagnosis and Treatment	139,388	—	28,032	17,825	185,245	76.73
Sub-Total	151,075	2,000	33,362	17,825	204,262	84.61
Research	5,330	7,000	5,070	12,800	30,200	12.50
Training	530	750	510	1,000	2,790	1.16
Facilities	1,330	225	1,330	1,300	4,185	1.73
TOTAL	158,265	9,975	40,272	32,925	241,437	100.00
Intermediate Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	14,977	4,000	10,954	—	29,931	9.00
Diagnosis and Treatment	140,275	—	32,442	43,200	215,917	64.93
Sub-Total	155,252	4,000	43,396	43,200	245,848	73.93
Research	7,330	11,000	6,200	18,700	43,230	12.99
Training	1,000	1,000	670	5,500	8,170	2.46
Facilities	10,670	10,670	10,670	3,300	35,310	10.62
TOTAL	174,252	26,670	60,936	70,700	332,558	100.00
Accelerated Expenditure Level*						
Diagnosis, Prevention, Treatment						
Prevention (including education & administration)	22,097	4,000	13,899	—	39,996	7.60
Diagnosis and Treatment	143,616	—	36,852	189,375	369,843	70.29
Sub-Total	165,713	4,000	50,751	189,375	409,839	77.89
Research	8,670	13,500	7,330	24,700	54,200	10.30
Training	1,300	1,000	1,900	10,000	14,200	2.70
Facilities	13,330	13,330	15,460	5,800	47,920	9.11
TOTAL	189,013	31,830	75,441	229,875	526,159	100.00
Accelerated Expenditure Level-1975**						
Diagnosis, Prevention, Treatment		{200,000-Vaccine				
Prevention (including education & administration)	25,190	{ 34,000	16,120	—	275,310	33.84
Diagnosis and Treatment	103,721	68,000	53,858	144,875	430,454	52.91
Sub-Total	188,911	302,000	69,978	144,875	705,764	86.75
Research	9,880	16,600	12,000	1,500	39,980	4.91
Training	1,480	2,490	4,000	5,000	12,970	1.60
Facilities	15,200	13,330	15,460	10,800	54,790	6.74
TOTAL	215,471	334,420	101,438	162,175 .	813,504	100.00

* Current State of the Art

** Advanced State of the Art

*** Attributable to renal disease associated with hypertension.

Source: See Chapter 6.

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Table III

PROGRAM BENEFITS

Program Level	Kidney Disease Categories				Total
	Infectious	Hypersensitivity	Hypertensive***	End-Stage	
Current Expenditure Level*					
Short-Term Benefit-Reductions:					
Mortality	70 Deaths	610 Deaths	2,190 Deaths	690 Deaths	3,560 Deaths
Prevalence	3,231,260 Cases	—	27,000 Cases	—	3,258,260 Cases
Morbid Days	15,962,420 Days	—	1,602,000 Days	—	17,764,420 Days
Long-Term Benefit-Reductions:					
Annual	1,750 Deaths	—	4,330 Deaths	—	6,080 Deaths
Cumulative	25,850 Deaths	—	86,560 Deaths	—	112,410 Deaths
Intermediate Expenditure Level*					
Short-Term Benefit-Reductions:					
Mortality	70 Deaths	610 Deaths	2,270 Deaths	1,560 Deaths	4,520 Deaths
Prevalence	3,243,860 Cases	—	34,680 Cases	—	3,278,740 Cases
Morbid Days	16,273,640 Days	—	2,056,820 Days	—	18,330,460 Days
Long-Term Benefit-Reductions:					
Annual	1,770 Deaths	—	4,820 Deaths	—	6,590 Deaths
Cumulative	26,190 Deaths	—	96,300 Deaths	—	122,490 Deaths
Accelerated Expenditure Level*					
Short-Term Benefit-Reductions:					
Mortality	70 Deaths	610 Deaths	2,380 Deaths	7,675 Deaths	10,735 Deaths
Prevalence	3,292,860 Cases	—	42,750 Cases	—	3,335,610 Cases
Morbid Days	17,483,880 Days	—	2,311,340 Days	—	19,795,220 Days
Long-Term Benefit-Reductions:					
Annual	1,870 Deaths	—	4,820 Deaths	—	6,690 Deaths
Cumulative	27,480 Deaths	—	96,300 Deaths	—	123,780 Deaths
Accelerated Expenditure Level-1975**					
Short-Term Benefit-Reductions:					
Mortality	80 Deaths	770 Deaths	9,300 Deaths	27,399 Deaths	37,549 Deaths
Prevalence	5,630,780 Cases	62,250 Cases	289,690 Cases	—	5,991,723 Cases
Morbid Days	26,064,430 Days	2,610,000 Days	5,578,860 Days	—	34,253,290 Days
Long-Term Benefit-Reductions:					
Annual	4,125 Deaths	8,610 Deaths	9,480 Deaths	—	21,090 Deaths
Cumulative	76,500 Deaths	320,000 Deaths	189,660 Deaths	—	586,160 Deaths

*   Current State of the Art

**   Advanced State of the Art

***   Renal disease associated with hypertension.

Source: See Chapter 6.

Short-term benefits - reduction in annual mortality, etc., when program is fully operative.

Long-term annual benefits - eventual annual reduction in number of cases reaching end-stage kidney disease.

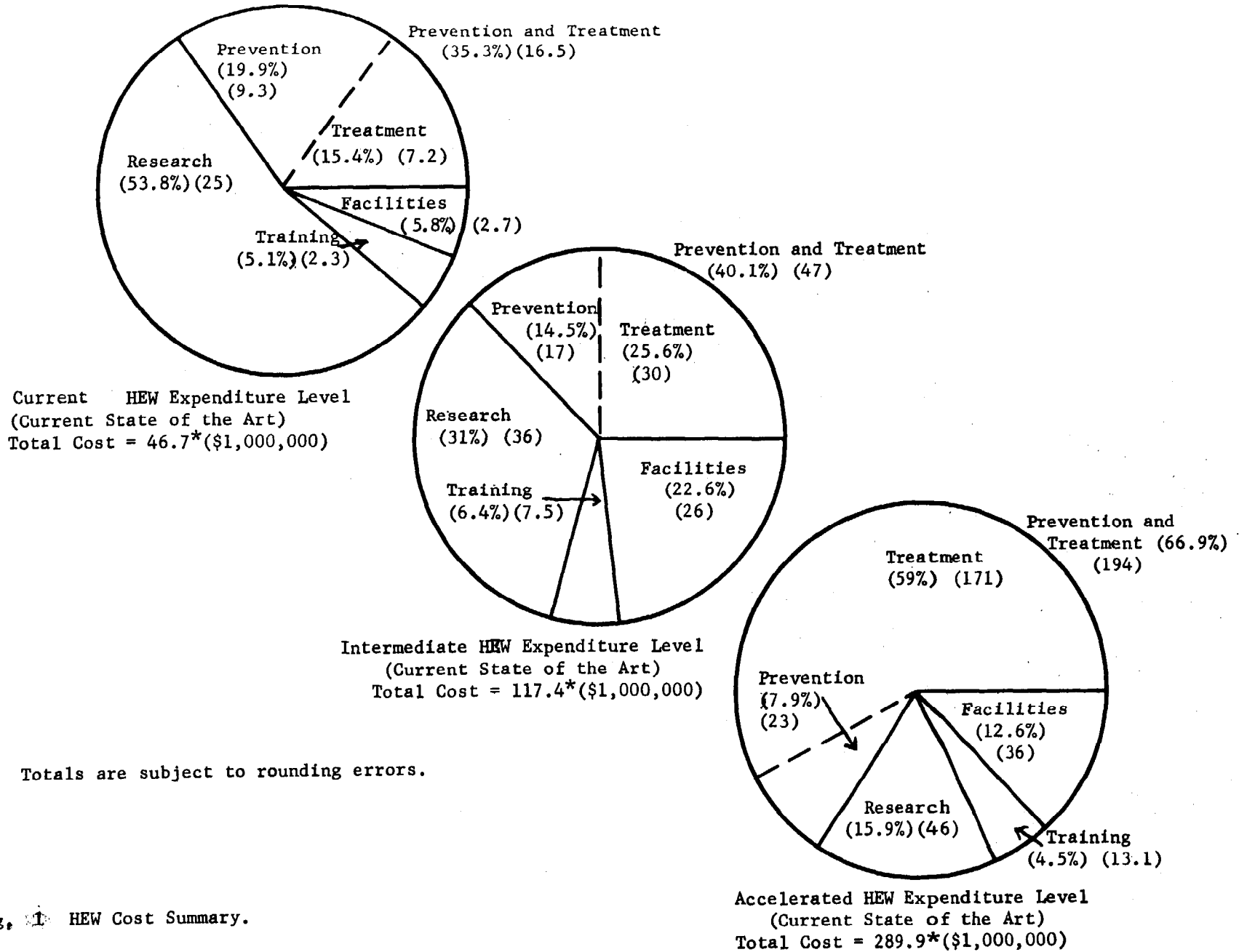Long-term cumulative benefits - sum total of long-term annual benefits.

Fig. 1 HEW Cost Summary.

Current HEW Expenditure Level
(Current State of the Art)
Total Cost = 46.7*($1,000,000)

Intermediate HEW Expenditure Level
(Current State of the Art)
Total Cost = 117.4*($1,000,000)

Accelerated HEW Expenditure Level
(Current State of the Art)
Total Cost = 289.9*($1,000,000)

* Totals are subject to rounding errors.

35d

Prevention and Treatment
(204.3) (304.59%)

Treatment
(276.22%)
(185.2)

Prevention (19.1)(28.37%)
Training
(4.18%)
(2.8)
Facilities
(3.60%)
(4.2)
Research
(45.00%)
(30.2)

Current   Total Expenditure Level
(Current State of the Art)
Total Cost = 241.5*($1,000,000)

35e

Treatment
(215.9) (233.74%)

Prevention and Treatment
(245.8) (266.14%)

(29.9)
(32.40%)
Prevention
Research
(43.2)
(46.76%)

Training
(8.1) (8.86%)

(25.5) Facilities
(38.23%)

Intermediate Total Expenditure Level
(Current State of the Art)
Total Cost = 322.6*($1,000,000)

* Totals are subject to
   rounding errors.

Prevention and
Treatment (409.7)
(280.40%)

Treatment
(369.8)
(253.04%)

(39.9)
(27.36%)
Prevention
Research
(54.2)
(37.08%)

Training
(14.2)(9.72%)
Facilities

(47.9)
(32.80%)

Accelerated Total Expenditure Level
(Current State of the Art)
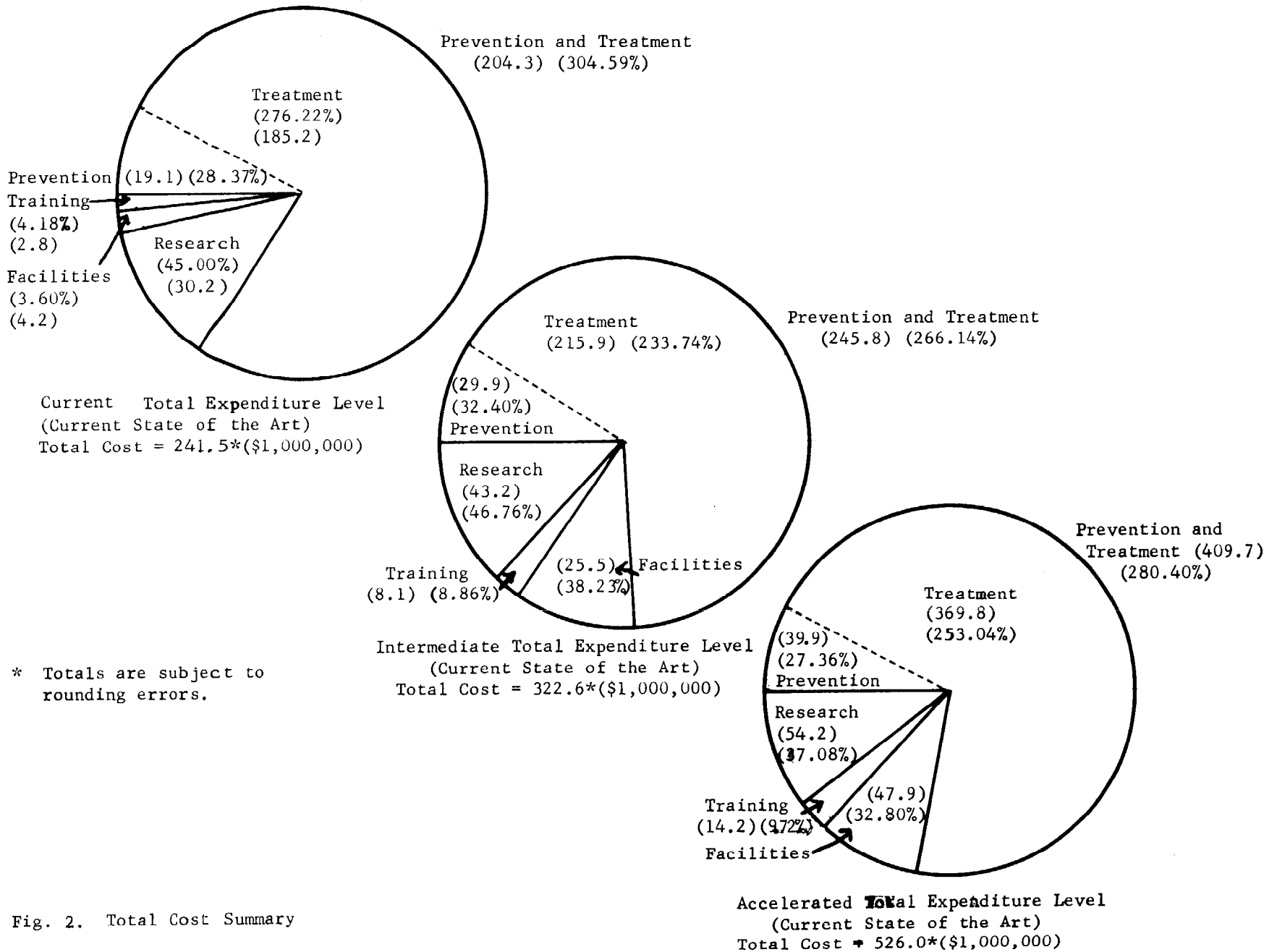Total Cost = 526.0*($1,000,000)

Fig. 2.   Total Cost Summary

be large. As the level of expenditure is liberalized this relationship

becomes reversed, although in each case the absolute expenditure for

each component still grows.

C. Future Shifting Proportions of Program Components

Figures 1 and 2 have illustrated the influence of the amount of avail-

able funds on the relative proportions of the various program components

in such total efforts. Another factor which will influence these proportions

very significantly is the prevailing state of the art with respect to the

various primary kidney diseases and end-stage kidney failure. This was

evident in the program analyses involving the individual groups of kidney

diseases; the same principle holds in relation to overall programs as

illustrated on Tables I and II. Here too, the total program mixes illus-

trated do not and should not represent static proportions to be followed in

future years. Depending on advances in knowledge and methodology which will

be derived from ongoing research efforts, these proportions will have to be

changed each year to obtain maximal benefits in terms of lives saved both in

the long run and in terms of the immediate future. Thus, as survival figures

for transplantation improve, more patients who would otherwise be maintained

permanently with the aid of dialysis will be treated by kidney transplant,

and proportionately more funds should be channeled in this direction. As

improved methods of primary prevention are developed (such as an anti-

streptococcal vaccine) more funds will have to be allocated for the

applications of the new techniques since their successful use will reduce

the long-term mortality at a relatively small per capita expense.

D. Outlook

With an advancing state of knowledge and with the passage of time, the

proportions of the optimal mix for a total program for the solution or

amelioration of the kidney problem will follow the general outlines of the diagram presented in Figure 3. It illustrates a gradually increasing emphasis on successful prevention and effective treatment of the various primary kidney diseases with progressively lesser needs for the saving of lives due to end-stage kidney disease. Given such a set of circumstances there will be a continued need for a repeated searching re-evaluation of the entire kidney disease problem, so that program decisions will continue to bring maximum benefits to patients afflicted with kidney disease.

100%

Treatment
of
End-Stage
Kidney
Disease

TRANSPLANTATION

DIALYSIS

Prevention
&
Treatment
of
Primary
Kidney
Diseases

TREATMENT of Primary
Kidney Diseases

PREVENTION of Primary
Kidney Diseases

RESEARCH

TRAINING

FACILITIES

100%

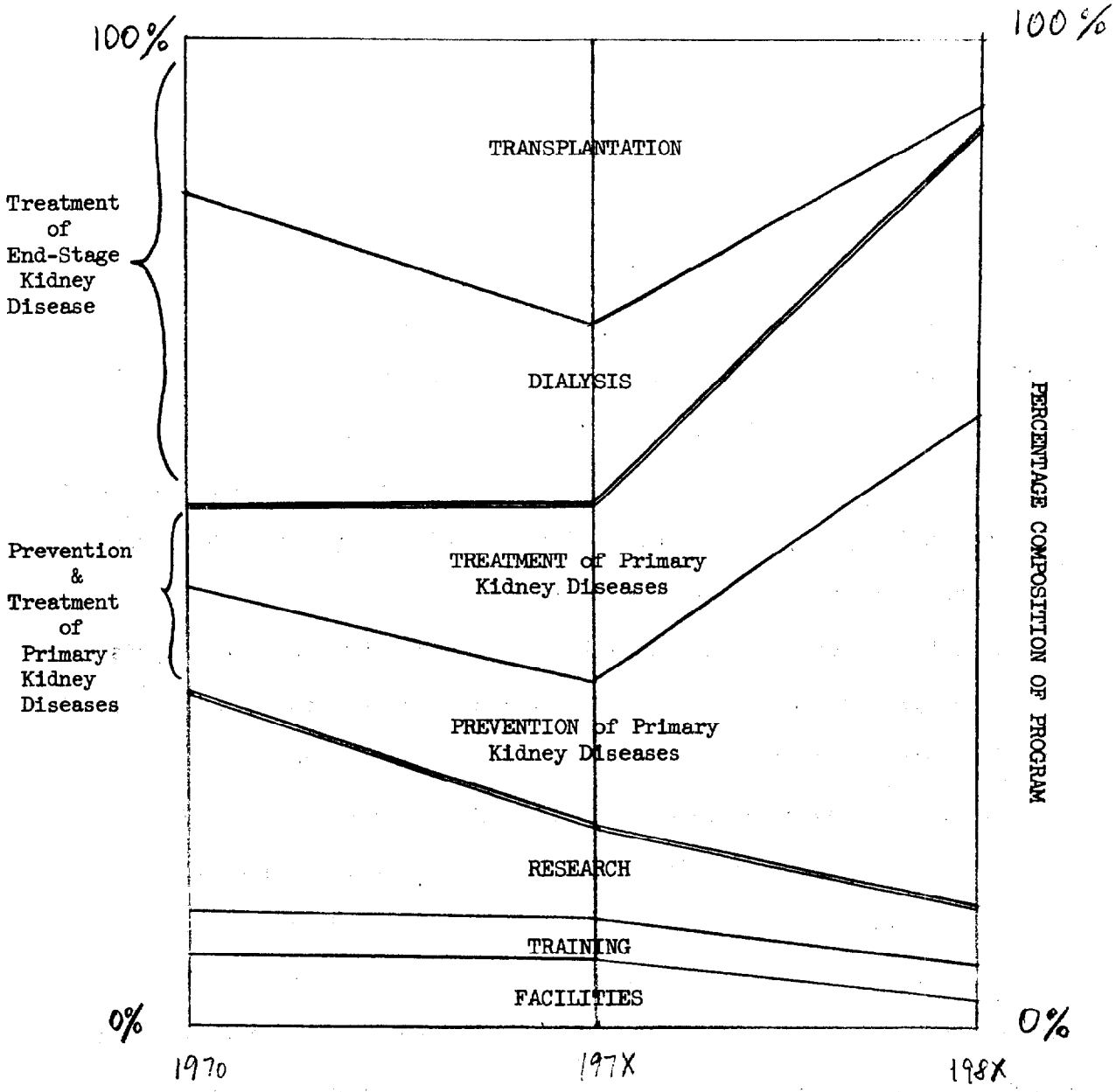PERCENTAGE COMPOSITION OF PROGRAM

0%

0%

1970

197X

198X

Figure 3. EFFECT OF ADVANCING STATE OF THE ART ON FUTURE PROGRAM
COMPOSITION
(Percentages are wholly arbitrary and merely serve to
illustrate shifting trends.)

37a

Chapter 2

Kidney Disease--Current Status

I. INTRODUCTION

Dramatic advances in the treatment of end-stage renal failure have

sparked new hope for people suffering from this hitherto fatal condition.

Today hundreds are living useful and productive lives while undergoing chronic

hemodialysis. Hundreds more have received successfully transplanted human

kidneys and carry on life with minimal interruption in their daily activities.

Current programs to increase research and development in transplantation and

chronic hemodialysis, and training of personnel to supervise these complex

procedures promise a wider application.

Yet, though dramatic and usually successful, chronic hemodialysis and

renal transplantation are difficult procedures associated with considerable

morbidity and mortality. At best these procedures are now applicable to a

relative few patients who reach the terminal stages of renal failure.

A rational program in kidney disease, therefore, requires that oppor-

tunities to interrupt all processes leading to renal disease be sought and

pursued vigorously. We must fill the gaps in our understanding of the path-

ogenesis of renal disease; we must define and isolate the etiologic factors,

and careful and detailed study must settle the areas of controversy.

II. THE DISEASE PROBLEM

As indicated in Chapter 1, diseases of the kidney have steadily gained

in significance as an area of social importance for both federal and nonfederal

research and service efforts during the last five years--primarily because

of the development of hemodialysis and kidney transplantation. In general,

however, mortality from kidney disease and other urinary system diseases has steadily declined since 1900 from about 100 deaths per 100,000 population in 1900 to 17.2 in 1964. Total mortality for all age groups among the four disease groups mentioned in Chapter 1 for 1964 was 58,788. The distribution of mortality among these disease groups is depicted in Figure 1. As can be seen, hypertensive renal cardiovascular diseases accounted for the greatest percentage (36%) of deaths among the kidney disease groups considered in the analysis.

Figures 2-5 graphically present the importance of morbidity associated with kidney diseases in terms of prevalence, days of restricted activity, days of bed disability and total work loss days. In general, there is little morbidity associated with hypersensitivity diseases of the kidney. Total morbid time of all types is generally evenly distributed among the remaining disease groups. During the period of July 1964 - June 1965, kidney diseases accounted for about 140,000,000 total days of restricted activity, 63,500,000 days of bed disability, 17,000,000 work loss days, with a prevalence of about 7,800,000 cases.

III. DISEASES OF INTEREST

A. Hypertension

1. Introduction

Arterial blood pressure is maintained by a variety of mechanisms and is subject to a number of influences such as posture, emotional state and exercise. When measured correctly in the steady resting state a diastolic blood pressure in excess of 90mm. of mercury is considered abnormal.

The conditions characterized by established diastolic hypertension
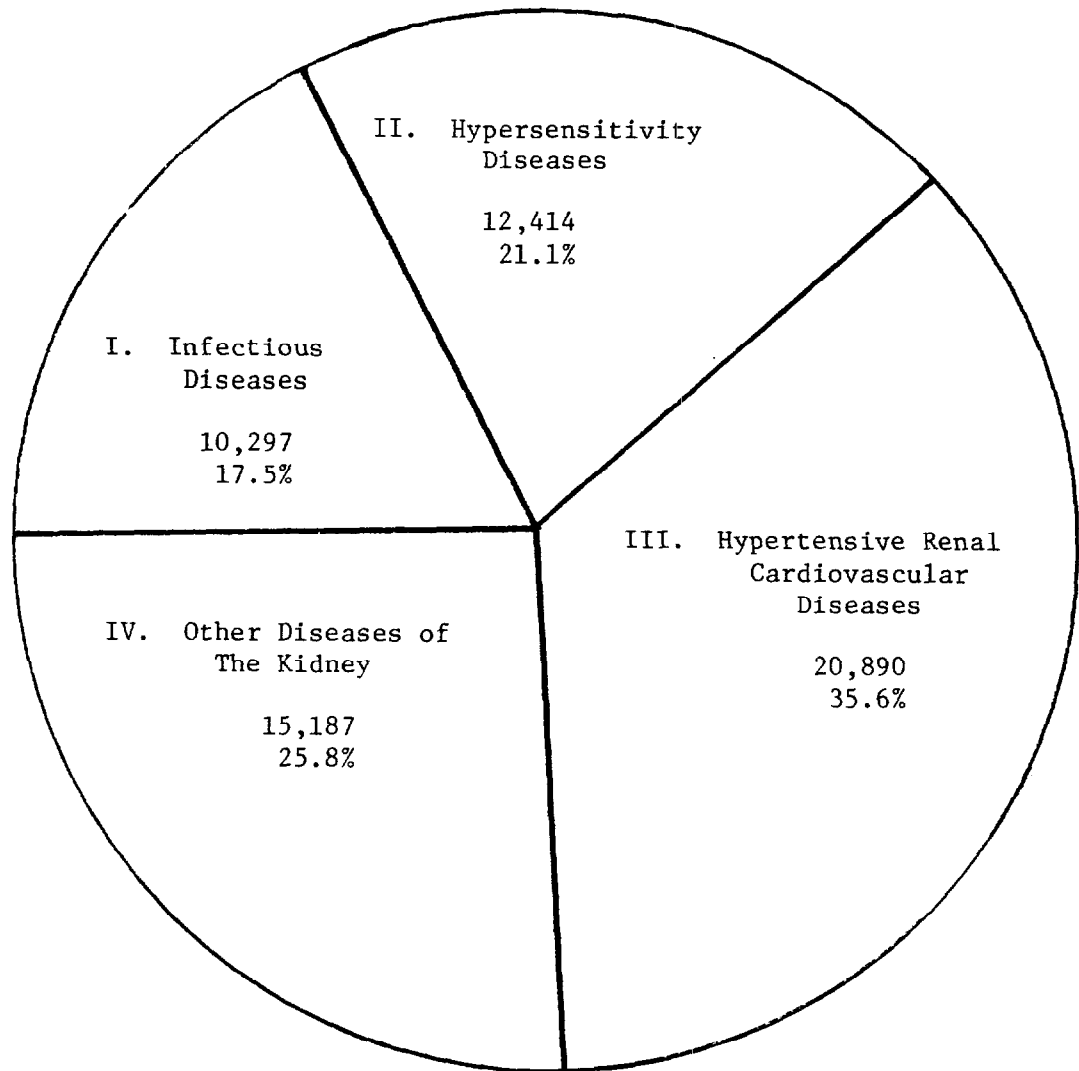
Total Mortality—58,788

Fig. 1. Mortality from Kidney Disease in 1964 by Disease Group.

Source: Unpublished data from the U.S. Department of Health, Education, and
Welfare, Public Health Service, National Center for Health Statistics,
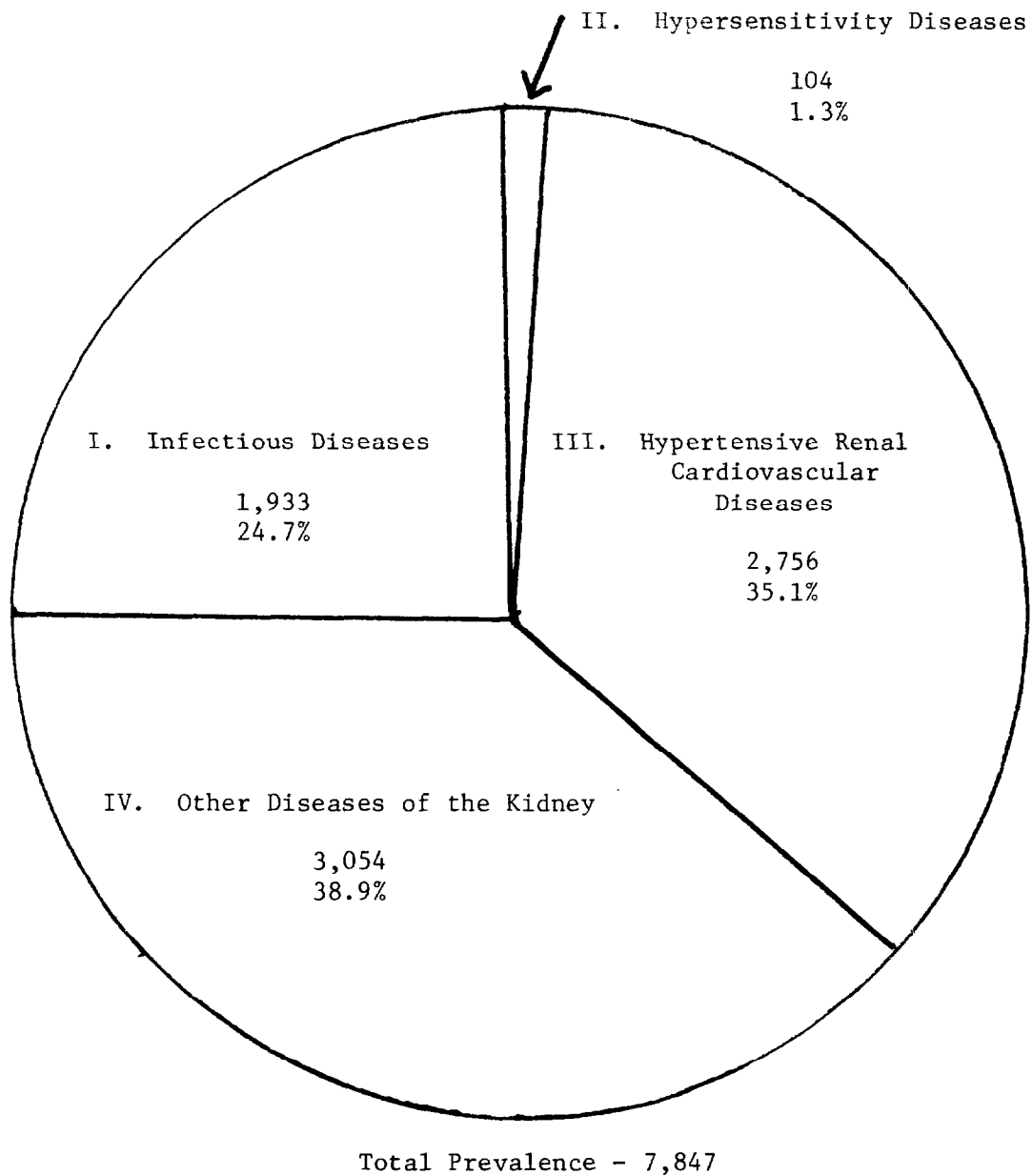Washington, D.C.

II. Hypersensitivity Diseases

104
1.3%

I. Infectious Diseases

1,933
24.7%

III. Hypertensive Renal
Cardiovascular
Diseases

2,756
35.1%

IV. Other Diseases of the Kidney
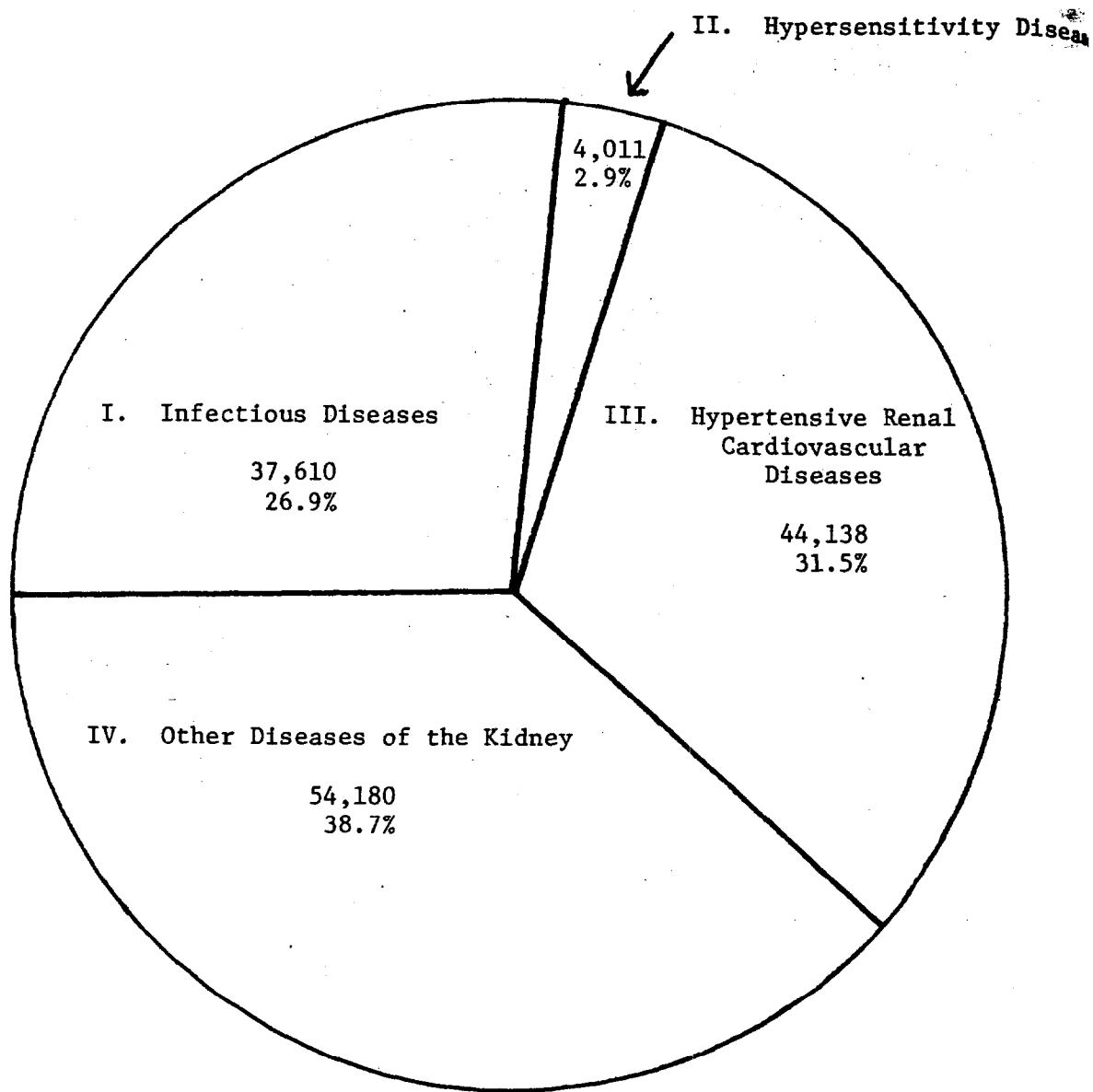
3,054
38.9%

Total Prevalence - 7,847

Fig. 2. Selected Chronic Conditions, Prevalence (1000's), United States,
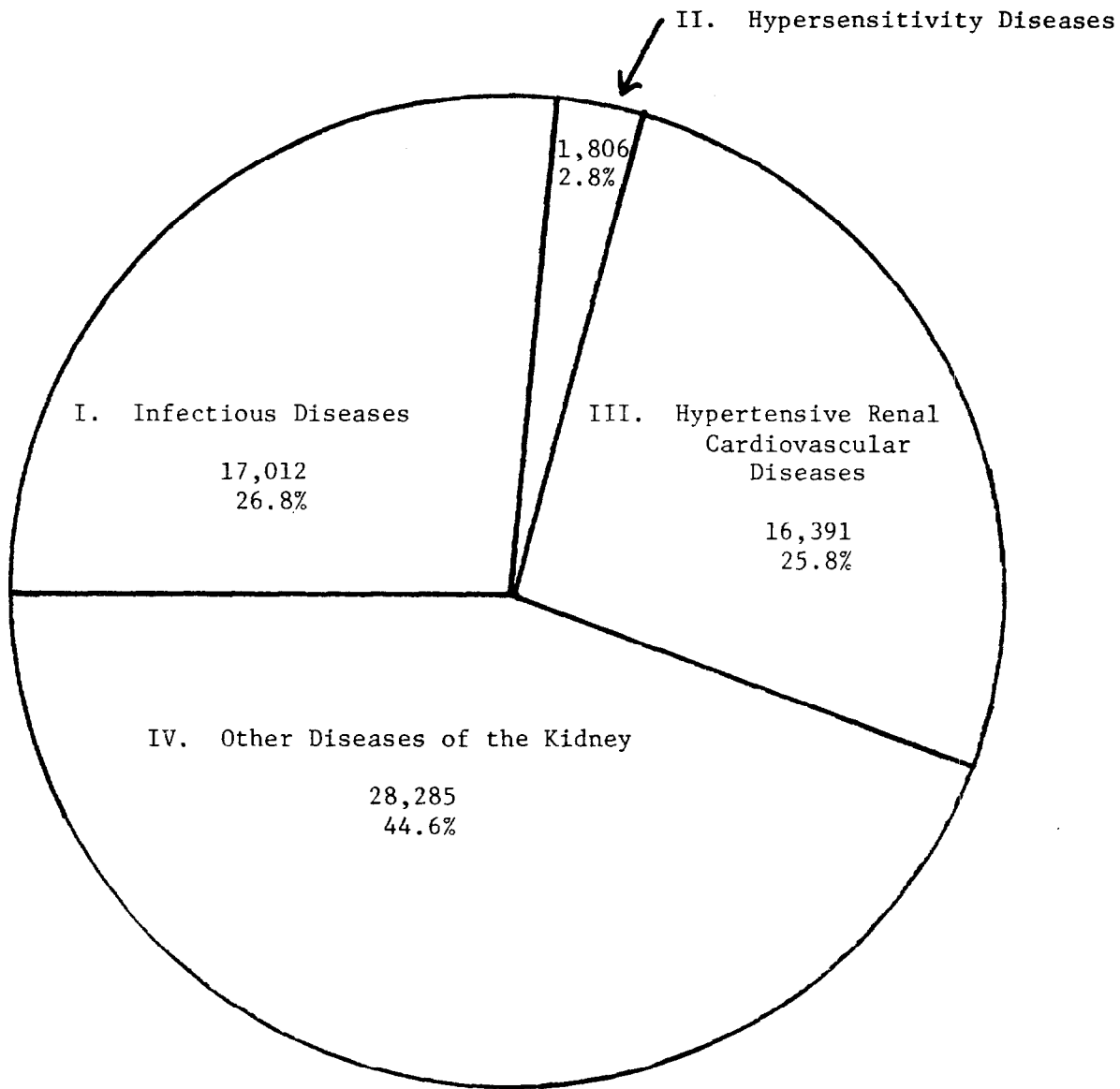July 1964 - June 1965.

Source: For civilian non-institutional population from unpublished data
from the U.S. Department of Health, Education, and Welfare,
Public Health Service, National Center for Health Statistics,
Washington, D.C.

II. Hypersensitivity Diseases

4,011
2.9%

I. Infectious Diseases

37,610
26.9%

III. Hypertensive Renal
Cardiovascular
Diseases

44,138
31.5%

IV. Other Diseases of the Kidney

54,180
38.7%

Total Days of Restricted Activity - 139,939

Fig. 3. Selected Chronic Conditions, Days of Restricted Activity
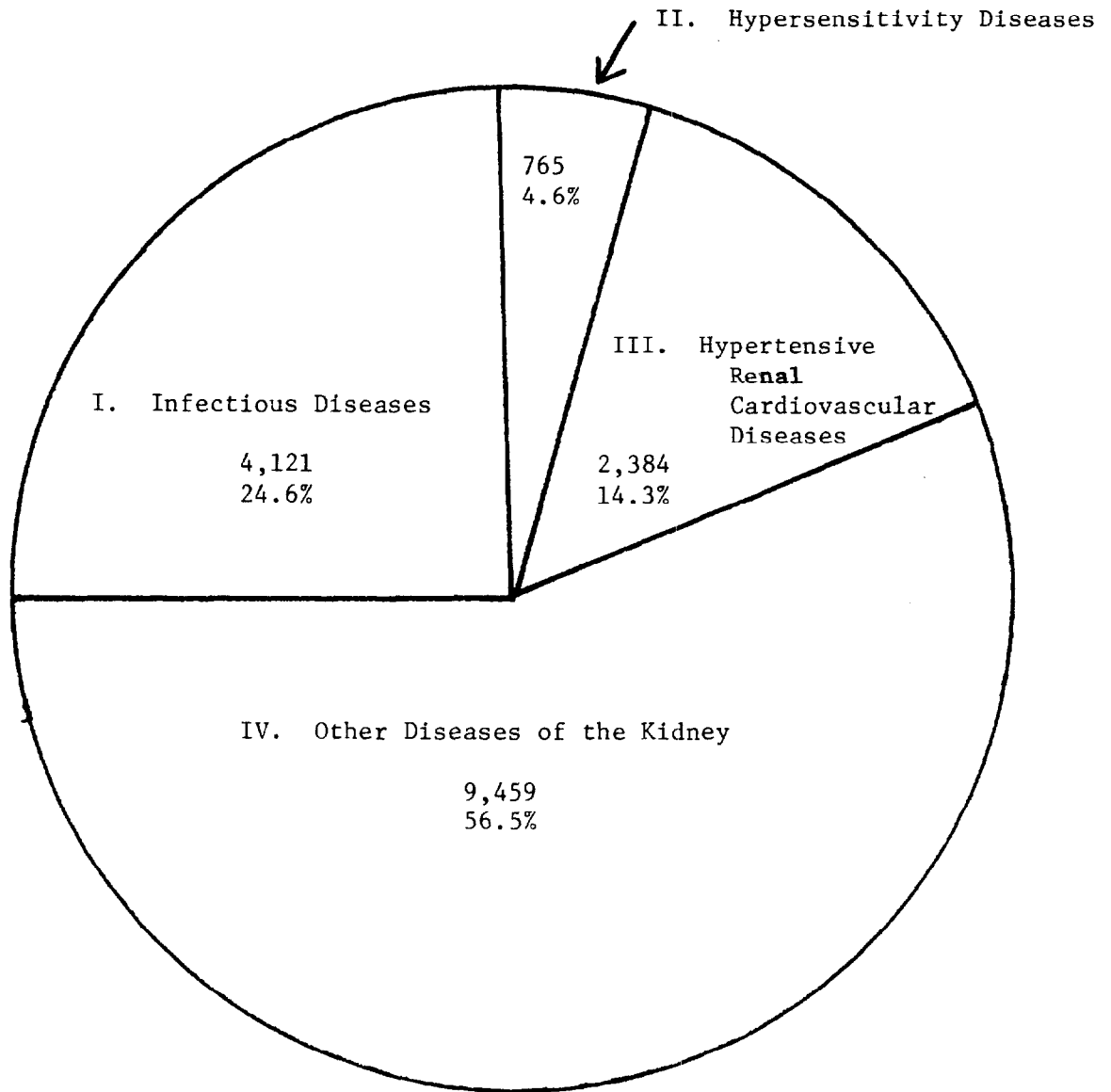(1000's), United States, July 1964 - June 1965.

Source: For Civilian non-institutional population from unpublished data
from the U.S. Department of Health, Education, and Welfare,
Public Health Service National Center for Health Statistics,
Washington, D.C.

II. Hypersensitivity Diseases

1,806
2.8%

I. Infectious Diseases

17,012
26.8%

III. Hypertensive Renal
Cardiovascular
Diseases

16,391
25.8%

IV. Other Diseases of the Kidney

28,285
44.6%

Total Days of Bed Disability - 63,494

Fig. 4. Selected Chronic Conditions, Days of Bed Disability (1000's),
United States, July 1964 - June 1965.

Source: For civilian non-institutional population from unpublished data
from the U.S. Department of Health, Education, and Welfare,
Public Health Service, National Center for Health Statistics,
Washington, D.C.

II. Hypersensitivity Diseases

765
4.6%

I. Infectious Diseases

4,121
24.6%

III. Hypertensive
Renal
Cardiovascular
Diseases

2,384
14.3%

IV. Other Diseases of the Kidney

9,459
56.5%

Total Work Loss Days - 16,729

Fig. 5. Selected Chronic Conditions, Work Loss Days (1000's), United States, July 1964 - June 1965.

Source: For civilian non-institutional population from unpublished data from the U.S. Department of Health, Education, and Welfare, Public Health Service, National Center for Health Statistics, Washington, D.C.

include primary (essential) hypertension, of unknown cause, comprising

80-90% of the total, and secondary hypertension accounting for 10-20%

of the hypertensive population. In the secondary group, the hyperten-

sion can be traced to some underlying process. This group is especially

important because often the hypertension can be cured. Processes leading

to secondary hypertension include: adrenal tumors, renal artery stenosis,

pyelonephritis, acute and chronic glomerulonephritis, pheochromocytoma,

coarctation of the aorta, and certain disorders of the central nervous system.

2. Primary (Essential) Hypertension

    a. Incidence

        Primary hypertension occurs in 5-10% of the adult population

of the United States. In 1965 it was estimated that 9,200,000

individuals had hypertension. It is twice as common in women as in

men and there is a strong familial tendency. The average age of

detection is about 32 and onset after 50 years of age is most

unusual. When followed from the onset of hypertension, the average

patient lives for a period of 20 years. (The average life expect-

ancy at 32 is 41.5 years.) The course of the individual patient

varies. Some patients may enter an accelerated phase in a few months;

others may survive with few complications for 40 or more years.

        Of those with essential hypertension 5-10% develop an accelerated

or malignant form which is fatal if untreated.

    b. Clinical Course--Benign Hypertension

        Initially there may be no symptoms and the patient is often

unaware of the illness until informed by his physician. The clinical

course roughly divided into an uncomplicated phase lasting an average

of 15 years and a complicated phase with progressive damage to the

heart, kidneys, brain, eyes, and other systems.

During the uncomplicated phase about 2/3 of the patients have
a variety of usually minor symptoms including fatigue, nervousness
and headaches. After an indefinite period, complications appear.
Atherosclerosis is common. Hypertension accelerates arterial damage
and predisposes to the deposition of lipid materials. In most there
is gradual enlargement of the heart. Congestive heart failure is
eventually responsible for about 25% of the deaths and is a contributing
factor in another 25%. About 10% of hypertensives die of a myocardial
infarction while another 10% die following cerebral thrombosis or
hemorrhage. Thus, some 70% die from major vascular problems.

In the kidneys, damage to the small arteries is found in a high
percentage of patients. Approximately one-half eventually develop
some evidence of renal damage (manifested by polyuria, diminished
concentrating power, or proteinuria), but uremia is only rarely the
cause of death unless there is an accelerated or malignant phase of
disease.

c. Accelerated or Malignant Form

Some 5-10% of patients with essential hypertension develop an
accelerated phase with progressive renal damage and higher fixed
diastolic blood pressure. The onset is usually abrupt and is
characterized by headaches, failing vision, nausea, and weight loss.
Unless the course is interrupted by treatment, complications develop
rapidly and death from brain, heart or kidney damage usually occurs
within two years. About one-third of these patients die with severe
renal complications. Early treatment of this group is important
since progressive changes in the small arteries of the kidney develop
rapidly. After these changes have developed to an advanced state,

lowering blood pressure may precipitate renal failure. Therapy started early significantly prolongs life in this group. The impact of successful drug therapy for malignant hypertension can be inferred from an almost 50% decline in the death rate from hypertensive heart disease since the introduction of antihypertensive agents in 1952.

3. Secondary Hypertension

In every patient with established diastolic hypertension, the possibility of secondary hypertension should be considered. Known causes must be systematically excluded by history, physical examination, appropriate laboratory tests and X-rays. The incidence of secondary hypertensions is estimated at from 10 to 20% of the total hypertensive population. Of these 5-15% are caused by renovascular (renal arterial) lesions. Another group of potentially curable hypertensives are those having hypertension secondary to aldosterone-producing adrenal tumors. Presently experts differ on the incidence of aldosterone-producing tumors in the hypertensive population. It is variously estimated that these tumors account for from 1 to 20% of the hypertensive population. Most investigators are now finding that 1% of their hypertensive patients have this condition. Other causes of secondary hypertension such as coarctation of the aorta, various renal diseases, Cushing's disease, pheochromocytoma and central nervous system disorders can be excluded only by careful and often extensive examination.

4. Etiology of Primary Hypertension

The cause or causes of hypertension have been and are the subject of intensive study by many distinguished investigators. There are three major theories relating to the development of hypertension. Some have stressed the importance of neurogenic factors and psychologic stress,

others have emphasized excessive sodium intake and abnormal endocrine control, while still others have concluded that renal circulation and renin are of primary importance in the development of hypertension. There is much evidence supporting each theory. Possibly one or all of these factors operates in a given individual who may be genetically predisposed to the development of hypertension. In this brief review emphasis will be placed on the renal relationships with hypertension without intending to imply that renal factors are the underlying cause of all primary hypertension.

The association between pyelonephritis and hypertension exists but the exact nature of the relationship has not been clarified. Patients with hypertension have a reported incidence of pyelonephritis varying from 14% to 51%. Conversely, from 12% to 85% of patients with histologic evidence of pyelonephritis are reported as having hypertension. The high incidence of pyelonephritic kidneys in hypertensives suggests that hypertension either predisposes to renal infection or is the direct cause of pathologic changes which are indistinguishable from those usually caused by infection. It has also been postulated that chronic renal infection is a major cause of hypertension. Current evidence is substantial regarding these views, but is not yet conclusive.

The relationship between hypertension and arteriolar nephrosclerosis (damage to the small arteries of the kidney), of the kidneys is also a subj of continuing controversy. Clearly, most hypertensives have nephrosclerosi to a greater or lesser extent. Now most investigators think that the nephrosclerosis is secondary to the hypertension. Some, however, maintain that the renal arteriolar lesions may be the precipitating cause of the hypertension. Whatever the underlying cause, it seems clear that once

established, hypertension accelerates the development of renal arteriolar stenosis and conversely that the arteriolar lesions may sustain and aggravate the increase in blood pressure. In malignant hypertension, renal ischemia leads to increased renin output with secondary hyperaldosteronism and an accelerated rate of hypertension which in turn leads to further renal arteriolar damage.

Further clarification of these important areas will have far-reaching therapeutic implications.

5. Management of Hypertension

With proper screening of the hypertensive population it is probable that 10-20% will be found to have underlying causes amenable to permanent cure. In malignant hypertension and in advanced diastolic hypertension (blood pressures in excess of 110mm. in men and 120mm. in women) early drug therapy and dietary management have been demonstrated sharply to reduce morbidity and mortality. In patients with lesser elevations of blood pressure the evidence favoring treatment is less substantial. Treatment must be individualized balancing the risks inherent in any chronic treatment against the potential benefits. Current long-term studies will help clarify this area.

B. Pyelonephritis and Infections of the Kidney

During the past 30 years since the reports of Longcope and Winkenwerder, and Weiss and Parker, the term pyelonephritis has been widely used to imply a pathologic process resulting from the immediate or late effects of bacterial infection of the kidneys. Unfortunately, the criteria used to diagnose pyelonephritis are not uniform.

1. Incidence

The incidence of chronic pyelonephritis varies widely among various

autopsy series from as low as 2% to as high as 35%. Reasons for these differences are the varying criteria used by pathologists to diagnose pyelonephritis and the differing populations studied. Kidney infections are more common in older populations, are more frequent in Negroes, and occur in higher incidence among lower socio-economic groups. In one careful study, pyelonephritis was found in 3.3% of 4,596 autopsies. Only 10% of these cases of pyelonephritis had demonstrable bacteriuria at death although previous treatment may have resulted in eradication of bacteria in some cases. In this same series 1.6% of 4,596 deaths were attributed to uremia. In another study acute and chronic pyelonephritis was found in 10% to 20% of the autopsies at two hospitals but was judged to be a major factor causing death in only one-third of these cases.

On a national basis in 1964, about 10,000 of the 1,800,000 deaths or 0.5% were attributed to infections of the kidney. This figure must be analyzed. It represents data from a wide variety of sources where there are considerable differences in the diagnostic criteria of pyelonephritis. It does not include cases of obstructive uropathy due to prostatic hypertrophy and prostatic cancer when these were ruled the underlying cause of death though renal infection may have precipitated death. On the other hand, this figure includes cases of renal disease in which there was no documentation of infection by bacteriologic or pathologic means. In other cases renal infection may have been recognized, but the underlying urologic or metabolic defect may not have been apparent.

Such incidence data of kidney infection and pyelonephritis must, therefore, be approached with caution in program planning. The final diagnosis of the cause of death is at best a good interpretation of events in the current state of the art. Many cases of infection are certainly

missed and others are classified erroneously as infection. The margin

of error is unknown, but could be large. A rational approach to the

control of pyelonephritis must include further research into all causes

of chronic interstitial nephritis as well as the search for methods to

control kidney infection.

2. Acute Pyelonephritis

Acute pyelonephritis is a common problem usually caused by gram

negative bacterial invasion of the kidney. The onset is usually abrupt

with characteristic symptoms although at times clinical symptoms may be

subtle or absent. The acute symptoms generally subside rapidly although

bacteriuria may persist without adequate treatment. Recurrences are common,

particularly during and following pregnancy. In recurrent cases, a careful

search for underlying predisposing factors such as prostatic hypertrophy,

stones, diabetes mellitus and congenital malformations should be made.

Remedial procedures are indicated where feasible.

3. Chronic Pyelonephritis

Symptoms of infection are frequently absent in patients with chronic

pyelonephritis although there may be a history of previous urinary tract

infection. The onset is usually insidious with gradual development of

the manifestations of chronic renal failure. This period of relative renal

insufficiency may be long. During this period many patients live in

comfort for years despite azotemia. Bacteriuria may be absent or present

only intermittently making accurate diagnosis difficult during life.

In such cases, other causes of nephritis must be considered. Eventually,

end-stage renal failure is reached unless intervention is undertaken.

4. Bacteriuria and Urinary Tract Infection

Bacteriuria may be defined as the presence of over 100,000 organisms per cc. of urine on a culture of clean fresh urine. Defined in this manner persistent bacteriuria indicates infection of the urinary tract. There has been much debate about the role of bacterial infection in the pathogenesis of chronic pyelonephritis. Repeated bouts of kidney infection whether manifest or silent lead to renal scarring and eventual renal failure. But in many cases bacteria cannot be isolated from kidneys in which the pathologic diagnosis is pyelonephritis. One current and controversial theory to explain this discrepancy is that bacteria may initiate a self-sustaining destructive process which persists after bacteria have been eradicated. Another possibility is that some cases classified as pyelonephritis are due to non-bacterial causes. It is not known how often bacteriuria per se is the forerunner of chronic pyelonephritis. Since bacteriuria is present in patients who do not subsequently develop pyelonephritis and since the source of bacteria may be the urethra, bladder or other lower urinary tract sites, there must be many cases in which ascending infection does not develop. On the other hand, bacteria in the lower urinary tract may lead to kidney infection, particularly in the presence of predisposing factors such as obstruction, stones, diabetes and gout. Furthermore, such bacterial infection can act as a source of virulent organisms in the development of septicemia. Thus, while bacteriuria may not always lead to the development of chronic pyelonephritis, its presence should be taken seriously, and careful consideration given to management.

In young patients persistence of bacteriuria should be confirmed
by a minimum of two cultures of clean voided specimens. If bacteriuria
persists in an asymptomatic patient, a short course of antibiotic treat-
ment should be followed with repeat culture at intervals. If bacteriuria
still persists, investigation to detect underlying correctable lesions is
indicated.

In later stages of pregnancy about 6% have asymptomatic bacteriuria.
Of these, at least 40% will develop pyelonephritis. It seems reasonable
to treat bacteriuric pregnant women for the duration of the pregnancy.
In older patients in whom the incidence of bacteriuria may be 10 to 20%,
treatment must be undertaken with some caution. The eradication of
bacteriuria in the elderly is difficult and the risk of complications
from over-zealous treatment seems great.

Carefully controlled long-term studies are necessary to determine
in which cases vigorous treatment of bacteriuria will prevent the develop-
ment of chronic pyelonephritis. Judicious application of current techniques
to control infection may result in eventual reduction in the number
reaching the end-stages of pyelonephritis.

Hypersensitivity Diseases

1. Acute Glomerulonephritis

Acute glomerulonephritis is a common disease affecting all age groups,
but it occurs predominantly in children. Almost all cases follow by one
to four weeks infection with hemolytic streptococci. These bacteria
initiate an immune process which is almost certainly responsible for the
subsequent renal damage. Only certain nephritogenic types of streptococci
are responsible for acute glomerulonephritis. Thus, in some epidemics
of hemolytic streptococcal infections, glomerulonephritis is not seen,

while in others the attack rate is high, the disease often striking several members of the same family.

Most cases are mild and some may go unnoticed. In mild symptomatic cases, renal damage is manifested by blood in the urine and puffiness due to salt and water retention. In more severe cases hypertension, anemia, and even acute renal failure may develop. As a rule most patients recover completely, but currently, about 2% of hospitalized patients die of acute renal failure. In 1964, 585 deaths were attributed to acute nephritis. An additional 2,900 died of nephritis not specified as acute or chronic. A few patients with the acute form enter a protracted subacute course with gradual deterioration of renal function over a 6 to 12 month period. Nephrosis seldom occurs in the acute phase.

In another group, comprising probably not much more than 1% of the total with acute post streptococcal glomerulonephritis, healing is incomplete. These patients show continuing proteinuria and eventually develop one type of chronic glomerulonephritis. Failure to heal is more common in adult cases of acute glomerulonephritis and seems to be associated with non-epidemic streptococcal infections. Estimates vary, but about one-tenth to one-third of all cases of chronic glomerulonephritis are post streptococcal in nature.

2. Chronic Glomerulonephritis

Chronic nephritis and nephrosis accounted for 8,800 deaths in 1964. Chronic glomerulonephritis cannot be defined as a single disease entity and probably has multiple causes. In most cases the etiology is obscure. In various autopsy series its frequency has been reported from 0.5% to 1.5% and is about one-third as frequent a cause of death as pyelonephritis. The onset occurs in all age groups. If those presenting with the nephrotic

syndrome are excluded, the greatest number are first noted between age 10 and 40.

Chronic glomerulonephritis usually begins quietly and progresses slowly. The first manifestation is frequently persistent protein in the urine. In other instances onset is abrupt with rapid development of nephrotic syndrome characterized by edema and massive proteinuria. Hypertension rarely appears until renal damage is severe. The course is variable lasting from one to about forty years. In one series the average duration was seven and one-half years in those who have died, however, many in this series are still living. The course may be punctuated by episodes of nephrosis and may terminate abruptly. Signs of renal failure appear gradually, but once azotemia appears, progress to end-stage renal failure is usually a matter of only a few years.

3. Nephrotic Syndrome

Massive loss of protein in the urine may be caused by a variety of renal diseases and leads to the development of the nephrotic syndrome. Clinically this syndrome is characterized by massive swelling of the body and face known as generalized edema. Underlying renal diseases such as lupus erythematosus, diabetic nephropathy and post streptococcal glomerulonephritis are occassionally recognized, but more often no underlying cause can be detected.

4. Idiopathic Nephrotic Syndrome

Nephrotic syndrome due to unknown causes is a major cause of morbidity and mortality, most often in children between the ages of one and six. The annual occurrence in this age group is estimated at 2 per 100,000.

Patients with the nephrotic syndrome present a variety of clinical pictures. In the idiopathic form glomerular lesions lead to urinary

protein loss with the development of generalized edema. Complications in severe cases include hypertension, malnutrition, anemia, infection and occasional vascular collapse. In children, about one-third heal spontaneously. Recently corticosteroid therapy and careful management appear to have improved survival rates. In adults with this disorder, the outlook is even more serious. Spontaneous healing is not common and progressive renal failure usually ensues.

5. Pathogenesis of Nephrotic Syndrome and Chronic Glomerulonephritis

The underlying causes of these renal diseases are not known. There is much evidence to indicate that immune mechanisms are responsible, but the precise sequence of events is not clear. The application of safe biopsy techniques, sophisticated biochemical methods and electron microscopy to the study of glomerular lesions has helped unravel this complex group of disorders. The application of new immunological concepts, combined with transplantation studies may finally yield answers to the remaining basic questions about these diseases.

6. Lupus Nephritis

Systemic lupus erythematosus is a generalized disease involving the kidneys, brain, lungs, skin, joints, and other organs. Nearly 300 deaths were listed in 1964. It is predominantly a disease of young women, but attacks both sexes through a wide age range. The incidence has increased markedly during the past two decades partly because of improved methods of diagnosis and almost certainly because of the more widespread use of sensitizing drugs. There is much evidence that an abnormal immune response, precipitated by a variety of agents, is responsible for this disease.

Renal involvement in patients with systemic lupus erythematosus is perhaps the most ominous of the many manifestations of the disease. In general, renal involvement is found in about two-thirds of lupus patients. Patients who exhibit renal involvement usually do so early in the course of their disease. The renal lesions run the gamut from a local glomerulitis involving parts of glomeruli, to a focal lesion involving some glomeruli, to generalized subacute or chronic glomerulonephritis, with or without the characteristic wire-loop lesion.

Clinical manifestations of renal lupus include hypertension, edema, and on occasion oliguria or anuria with rapidly progressing uremia. Many patients with lupus nephritis show at some stage the nephrotic syndrome. Usually, this group does poorly.

Corticosteroids have become a mainstay of lupus nephritis therapy, though there are divergent opinions as to the effectiveness of these drugs in various stages of the disease. Recently antimetabolites have been used and present information suggests a significant measure of success. Additional information about the nature of the renal changes in this disease has been obtained by attempts to relate ultrastructure and functional derangements. Studies are under way to elucidate the role played by plasma proteins in the evolution of this disease. Important work is being done correlating the histologic changes in the kidney with clinical course. Understanding of the pathogenesis of this disease has important implications for all hypersensitivity diseases such as rheumatoid arthritis, all chronic nephritis and rheumatic fever and has relativity to transplantation immunology.

D. Other Related Renal Diseases

Many kidney diseases and other diseases which often lead to severe renal disease were not included in this initial analysis. These are described briefly in this section.

1. Polycystic Disease of the Kidneys

This disease is by far the most important of the developmental anomalies of the kidneys. This anomaly was held responsible for 1,061 deaths in the United States in 1964. In this group over three-fourths of the deaths occurred before the age of 60. This disease masquerades in a variety of forms including vascular accidents, hypertension, pyelonephritis and chronic renal failure. There are two forms: one inherited as a dominant trait which usually becomes manifest in adult patients, and one which appears to be inherited as a recessive trait primarily manifested in children. A history of polycystic disease is usually readily obtained in other family members; unfortunately in some families there is a pathetic desire to hide the trait. Conventional treatment helps these patients. But, as end-stage renal failure approaches, hemodialysis and eventual renal transplantation are their only hope for survival.

2. Gouty Nephropathy

An estimated 250,000 people in this country are suffering from some form of gout. In 1964, 130 deaths were attributed to gout. In the advanced stages of gout one of the major causes of death is renal insufficiency. Some reports suggest that albuminuria occurs in up to 40% of patients with gout, renal calculi in 17% and that the development of renal insufficiency in 18% of cases. The only distinctive pathologic feature of the gouty kidney is the presence of urate crystals. The precipitation of this material in the kidney may be responsible for the frequently observed

pathologic picture of pyelonephritis or nephrosclerosis and less often
amyloidosis.

Management of gout has until recently been limited to the relief
of joint symptoms primarily through the use of colchicine and the
reduction of elevated blood uric acid levels by increasing uric acid
excretion primarily through the use of probenecid. A new approach to
reduction of blood uric acid levels has been provided by the introduction
of allopurinol, a xanthine oxidase inhibitor, which acts by decreasing
the production rather than the excretion of uric acid. Important avenues
of investigation have been opened not only in primary gout but in other
diseases associated with increased uric acid levels. The promise of
reduction in morbidity and mortality from gout is great.

3. Hypercalcemia

Hypercalcemia from a variety of causes may produce secondary renal
disease which if uninterrupted is often lethal. Calcification of the
kidney tissue, formation of stones, and secondary pyelonephritis are
common in advanced cases and usually lead to end-stage renal failure.
Such diverse entities as hyperparathyroidism, sarcoidosis, vitamin D
intoxication, excessive ingestion of milk and alkali, and immobilization
in bed can lead to hypercalcemic nephropathy. In many of these cases
therapy directed at the underlying problem is successful in arresting
the progress of renal damage. Often, however, the process is not recog-
nized until renal damage has progressed to an advanced state. In this
stage, particularly if hypertension has supervened, reversal of the
process is usually impossible and terminal renal failure ensues.

4. Diabetes

As the life span of diabetics has increased, renal disease has become an increasingly important cause of morbidity and mortality. The renal complications of diabetes are manifold and include acute and chronic infection, renal arterio-sclerosis and arteriolar sclerosis with hypertension, and finally intercapillary glomerulosclerosis, a process seen only in association with diabetes mellitus. Renal diseases account for over 10% of the deaths in diabetics.

The management of these renal problems is only moderately successful. Eradication of urinary tract infection is particularly difficult in diabetics, but should be pursued with vigor since this may retard the progress of renal damage and prevent septicemia. Hypertension may be ameliorated by conventional therapy.

Unfortunately, chronic hemodialysis and transplantation offer little chance for long-term survival in most of these patients since severe arterial disease is usually **widespread** in affected patients. Better understanding of the mechanisms of development of atherosclerosis and of lipid metabolism and changes occurring in the capillary basement membrane offer the best hope for improving the outlook of these patients.

5. Miscellaneous Renal and Renal Related Diseases

Many other diseases are of importance in any discussion of kidney diseases. Malignant diseases of the prostate account for over 15,000 deaths annually. In this usually indolent malignancy early detection may cure many patients, while hormonal therapy will help others. Prompt treatment of renal infections and alleviation of urinary obstruction reduces renal deaths. Benign prostatic hypertrophy leads to urinary tract obstruction with frequent development of hydronephrosis and pyelonephritis.

New cryosurgical techniques are promising for this group and there is indication that hormonal therapy may be beneficial.

Kidney Stones often lead to obstruction and infection. In cases due to gout and hypercalcemia the treatment of the underlying disorder may be effective. In other cases the cause is not clear, but may be related to individual habits or peculiarities of the environment. Recent identification and isolation of an "anti-stone substance" which is absent in the urine of some who develop kidney stones may lead to new therapeutic methods. In still other cases, such as cystinuria and oxalosis, the metabolic defects have been identified and corrective therapy may be forth-coming.

A number of urinary tract anomalies are lethal in infancy. Other obstructive and muscular lesions may respond to treatment in later life.

Tuberculosis of the genitourinary tract still accounts for almost 100 deaths per year and if recognized may respond to a variety of measures. Toxemias of pregnancy still account for over 200 deaths per year. Renal amyloidosis secondary to rheumatoid arthritis, ulcerative colitis and leprosy accounts for many deaths. Amyloidosis of the kidney due to chronic infectious diseases is a major world cause of renal deaths.

E. Acute Renal Failure

Acute renal failure may appear suddenly following a massive kidney injury or develop in the course of a chronic renal disease. In either case urine flow is greatly diminished and the kidneys are temporarily unable to perform their usual functions. The incidence of acute renal failure is difficult to determine, however, in one university referral center, acute renal failure accounted for half of the patients seen with uremia. In a nationwide sample

the proportion of patients with uremia who present with acute renal failure would probably be much lower.

Acute renal failure may be due to a number of causes including insufficient renal blood flow, transfusion reactions from mis-matched blood, fulminating infections, kidney poisons, acute urinary tract obstruction and acute glomerulonephritis. Prompt restoration of blood flow, relief of obstruction and effective treatment of infection are essential in preventing further renal damage. Toxic substances must be immediately identified and measures taken to remove them by dialysis or chemical binding whenever possible.

After all available measures have been taken to arrest further damage, assessment of the degree of damage must be undertaken and management planned. In a few cases the damage is mild and no further measures are necessary. In others, renal function ceases completely and the patients must be sustained by a combination of dialysis and dietary regulation while healing takes place. In these cases after a period of days or weeks the kidney gradually resumes its function and may eventually show return to normal function.

Broad advances in our knowledge of kidney function, wide use of hemo-dialysis and availability of remarkable new therapeutic agents have resulted in a gradual increase in the number of patients surviving. Now over 50% of patients with severe acute renal failure recover.

In other patients kidney damage is too severe and effective renal function does not return. Some die of other underlying processes or infection while others have little or no return of function and enter a period of chronic renal failure.

F. Chronic Renal Failure

Despite current screening programs and early medical intervention in many cases of renal diseases, many patients do not seek medical attention

until irreversible renal damage has progressed to an advanced state. Often destructive kidney lesions are painless and indeed asymptomatic. Symptoms may not be noticed by the patient until 50 to 80% of his kidneys have been destroyed. If at this point the patient seeks the help of his physician it may still be possible, depending on the underlying disease, to arrest renal destruction, prolong life and reduce complications. For example, in chronic pyelonephritis due to bacterial infection, relief of obstruction or removal of stones combined with selective antibiotic therapy may arrest renal destruction and in lupus erythematosus steroid and immunosuppressive therapy often retard the progress of renal destruction. In other cases such as chronic glomerulonephritis, congenital polycystic disease, diabetic glomerulosclerosis, and some cases of chronic pyelonephritis, there is no current effective therapy to arrest renal destruction.

1. Dietary Therapy

In these cases careful intelligent management has much to offer. Three major kidney functions are the regulation of water and electrolytes, the excretion of nitrogenous waste products and the excretion of excess acid. By careful regulation of dietary intake of sodium and potassium, restriction of protein intake to a minimum balanced mixture of essential amino acids, and limitation of the acid forming potential of the diet it is possible to reduce considerably the morbidity of patients with chronic renal failure. In cooperative patients, the frequency of dialysis can be greatly reduced. Anemia, hypertension and certain metabolic disturbances remain severe problems in some patients.

2. Hemodialysis and Transplantation

In those patients who have progressed to the end-stages of renal failure or who have other threatening complications which can no longer

be managed by selective management of intake, chronic hemodialysis and
renal transplantation now offer a new hope for survival. Because
experience is limited, it is difficult to predict the eventual applicability
of these two procedures to the total population with end-stage renal
failure. Further research into improved dialysis membranes, combinations
of hemodialysis with various ion exchange methods and/or selective adsorption
procedures, and better understanding of complex metabolic problems will
reduce the morbidity and mortality associated with hemodialysis and may
yield entirely new methods with wider application and reduced cost. Home
dialysis is promising. In the field of organ transplantation experience
in management of transplant recipients and improved matching of donor
kidney and recipient have resulted in substantial reduction in morbidity
and mortality. Now this procedure is performed with remarkable success
in a number of centers. Further advances in histocompatibility typing,
selective immunosuppression and patient management can be expected.

a. Hemodialysis

Hemodialysis has been used with success in acute renal failure
since 1947. The development of the indwelling arteriovenous shunt
in 1960 made possible the use of intermittent hemodialysis to prolong
life in irreversible uremia. In the current state of the art, a
number of problems are apparent in the application of this procedure.

b. Factors Limiting Application of Hemodialysis

Partly because of limited facilities and personnel and because
of the limitations of current techniques, experience has largely
been limited to patients between ages 20 and 55. Unfortunately, about
three fourths of patients reaching end-stage renal failure and who
thus might benefit from hemodialysis are beyond the age of 60.

Within the mid-age group, psychological problems have presented
a serious obstacle to some who might have benefited from hemodialysis.
A number of patients have developed problems in accepting their dependence
on dialysis machines and their attending medical personnel while
others have suffered a change in self image which has led to serious
social difficulties. The motivation and intelligence of the patient
are crucial to success.

The medical problems associated with chronic hemodialysis are
formidable. Peripheral neuropathy and metastatic calcification are
common. Hypertension is often difficult to control. The anemia of
chronic renal failure often requires transfusions which eventually
may lead to hemosiderosis. Serum hepatitis is a danger to the patient
and the attending personnel as well. Infection at the cannula site
and clotting of the cannula are persistent problems. Severe metabolic
bone disease is still frequent although some progress has been made
in its control. Human errors and mechanical difficulties are occasionally
responsible for failures. Well trained, highly motivated and experi-
enced medical personnel are scarce.

Despite these problems many live useful, productive lives. While
extension of hemodialysis to older age groups presents difficult
problems, technical improvements and increased experience may prove
intermittent hemodialysis feasible in some older patients. Intermittent
hemodialysis combined with dietary therapy may prolong useful life in
many and sustain others who might benefit from renal transplantation.

Clearly, many now face death who could be helped by intermittent
hemodialysis.

c. Kidney Transplantation

Renal transplantation offers another future hope for those afflicted with end-stage renal failure. Currently 30-month survival rates range from 17 to 47% for patients with cadaver transplants and 60% or more for living related donors. In cases where a good histocompatibility match has been obtained and no rejection crisis has occurred in the first few months after transplantation, good renal function has been reported in up to 93% of patients after three and one-half years.

d. Limitations

Aside from the operative morbidity and mortality associated with renal transplantation there are currently several major obstacles to greater use of renal transplantation for end-stage renal failure. The availability of viable human kidneys presents a major problem. The use of living related donors raises serious moral questions and such donors will provide only a limited number of kidneys. Cadaver kidneys are a major potential source of viable kidneys; however, the problems of histocompatibility matching, the ethical and legal questions of consent, and the logistical problems of preservation and trans-portation have not yet been solved. Immunosuppressive therapy has been successful in preventing homograft rejection in many cases, but has often led to serious and sometimes fatal infection in the recipient. Although the development of more selective immunosuppressive agents has been promising, the problem of complicating infections has not been overcome.

Large areas of investigation offering significant conceptual advances in the field of tissue transplantation remain to be explored. Induction of adult tolerance, detailed analysis of histocompatibility

antigens and work on the non-immunologic mechanisms of cell to cell

interaction are some of these.

e. Peritoneal Dialysis

Peritoneal dialysis offers a useful, but a present limited alternative

to hemodialysis. Exchange of chemicals is less efficient, leading

to longer treatment periods than with hemodialysis, and infection

remains a major obstacle. Intermittent catheterization, new flexible

catheters, and automated flushing have improved this method.

F. Poisoning

In 1964, over 1,000 deaths resulted from accidental poisonings from

salicylates, barbiturates and other analgesic and soporific agents. In addition,

over 2,400 suicides resulted from use of these agents. Hemodialysis techniques

are of great value in most of these poisonings and it is reasonable to assume

that a significant number of these deaths could have been avoided if personnel

trained in the techniques of emergency hemodialysis had been widely available.

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Current Kidney Disease Control Programs

I. INTRODUCTION

This chapter is devoted to a brief description of current kidney disease "program" activities and deficiencies. "Program" as used herein refers to an organized effort directed toward the eradication or alleviation of kidney disease problems. Kidney disease program efforts may have an active nature, such as a research project in kidney disease, or passive nature such as a hospital renal clinic.

Kidney disease program efforts in this chapter are viewed from the standpoint of program source and by program objective. Program source is considered in terms of federal and nonfederal. The latter includes state and local government, individual, philanthropic, and nongovernment institutional financial expenditures for or on behalf of kidney disease.

Kidney disease programs objectives may be separated into the following functional areas:

1) Research--Includes laboratory and clinical investigations and developmental research efforts.

2) Other Methodological Studies in Kidney Disease--Includes operational studies, screening and detection programs, and demonstration projects.

3) Treatment--Includes hospital, nursing home, physician and other professional services for diagnosis and therapy of kidney diseases.

4) Facilities--Includes aid in construction, remodeling or expansion of facilities for activities in kidney disease treatment, research, and training.

5) Education and Training--Includes basic education (fellowships),

specialized on-the-job training (training grants), and postgraduate education in kidney diseases.

The ability to describe many federal and particularly nonfederal kidney disease program efforts in terms of expenditures is highly variable because of insufficient or inadequate data. In many instances kidney disease program efforts are merged with others thereby making it difficult to proportion accurately kidney-related expenditures among general programs. In some instances it was necessary to use data for the year 1964 because of its completeness and availability. Whenever possible, programs for more recent years are used in order to make this document action-oriented for imminent budgetary periods, and to take into consideration increased efforts in this disease area.

II. SPECIFIC FEDERAL KIDNEY DISEASE PROGRAM EFFORTS

A number of federal agencies are currently active in kidney disease. Some have primary responsibilities in providing patient care and others are interested in basic and developmental research. As in most other diseases, there is no single federal agency charged with the responsibility for kidney disease programs. PHS recently indicated that there is no comprehensive plan for coordinated attacks against kidney disease because:

1) Kidney disease is notoriously difficult to pinpoint as a cause for morbidity and mortality in the population;

2) The variation in opinion within the medical community as to the desirability of large-scale dialysis and transplantation efforts;

3) The need for more time to improve and develop research; and

4) No single agency or organization has taken on itself the

leadership in bringing together all interested groups in kidney disease. Kidney disease program activities of specific Federal Agencies follow.

A. U. S. Department of Health Education and Welfare (HEW)

HEW has undertaken major responsibility of kidney disease control programs in the U. S. Its activities range from laboratory and clinical research performed or supported by the National Institutes of Health (NIH) to support of dialysis center demonstration projects by the Kidney Disease Control Program of the National Center for Chronic Disease Control. Specific groups and activities follow.

1. National Institutes of Health (NIH)

   a. National Institute of Arthritis and Metabolic Diseases (NIAMD)

   NIAMD's primary efforts are in the area of laboratory and clinical research and in urology and kidney diseases in general, and research and development in chronic uremia, hemodialysis and artificial kidney development.

   The NIAMD has traditionally invested major funds in extramural support of laboratory and clinical research in kidney diseases and urologic disorders. It was a group of Institute grantees that developed the permanently indwelling polymer shunts which made chronic intermittent hemodialysis possible. The emergence of this new treatment modality encouraged the Congress, in the summer of 1965, to appropriate funds to this Institute for the pursuit of a centrally directed program of research and development in chronic uremia, hemodialysis and artificial kidney development, utilizing predominantly a direct contract approach as well as increased research grant support.

   A thorough study of the state of the art made it apparent that no single specific direction should be followed which would exclude others which might be relevant. Several different types of

artificial kidneys are in use at the moment, and different

methodologies are being advocated by the various workers in

the field. Therefore, at this time, a variety of approaches

in artificial kidney development are being supported. Once it

becomes evident that one or more approaches show greater

promise, efforts will be concentrated in these directions.

The Artificial Kidney-Chronic Uremia Program was mounted

with the placement of carefully selected research and develop-

ment contracts with universities, nonprofit research laboratories

and industrial concerns which possessed relevant talents and

facilities. These projects involve development of improved

blood cannulas; evaluation and development of new polymer surfaces

for artificial kidneys; cannulas and membranes which do not

induce blood coagulation; design of more efficient, compact,

and less costly dialyzer systems; development of a new concept

of artificial kidney dialysis ("hollow fiber" or "capillary"

kidneys); research on and development of absorption cartridges

for blood purification; research on the utilization of ultra-

sonics to speed up dialysis in artificial kidneys; development

of inexpensive disposable dialysis units; improvement and design

of new dialysis units with automated failsafe mechanisms;

design and development of a prototype for a portable artificial

kidney; evaluation of a special protein restricted diet in

the maintenance of uremic patients for whom chronic dialysis

is deemed not feasible or unobtainable; isolation from dialysates and identification of the as yet unknown compound(s) which is (are) specifically responsible for the toxic symptomatology in uremia; and many other projects related to improved dialysis methodology or apparatus.

An important new activity involves the establishment of a long term central patient registry and medical information system involving all patients maintained with the aid of chronic dialysis in the United States (and, through cooperation of the European Dialysis and Transplant Association, of similar patients in Europe). This activity, which involves very close collaboration with the Kidney Disease Control Program of PHS and with the Veterans Administration, will permit a comparative evaluation of different dialysis treatment methods and equipment based on a longitudinal study of all patients involved, from their selection for chronic dialysis treatment onward.

The portion of the program which is funded by extramural research grants complements closely the contract program described above, but is oriented more toward elucidation of clinical and fundamental biological problems related to the treatment of chronic uremia rather than toward hardware development. It involves studies on urea metabolism in uremic patients undergoing chronic dialysis; the effectiveness of peritoneal dialysis in uremia patients; other novel approaches to blood purification in chronic kidney failure such as dialysis of a surgically relocated, isolated intestinal loop, lymph dialysis and dialysis in the home; and the nature of the biochemical defects in advanced uremia.

A summary of NIAMD kidney disease program expenditures is presented in Table I.

Table I

NIAMD KIDNEY DISEASE PROGRAM EXPENDITURES FOR 1966

Program	1966 Expenditures
Research and Development:	
Artificial Kidney and Dialysis	$3,151,000
Kidney Transplant Research	593,000
Other Renal and Urology Research	2,894,000
Total	$6,638,000

b. **National Institute of Allergy and Infectious Diseases (NIAID)**

NIAID's efforts are devoted to fundamental research and applied research and development in kidney transplantation including typing systems, immunosuppression and organ preservation.

Grant-supported research projects, intramural studies, and organized developmental work in medical centers and industry have been stepped up in recent years.

The urgent need, and the short-term goal, of the tissue transplantation immunology program is the identification of all the tissue transplantation antigens and their classification according to relative strength. Experimental work has shown that there are apparently only 6 to 10 major transplantation antigens rather than the 15 to 30 which had been predicted on the basis of animal studies.

Certain immunosuppressive drugs for use in the prevention or control of the rejection phenomenon are being studied. Studies are being conducted to find more effective and less toxic drugs to control the immune response.

Two groups of investigators have produced specific immunologic

tolerance to grafts in mice and in dogs by administration of anti-
lymphocyte serum before the transplant operation. This procedure
resulted in striking prolongation of the graft and apparently
induced tolerance also to second grafts. Another group found that
antiserum to thymus prolonged skin graft survival in rats twice
as long as antiserum to lymphocytes.

In addition to antilymphocyte serum, total and sub-total body
irradiation, cytotoxic drugs, and surgical alterations of the lympha-
tic system have been used in attempts to reduce or eliminate the
lymphocyte population and thus increase tolerance to homografts.
These methods, however, also cause undesirable general effects, such
as depression of bone marrow and red blood cell formation.

Paralleling the efforts to develop reagents, tests, and techniques
for applying the knowledge already gained are research projects
aimed at understanding the basic immunologic processes of the human
body. Intramural projects in Bethesda on immunology focus on such
areas as hypersensitivity, mechanisms of the immune response,
immunochemistry of serum antibodies and antisera, and induction of
delayed hypersensitivity. Many of these studies are closely related
to the problems of transplantation. Fifty-nine research grants and
fifteen collaborative research contracts were supported in 1966. A
summary of NIAID kidney disease program expenditures for 1966 is
presented in Table II.

Table II

NIAID KIDNEY DISEASE PROGRAM EXPENDITURES FOR 1966

Program	1966 Expenditures
Intramural Research in Transplantation Immunology	$ 190,000
Research Grants--Transplantation Immunology	3,100,000
Collaborative Research Contracts-- Transplantation and Immunology	849,000
Total	$4,139,000

c. National Heart Institute (NHI)

Through the years, the National Heart Institute has supported a wide variety of basic and applied research in kidney diseases and hypertension. One hundred and thirty research grants were awarded in the area of renal diseases, including somewhat less than 10% in studies on fluids and electrolytes, totaling about 5.0 million dollars, or 6.0% of Heart Institute research grant funds for FY 66. Another 130 projects dealt predominantly with hypertension, totaling 3.6 million dollars, or 4.3% of funds, and 83 grants for 3.0 million dollars representing 3.6% of research grant funds, devoted to studies combining renal and hypertension interests. While these reflect primarily numbers and costs of research grants, it may be noted that approximately another 10% of these figures were expended to support training grants and fellowships in the same areas of research.

In FY 66, 53 of these 343 research grants were in the areas of

artificial kidney and kidney transplantation. This includes a
significant number of projects where relatively minor commitments
are in the categories noted.

While the National Heart Institute conducts no organized
programs in kidney disease, certain coordinated efforts can be
mentioned. These take two forms of multi-disciplinary approach:

1) Intra-institutional, inter-departmental program projects;
    and

2) Inter-institutional cooperative studies.

Of the 226 research grants in the etiology of kidney diseases,
two are program projects dealing with renal diseases, and two other
combine attacks on renal disease and hypertension. Support to these
four projects amounted to $838,000 in FY 66, averaging about
$210,000 per project. Two more program projects were supported in
the renal area, directing their efforts to therapeutic implications,
and costing $905,000 or about $450,000 per project. It may be noted
also that both these latter projects deal with kidney transplantation.

Cooperative studies represent another coordinated type of attack
on disease problems. The Heart Institute in FY 66 supported 36
projects in three separate cooperative studies, the total cost of
which in that year was $1,374,000. All three of these cooperative
studies emphasized clinical testing of surgical or drug therapeutic
measures, although not without inclusion also of a significant stress
on diagnostic techniques particularly in the extensive 20-project
Cooperative Study on Renovascular Hypertension. It is of interest
that the two other studies, one on drug therapies and hypertension,
and the other dealing with antibiotic therapy of pyelonephritis in

relation to hypertension, both are conducted entirely in PHS hospitals. A good deal of the higher cost per project in the Renovascular Hypertension Study reflects costs of hospitalization and other patient care, which are not carried by the grants to the PHS hospitals.

All together, these coordinated efforts supported by the Heart Institute amount to 42 projects, or 12% of those in the total area of kidney and hypertension research, with a support level of slightly over $3,000,000 (see Table III), or about a quarter of the total research grant budget for these areas. Thus, while the Institute continues to emphasize support of individual, unstructured, non-directed research on hypertension and kidney disease, these more coordinated program projects and cooperative studies represent significant portions of Heart Institute support to these fields, stressing particularly many aspects of therapeutic measures.

Table III

NHI RESEARCH EXPENDITURES ON KIDNEY DISEASE

Program	1966 Expenditures
Renal Disease and Hypertension	$1,743,000
Cooperative Studies	1,374,000
Total	$3,117,000

d. Division of Research Facilities and Resources (DRFR)

Several programs are administered by DRFR which include
support of research in kidney diseases.

In FY 1966, the General Clinical Research Centers program
provided an estimated $4.5 million for kidney disease research
not including research in hypertension and diabetes. This
program provides for the cost of remodeling and renovation
necessary to establish the resource and for operating costs such
as hospitalization, research nursing care and support of specialized
technical personnel. Laboratory support in these centers is limited
to procedures required by several different investigators. The
research conducted in these centers is controlled through competi-
tion adjudicated by a local advisory committee. Since many of the
investigators utilize the resource simultaneously, the award pro-
vides a flexible mechanism of bed-support which can readily adapt
to the needs of many investigators at any particular time.

The Division has two other programs on which kidney research
depends indirectly. The Health Research Facilities Program, budgeted
at $50 million, provides matching funds for the construction of
research facilities. Any future research programs in renal diseases
requiring additional space may depend heavily on this program.

A second program is the General Research Support Program,
currently budgeted at $61 million. This program assists institutions
heavily involved in sponsored biomedical research to maintain a
degree of flexibility in furthering their own biomedical research
and research training goals. Thus this program provides backup

support for many of the categorical grants from the institutes.

A summary of pertinent Division of Research Facilities and

Resources expenditures is presented in Table IV.

Table IV

ESTIMATED DRFR DIRECT KIDNEY DISEASE PROGRAM EXPENDITURES

Program	1966 Expenditures
General Clinical Research Centers: Kidney Disease	$4,500,000

2. Kidney Disease Control Branch, National Center for Chronic Disease
Control

The Kidney Disease Control Program of the National Center for

Chronic Disease Control has responsibilities in all areas relating

to the development and demonstration of the dialysis method in commu-

nities, the training of professional and technical personnel in

dialysis therapy, public and professional information and education

activities, and appropriate related data collection and analysis. The

Branch serves as the Public Health Service's consultative unit in

dealing with official and other health agencies, hospitals, and

practitioners in all aspects of the provision of dialysis services.

In addition to these dialysis-related activities, the Kidney Disease

Control Program conducts a broad range of preventive and educational

activities in the broad kidney disease field.

Specific responsibilities in the dialysis-related areas follow.

a. Development and Demonstration Activities

Utilizing the grant authority of Section 316 of the Public

Health Services Act, the Kidney Disease Control Program actively

promotes the development of community dialysis demonstration

programs in various areas of the country. In addition to demon-

strating the feasibility of the treatment in the community setting,

these programs allow exploration of methods of financing dialysis

programs, provide expanded training opportunities, and allow

testing of new patterns in the provision of dialysis services. A

total of 15 community dialysis programs are presently being funded.

b. Training Activities

In addition to providing training opportunities through the

grant program, the Branch is responsible for development of train-

ing materials and techniques for use in both community centers and

home dialysis programs. This extends to all types of professional

and technical personnel and complements the limited direct assist-

ance for training in centers receiving grants.

c. Public and Professional Information and Education

In this area, the Branch is responsible for the development

and distribution of both technical and non-technical materials

related to the dialysis method, and for the provision of accurate

information on all aspects of the problem to the public through

the various media.

d. Data Collection and Analysis

The Branch engages in a continuing data collection and analysis

function directed towards the acquisition of quantitative information

from dialysis programs--regardless of the mode of support--and

analysis of the information in order to gain an accurate assess-

ment of the current status of the method. The data is disseminated

to interested parties inside and outside government, and is

utilized in the long-range planning functions of the Branch.

A summary of the Kidney Disease Control Branch Program's expenditures

are presented in Table V.

Table V

SUMMARY OF KIDNEY DISEASE CONTROL BRANCH PROGRAM EXPENDITURES IN 1966

Program	1966 Expenditures
Community Dialysis	$2,617,000
Prevention	385,000
Basic Data Development	156,000
Information and Training Materials	249,000
Total	$3,407,000

3. Bureau of Health Services

Present program activities of the Bureau of Health Services related

to kidney problems include basic and clinical research programs which

are being conducted at four Public Health Service general hospitals.

These programs encompass investigations in normal renal physiology as

well as a broad range of primary and secondary renal abnormalities. A

cooperative study involving seven general hospitals is attempting to

define the pathogenesis and natural history of chronic pyelonephritis
and to assess the response to long-term suppressive antibiotic therapy.
One of the hospitals has established a kidney disease screening clinic
to evaluate patients with suspected renal abnormalities. A second
cooperative study of hypertension includes the renal causes and com-
plications of this entity. Both cooperative studies are funded by the NHI.

With regard to training in this subspecialty, it has been necessary
until recently to provide training outside-the-Service in order to
develop career investigators for the Bureau and the Service. Individuals,
who received this training, now provide the competence for the present
research programs and for future training programs.

Expenditures by the Bureau of Health Services for research and train-
ing for 1966 are presented in Table VI.

Table VI

BUREAU OF HEALTH SERVICES KIDNEY DISEASE RESEARCH AND
TRAINING EXPENDITURES FOR 1966

Program	1966 Expenditures
Training	$24,000
Research	50,000
Total	$74,000

4. Vocational Rehabilitation Administration

At present the magnitude of specifically identified support for the
Vocational Rehabilitation Administration for patients with kidney disease
is not readily ascertainable.

B. The Veteran's Administration

The Veteran's Administration is charged with the responsibility of providing medical care, and to conduct medical research, designed to maintain or improve the health of its beneficiaries. Within this broad mandate the Veteran's Administration has exerted a significant effort in the kidney disease area.

The large majority of Veteran's Administration funds directed towards kidney diseases is expended in the area of clinical care. Information as to the level of effort in this area is scanty, and overall costs are not available. However, discharge diagnoses from the Veteran's Administration hospitals can provide clues on the size of the problem. In calendar years 1962-64, patients discharged from Veteran's Administration hospitals with selected principal and associated renal diagnoses averaged nearly 50,000 per year. The number of deaths with kidney disease as a principal diagnosis has remained relatively constant at roughly 1,600 per year although the distribution of diagnoses has changed somewhat.

A little over three years ago the Veteran's Administration decided to include a chronic hemodialysis capability within its hospital system. Since that time, 13 hospital units have been established. Actual cost analysis of this program is very difficult since a large share of the cost of the activity is supported from basic hospital budgets and is not separately identifiable. Specific allocations by the Veteran's Administration Central Office for unit activation over and above these basic hospital costs has been estimated at $2,476,000.

At the present time, the Veteran's Administration estimates that approximately 175 patients are being maintained on chronic intermittent hemodialysis. It further estimates that the future development of units already established

would enable it to perhaps double this caseload. Analysis of the mortality data mentioned earlier has led the Veteran's Administration to estimate that roughly 200 to 600 of the 1,600 individuals dying each year due to kidney disease would be suitable candidates for chronic hemodialysis programs.

Kidney transplant efforts are being conducted within the hospital system of the Veteran's Administration and generally are associated with a chronic hemodialysis program. Reliable data on veterans treated with kidney transplantation, however, are not available. At a recent meeting, surgeons from most of the Veteran's Administration hospitals estimated that approximately 100 such operations were reported as having been performed during the past three years. However, a considerable number of veterans have been referred to non-Federal institutions for transplants.

Research efforts sponsored directly by the Veterans Administration constitute only a very modest part of the overall national investment in kidney research. Research projects are underway in transplantation and dialysis as well as in other kidney research areas.

A summary of estimated expenditures for VA kidney disease research programs in 1966 is presented in Table VII.

Table VII

ESTIMATED VA EXPENDITURES FOR KIDNEY DISEASE RESEARCH PROGRAMS IN 1966

Program	1966 Expenditures
Research (dialysis and transplantation)	$ 734,000

C. Other Federal Agencies

Program efforts by other Federal agencies include those of research by
the Department of Defense, Atomic Energy Commission, U. S. Department of
Agriculture, National Aeronautics Space Administration, and National
Science Foundation.

With the exception of the Department of Defense, expenditures by other
Federal agencies in kidney disease are for research and are summarized in
Table VIII. Expenditures by the Department of Defense for treatment of kidney
disease have not been included.

Table VIII

KIDNEY DISEASE RESEARCH PROGRAM EXPENDITURES BY
OTHER FEDERAL AGENCIES IN 1966

Agency	1966 Expenditures
DOD	$ 440,000
AEC	65,000
USDA	105,276
NASA	85,400
NSF	22,034
Other Nonspecified	617,290
Total	$1,335,000

III. NONFEDERAL EXPENDITURES FOR KIDNEY DISEASE PROGRAMS

There are numerous state and local programs which expend money for various types of kidney disease programs including construction of facilities, treatment and prevention. These have not been included in this report.

Certain nonfederal agencies carry on active research, education, and general service programs in kidney disease. A description of some of these follows.

A. The American Heart Association

In general, the aims of the American Heart Association are to combat diseases of the heart and circulation and to provide positive benefits for the health of the people of the United States. Because of the association of renal diseases to those of the circulation, the American Heart Association's program activities include a substantial effort directed toward the control of renal diseases. Although the Heart Association has traditionally placed its primary emphasis on the support of the acquisition of new knowledge through research, it also has embarked on broad programs of public and professional education and has supported specific community programs designed to contribute to the understanding and prevention of cardiovascular diseases as well as to provide support for the individual patient with cardiovascular disease. In the renal disease area, the largest portion of effort has been expended in the areas of research with particular emphasis on the relationship between hypertension and kidney disease. It is anticipated that future efforts to be expended in this area will remain at approximately the present level and the Heart Association does not plan to extend its efforts in renal disease into areas of other than research. Table IX shows the 1966 level of effort in renal and directly related research.

Table IX

AMERICAN HEART ASSOCIATION EXPENDITURES IN RENAL RESEARCH FOR 1966

Program	1966 Expenditures
National	$ 618,000
Local	442,000
Total	$1,060,000

B. National Kidney Foundation

The aim of the National Kidney Foundation is to improve the care and treatment of those afflicted with kidney disease through the support of research into the incidence, causes, treatment, prevention, and cure of kidney diseases. The foundation also aims to promote professional and public education directed toward improving care and treatment of those afflicted with kidney disease. Through its lay and scientific advisory groups, the National Kidney Foundation cooperates with other agencies, public and private, to achieve these aims. Over the last five years the National Kidney Foundation has engaged in several broad areas of activity. Patient care services have included the distribution of drugs and medication, at cost or gratis, through its Drug Bank Program. A number of renal clinics has been promoted and assisted throughout the United States. Direct support of research activities has consumed the major portion of its resources, although a substantial effort also has been directed toward public and professional education. Table X shows the 1966 level of expenditures by the National Kidney Foundation for renal research, services, and education.

Table X

NATIONAL KIDNEY FOUNDATION EXPENDITURES FOR 1966

Program	1966 Expenditures
Research	$350,000
Services	200,000
Education	200,000
Total	$750,000

C. John Hartford Foundation

The John Hartford Foundation expended money for renal disease primarily in the area of research on dialysis and urinary disease problems. Expenditures for 1964 totaled about $796,000.

Chapter 4

Research Methodology

I.   INTRODUCTION

This chapter presents the methodology used in the analysis of projected
kidney disease programs. This methodology is designed to identify significant
kidney diseases in the United States, to postulate programs designed to
alleviate the effects of these diseases, and to estimate the benefits and
costs associated with such programs. A schematic of this methodology is
presented in Figure 1.

II.   DISEASES STUDIED

Because of the complex diffuse etiologies and the large variety of
diseases that affect the kidney, it was imperative that the disease spectrum
be narrowed in order to identify meaningful categories of kidney disease
which will serve as foci for important research and control programs (please
see Chapter 2). Prominent kidney diseases were identified and grouped in
the following manner:*

1)   Infectious Diseases of the Urinary Tract

Disease	ICD Code
Infections of the kidney	600
Cystitis	605
Urethritis (non-venereal)	607
Pyelitis and pyelonephritis of pregnancy	640

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*
    ICD—[1] codes and nomenclatures were used to identify diseases of interest
    as most available statistics on mortality and morbidity follow these
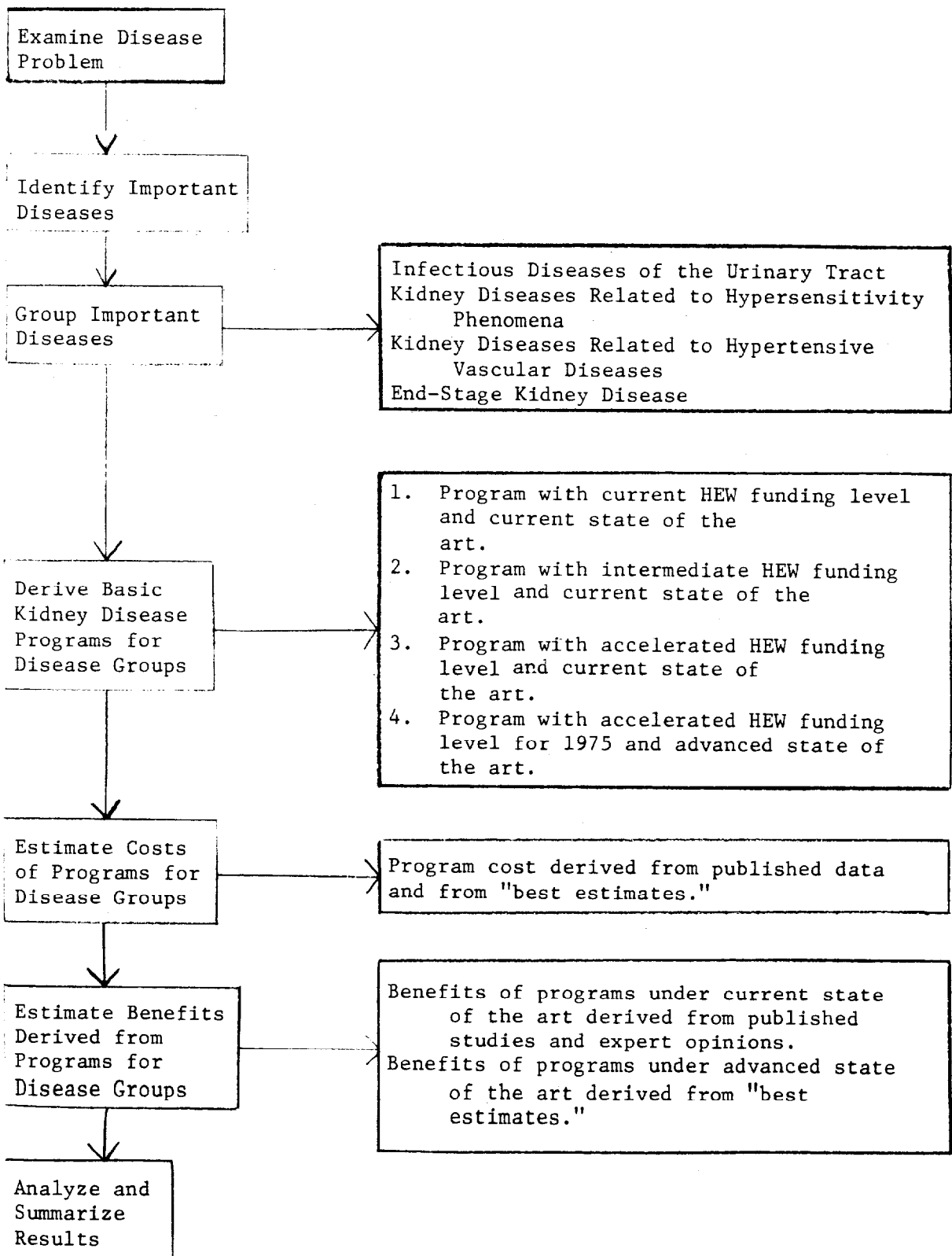   classifications.

```
┌──────────────────┐
│ Examine Disease  │
│ Problem          │
└──────────────────┘
         │
         V
┌──────────────────┐
│ Identify Important│
│ Diseases         │
└──────────────────┘
         │
         V
┌──────────────────┐        ┌─────────────────────────────────────────────┐
│ Group Important  │───────▶│ Infectious Diseases of the Urinary Tract    │
│ Diseases         │        │ Kidney Diseases Related to Hypersensitivity │
└──────────────────┘        │       Phenomena                             │
                            │ Kidney Diseases Related to Hypertensive      │
                            │       Vascular Diseases                      │
                            │ End-Stage Kidney Disease                     │
                            └─────────────────────────────────────────────┘
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┌─────────────────────────────────────────────┐
│ 1.  Program with current HEW funding level   │
│     and current state of the                 │
│     art.                                     │
│ 2.  Program with intermediate HEW funding    │
│     level and current state of the           │
│     art.                                     │
│ 3.  Program with accelerated HEW funding     │
│     level and current state of               │
│     the art.                                 │
│ 4.  Program with accelerated HEW funding     │
│     level for 1975 and advanced state of     │
│     the art.                                 │
└─────────────────────────────────────────────┘
```

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┌──────────────────┐
│ Derive Basic     │──────▶ (to box above)
│ Kidney Disease   │
│ Programs for     │
│ Disease Groups   │
└──────────────────┘
         │
         V
┌──────────────────┐        ┌─────────────────────────────────────────────┐
│ Estimate Costs   │───────▶│ Program cost derived from published data     │
│ of Programs for  │        │ and from "best estimates."                   │
│ Disease Groups   │        └─────────────────────────────────────────────┘
└──────────────────┘
         │
         V
┌──────────────────┐        ┌─────────────────────────────────────────────┐
│ Estimate Benefits│───────▶│ Benefits of programs under current state     │
│ Derived from     │        │     of the art derived from published        │
│ Programs for     │        │     studies and expert opinions.             │
│ Disease Groups   │        │ Benefits of programs under advanced state    │
└──────────────────┘        │     of the art derived from "best            │
         │                  │     estimates."                              │
         V                  └─────────────────────────────────────────────┘
┌──────────────────┐
│ Analyze and      │
│ Summarize        │
│ Results          │
└──────────────────┘
```

Fig. 1. Methodology Schematic.

2) <u>Kidney Diseases Related to Hypersensitivity</u>
   <u>Phenomena</u>

<u>Disease</u>	<u>ICD Code</u>
Acute nephritis	590
Nephritis with edema, including nephrosis	591
Chronic nephritis	592
Nephritis not specified as acute or chronic	593
Other renal sclerosis	594

3) <u>Kidney Diseases Related to Hypertensive Vascular</u>
   <u>Diseases</u>

<u>Disease</u>	<u>ICD Code</u>
Essential benign hypertensive heart disease	440
Essential malignant hypertensive heart disease	441
Hypertensive heart disease with arteriolar nephrosclerosis	442
Other and unspecified hypertensive heart disease	443
Essential benign hypertension	444
Essential malignant hypertension	445
Hypertension with arteriolar nephrosclerosis	446
Other hypertensive disease without mention of heart	447

4) <u>End-Stage Kidney Disease</u>

Although end-stage kidney disease is the eventual result of advanced or untreated primary renal disease, it is considered separately because of the unique treatments which can be employed; i.e., chronic intermittent dialysis and kidney transplantation.

5) <u>Other Diseases Affecting the Kidney</u>

A variety of other diseases falls within this category. Some

(i.e., neoplasms of the kidney) fall within other disease control programs. These diseases have not been considered in the detailed analysis for reasons stated in Chapter I, E, 1 & 2, but many should be considered in a more comprehensive study.

III. KIDNEY DISEASE PROGRAMS STUDIED

A limited number of hypothetical kidney disease programs were studied. These programs are delineated by time, state of the art, and funding level. The time periods used included fiscal year 1966 (a year for which reasonably complete costing data are available) and 1975 (a year for which significant advances in the state of the art are anticipated). Both current and advanced states of the art are considered in this analysis; the current state of the art refers to 1966 modus operandi in the control of kidney disease. The advanced state is that which would exist following significant research advances in kidney disease. Program funding levels were considered from the standpoint of HEW participation (third party payments and general direct health expenditures were not considered) and include the current level of expenditures (1966), an intermediate level of spending, and an accelerated expenditure level. The hypothetical intermediate funding level is two to three times greater than the current level and is used to analyze various programming possibilities at a more accelerated level. The hypothetical accelerated funding level is even greater than the intermediate level (about six times greater than the current level). Using these parameters, four major programs were developed under which each disease group is studied. These are:

1) Program A

This program describes the distribution of the total funds available from HEW (currently approximately $47,000,000) and other kidney disease programs for fiscal year 1966 for which benefits are maximized within the current state of the art for 1966.

2) Program B

This program describes an intermediate HEW funding level (two to three times greater than the amount available for fiscal year 1966) for which benefits are maximized within the current state of the art for 1966.

3) Program C

This program presents an "accelerated" HEW funding level (about six times greater than fiscal year 1966) for which benefits are maximized within the current state of the art for 1966.

4) Program D

This program describes an accelerated HEW funding level (as in Program C) for which benefits are maximized within an advanced state of the art for 1975. The advanced state of the art as used here implies that significant advances in research have been made and that the control of renal disease is operational.

In general, the effects of the various programs projected are mutually exclusive. First, the programs proposed for any given year do not affect the programs proposed for any other year; this assumption is necessary in order to estimate fully the benefits and costs of a single program. Secondly, the programs proposed for a given disease group are not assumed to affect the programs for other disease groupings. Again, this is done to estimate

closely the effects of a single program. Moreover, within the imposed

time period (1966 to 1975) it is felt that important inter-effects would

not have occurred; this is especially true when considering the preventive

program components and their effects on end-stage kidney disease.

In addition, the programs are in a steady state, that is, the full

effect of the programs is assumed to have been attained within the year

under consideration. It is assumed that personnel build-up, initial costs,

etc., which are inevitable in establishing a program, have already been

arranged.

IV. COSTS OF KIDNEY DISEASE PROGRAMS

The costs associated with the various kidney disease programs were

arrived at by utilizing various sources and assuming a constant 1966 dollar

value throughout. PHS publications[2] and a current study at the Research

Triangle Institute[3] provided basic cost data. Unpublished data from the

National Center for Health Statistics,[4] the National Drug and Therapeutic

Index,[5] the Professional Activities Service,[6] and published data from

the American Hospital Association[7] provided information on the costs

associated with morbidity and mortality relating to kidney diseases. "Cost

to HEW" refers only to the direct health expenditures of HEW (excluding

third party payments) generated by the programs described. "Total cost"

refers to all expenditures anticipated for the programs described.

While the costs of certain specific treatments such as dialysis are

available (although subject to range errors), other costs such as that

of implementing kidney disease prevention programs, including mass screening,

were not generally available. Accordingly, it was necessary to make "best estimates" based upon informed medical judgment. As such, these figures represent a first approximation of the desired data. Implicit in such methodology is that as more data becomes available, these estimates can be refined.

When screening and educational programs are described in the text, the assumption is always made that the particular program component studied is part of a general screening and educational program.

V. BENEFITS OF KIDNEY DISEASE PROGRAMS

Benefits derived from proposed kidney disease programs are measured only in terms of the impact upon mortality, prevalence, and morbid days in select population groups, i.e., number of lives saved, number of cases reduced, and number of morbid days prevented. Reduced mortality, reduced prevalence, and reduced morbid days (defined as days of restricted activity), are benefits measured in disease groups 1, 2 and 3 above. Reduced mortality only was used for disease group 4 above. No attempt was made to estimate the benefits derived from a reduction of indirect costs. In addition, no attempts were made to estimate the returns made to the general economy by an individua: whose life has been saved or lengthened or where disease has been terminated.

In the case of the disease groups related to infection, hypersensitivity, and hypertension, a select or high-risk population group was identified and data were collected on current mortality, prevalence, and morbidity. Estimate were then made on the effect of a projected program on morbidity and mortality for these groups. The difference between current mortality and morbidity per year and those estimated to be the effect of the proposed program

(assuming the program has become fully established) comprise the short-term

benefits discussed in this analysis. Long-term benefits for these groups

(not accounting for changes in these groups over the years) were estimated

in terms of reduction in the number of cases of end-stage kidney disease,

both on an annual and on a cumulative basis.

Annual long-term benefits assume that a sufficient length of time has

elapsed after the implementation of the programs to decrease maximally the yearly

number of cases of end-stage kidney disease which would eventually have

occurred in the high-risk groups without such a program.

Cumulative long-term benefits refer to the summary effect on the number

of cases of end-stage kidney disease which would have occurred without the

projected program. Each program is analyzed for a surveyed population and

does not take into account changes in that population over the years.

For the end-stage kidney disease group, the treated population was

identified and estimates made as to the number of deaths prevented as a

result of the program in a particular year. No attempt was made to measure

short-term benefits in terms of reduced morbid days. Because of the relatively

high incidence of death in these groups, the uncritical estimation of morbid

days can be very misleading. For example, it can be shown in some cases

that a patient in kidney failure may have _fewer_ morbid days if he succumbs

to his disease after conservative treatment only, rather than if his life

were prolonged with the aid of chronic dialysis.

VI. METHODOLOGY LIMITATIONS

Because of the time limits involved, this study has several limitations.

Among these are:

1) A limited number of kidney disease control programs were considered;

2) A limited number of diseases were analyzed;

3) Diseases were grouped rather than studied singly;

4) Benefit measures employed did not include reduction in indirect costs;

5) Only two time periods, 10 years apart, were studied;

6) Only 4 funding levels were considered;

7) Only high-risk population groups were considered;

8) Cohort analysis was not used in estimating benefits. In future studies the benefits attributed to various programs could be followed in a cohort of some fixed size from birth to death;

9) Inflationary trends were not taken into account;

10) Associated benefits such as the simultaneous effect on rheumatic heart disease of a program to control acute glomerulonephritis were pointed out but not measured; and

11) The effect of possible changes in the general standard of living was not taken into account.

All of the above limitations should be examined in any continuation of this study. Despite these limitations, however, the results of this study are significant insofar as it provides some idea of the dimension of the problem and a rather specific indication of benefits to be derived from alternative programs and funding levels.

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Chapter 5

Program Analysis

I. INTRODUCTION

This chapter discusses in detail the programs designed for the four

disease groups under consideration in this study. As mentioned earlier,

the disease groups include infectious diseases of the kidney and urinary

tract, hypersensitivity diseases of the kidney, kidney disease related to

hypertensive vascular diseases, and end-stage kidney disease. These disease

groups are studied within the constraints of four hypothetical programs

varying in budgetary level, state of the art, and time. Three hypothetical

programs for fiscal year 1966 have been postulated based on a low (reflecting

current HEW expenditures of about $47,000,000), intermediate (with

$117,000,000 HEW support), and high (with $290,000,000 HEW support) expendi-

ture level. In addition to these three programs, a fourth program reflecting

advances in the state of the art on an accelerated ($293,000,000 HEW support)

level which could be operational by 1975, is considered. Possible activities

for each disease group are projected within the framework of each of the

four programs mentioned above. In each case attempts have been made realistiç-

ally to evaluate what will happen within the constraints of the program and

the disease under consideration.

As each disease group was being studied within the program constraints,

realistic program components were postulated including their costs and

estimated benefits. The following components were used:

1) Prevention, Diagnosis, and Treatment

This component refers to the screening, confirmatory diagnostic tests, relevant treatment follow-up, and related general educational and administrative steps needed to ameliorate or control the disease. (This includes postgraduate physician education and relevant lay education).

2) Research

Research includes problem-focussed laboratory and clinical studies as well as fundamental, individually oriented research supported by grants.

3) Training

The training of researcher workers and other specialized medical personnel other than the general educational efforts referred to in the first program component is of concern here.

4) Facilities

Included here is the real estate and hard core equipment that support any disease control program.

Both short and long-term benefits were estimated. Short-term benefits were determined in terms of reduction per year in mortality, prevalence and morbid days. Long-term benefits were determined on the basis of an annual reduction in end-stage uremia, and on a cumulative (life-long) basis for the high-risk population being considered by the specific program.

As indicated in the methodology, in many instances it was necessary to use "best estimates" based on informed medical judgment. These estimates are obviously subject to range errors, but are representative, by and large, of the facts that can be drawn from current information.

The remainder of this chapter is divided into major sections, according to the various disease groups. Within each of these sections the four hypothetical programs are considered.

Benefit-cost tables summarize the analysis of each hypothetical program.

The reader of this chapter is referred to Chapter 1 of the report (Introduction and Overall Summary) for a textual summary of the various analyses and for a discussion of the findings within the overall framework of the kidney disease problem.

II. INFECTIOUS DISEASES OF THE URINARY TRACT

A. Introduction

This section pertains to programs needed for the control of infectious diseases of the urinary tract.

In 1966, 10,550 deaths[1] were estimated to have had infectious disease of the urinary tract as the underlying cause of death. In 1966, there were an estimated 1,963,000 cases of known infections of the urinary tract and an associated 38,197,000 days of restricted activity, 17,277,000 days of bed disability, and 4,185,000 work-loss days.[2] The actual prevalence of the disease is at least 3 to 4 times higher (i.e., 6,000,000 to 8,000,000).[3] The discrepancy is due to the presence of numerous asymptomatic and unreported cases.

The statistics and estimates used and described in the text are based, in most cases, on information gathered from the literature. In many instances the validity of such data, upon which projections are based, might be questionable. However, the information is often quite reliable and has been used realistically to project the findings onto overall population figures.

Four programs have been considered in this analysis (see Chapter 4, Research Methodology). The following sections describe these in detail.
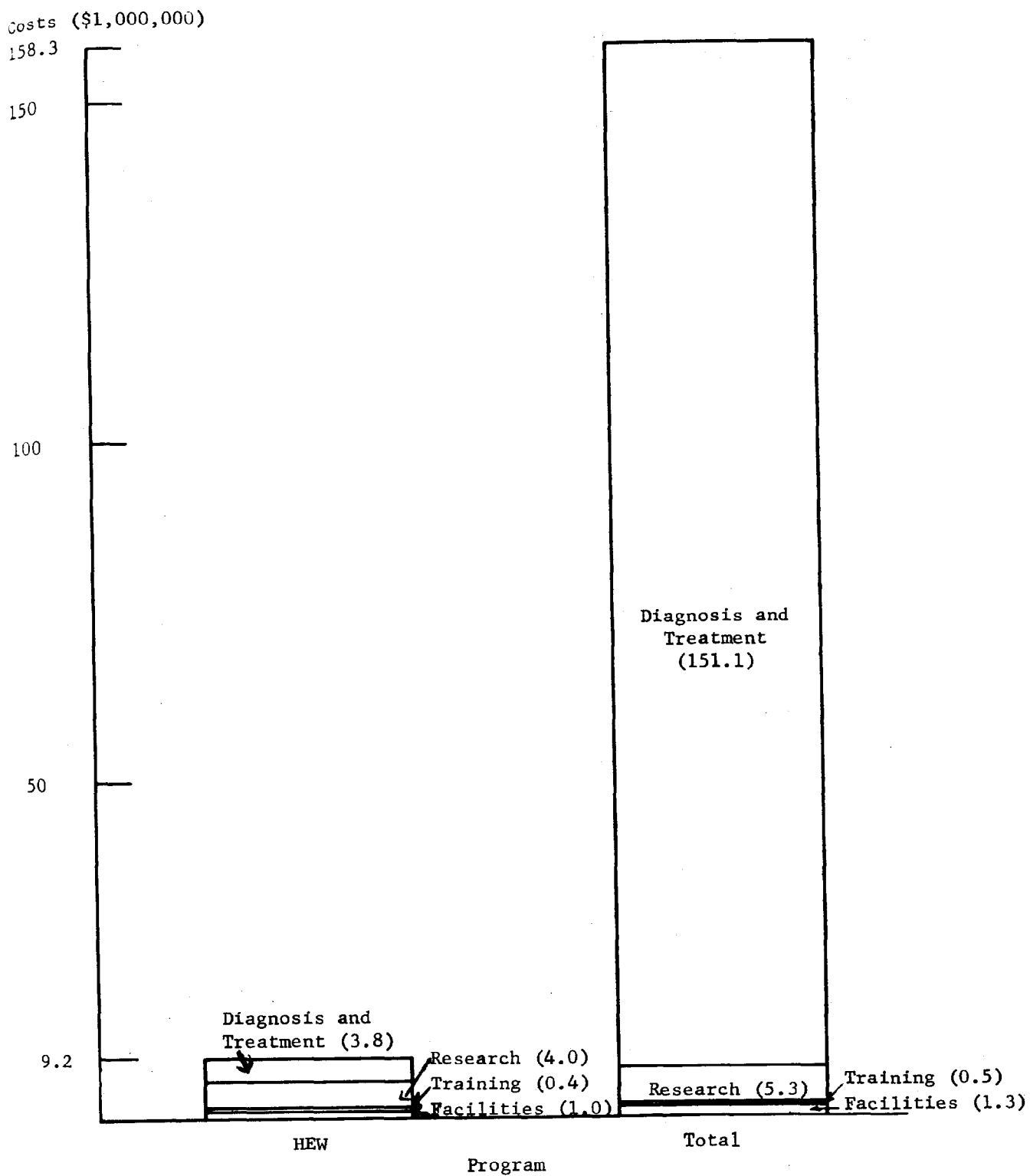
B. Infectious Diseases of the Urinary Tract, Hypothetical Program at Current HEW Expenditure Level, Based on Current State of the Art

1. Introduction

This program has four components:

1) Screening, diagnosis, treatment, and supportive physician and lay education and administration;

2) Research;

3) Training; and

4) Facilities.

As illustrated in Figure 1, the total cost for this program is estimated to be $158,265,000. Of this amount, HEW funds would account for $9,203,000. A discussion of the various program components follows.

2. Screening, Diagnosis, Treatment, and Supportive Education and Administration

Within the present state of the art, a program would be developed to screen high-risk patient groups for the presence of urinary tract infections. The highest number would probably come from:

1) Hospitalized in-patients,

2) Non-hospitalized pregnant females, and

3) Non-hospitalized diabetic patients.

These population groups are known to have a high incidence of urinary tract infections.[4/] Furthermore, screening tests can be applied to these groups with a minimum of organizational development, since they are usually already under a physician's care. The development of this program presupposes the presence of an accurate screening test, such as a refined Greiss Test (nitrate reduction test), which will be incorporated into a routine examination of the urine in these population groups. The selection of these high-risk groups has been somewhat arbitrary, and further study may indicate that other groups such as school children and college students should also be screened. It was felt, however, that the groups selected would be most likely to derive maximum benefits under this program.

a. Relevant Population and Program Component Costs

It is estimated that during 1966, 29,147,000 individuals were

Fig. 1. Infectious Diseases of the Urinary Tract, Hypothetical Program Costs at Current HEW Expenditure Level, Based on the Current State of the Art.

98a

short and long-term residents in hospitals and nursing homes in the

U. S.[5/] In addition, in the U. S. it is estimated that there were

4,497,000 non-hospitalized pregnant females[6/] and 2,422,000 non-

hospitalized diabetics.[7/] Thus, the total high risk group was comprised

of 36,066,000 individuals. It is also estimated that significant

bacteriuria exists in 20% of the hospitalized in-patient population,

6% of non-hospitalized pregnant females, and 15% of non-hospitalized

diabetics.[8/] The projected prevalence in this population is then estimated

to be 6,462,520 cases of bacteriuria[9/] (about 18% of the population

at risk).

It is also estimated that a screening program will be able to

detect 85% (5,493,140) of the patients having significant bacteriuria.[10/]

Assuming a 5% false positive screening rate, 5,767,800 positive tests

will appear in this program (105% of 5,493,140).[11/] Those individuals

with positive screening results will require a confirmatory urine test

(urine culture, bacterial colony count and antibiotic sensitivity test).

A second repeat procedure for the 5,493,140 confirmed cases is necessary

following therapy in order to ascertain the degree of success of treatment.

The estimated cost for the detection test as part of a general

screening program is $0.25 per person tested ($0.125 for the cost of

the test and $0.125 for the cost of administration).[12/] The total cost

is calculated to be $9,017,000[13/] of which HEW will contribute $1,803,000

for technical and financial support. The cost for a single confirmatory

urine culture, colony count, and sensitivity test is $7.50,[14/] and the total

cost for confirmatory tests is then $84,457,000 which will be contributed

by sources other than HEW.

Treatment costs are estimated at $10.00 per patient (note that

these individuals are already under physicians' care and that most of

this cost is for drugs). The total cost of therapy would be
$54,931,400 for the 5,493,140 individuals with confirmed infections.
This method of detection and treatment would not require individuals
who are not already hospitalized to be placed in such treatment care
facilities; therefore, additional costs for hospitalization are not
anticipated. However, it is quite probable that an individual with
an infection of the kidney may require hospitalization. It should
also be emphasized that this projected cost (most of which will be
borne by sources other than HEW) is a bare minimum estimate and
allows only for detection, diagnosis, and drug treatment. It does
not allow for inquiries into associated or predisposing factors of
infection, follow-up therapeutic courses, or laboratory studies when
needed.

Extensive educational and administrative financial support is
anticipated from HEW. Any screening program that is to be instituted
in hospitals throughuut the country would require a vigorous educa-
tional program concerning proper interpretation of tests, adequate
therapy, and appropriate follow-up procedures. It is felt that the
7,000 or so hospitals in the U. S. should be exposed to an educational
program regarding the entire problem of urinary tract infections in
order to achieve maximum program effectiveness (i.e., eradication of
bacteriuria). About $1,000,000 ($140 per hospital) as part of a kidney
disease general education program will be required from HEW, and $335,000
is expected from other sources for the education of medical personnel.[15]

$1,000,000 is required from HEW for administrative purposes plus
$335,000 from other sources.[16] The total cost to HEW is $2,000,000,

and $670,000 is to be spent by other agencies.

b. Short-Term Benefits

From an estimated base of 6,800 deaths in the population screened which would occur without this program component,[17] a 1% reduction in immediate mortality is anticipated due to the successful treatment of acute pyelonephritis (if it is detected at an early stage before severe tissue damage has occurred).[18] Therefore, a reduction in mortality of 70 deaths per year is estimated.

In addition, there is a reduction in the prevalence of significant bacteriuria in 3,231,260 patients (50% of 6,462,520). This 50% reduction is based on the supposition that the majority of cases detected will be of simple bacteriuria, in the absence of tissue infection, which responds well to treatment. It is understood that the first course of therapy for patients with bacteriuria in acute infections would be highly successful, but is is not anticipated that a permanent cure will be achieved in individuals with chronic urinary tract infections.

With therapy, the number of morbid days could be reduced by 65% from the base of 24,557,580 to 15,962,427.[19]

c. Long-Term Benefits

A significant benefit from this early detection program will be an ultimate reduction in mortality due to end-stage renal disease resulting from earlier urinary tract infections.[19A] After a diagnosis of infection is made, further study of the patient would lead to the detection of factors predisposing to or associated with that infection. It should be pointed out that new methods of anti-infectious therapy could possibly increase the cure rate for the population-at-risk to 75%.[20]

(1) <u>Annual Long-Term Benefits</u>

At present, it is estimated that 20% (1,750) of an esti-

mated total cases (8,500) of end-stage kidney disease per year

can be averted by current medical therapy.$\frac{21/}{}$

(2) <u>Cumulative Long-Term Benefits</u>

It is estimated that in time 5% (323,126) of the 6,462,520

individuals having significant bacteriuria may have developed a

significant urinary tract infection. Of this 5%, approximately

40% (129,250) may eventually die in renal failure. Implementation

of the above program would be expected to reduce this mortality by

20% (25,850) based on current methods of therapy.$\frac{22/}{}$

3. <u>Research</u>

Because of problems peculiar to urinary tract infection, [i.e., the

poor response to therapy (20% cure rate) and the difficulty in isolating

bacteria from end-stage kidneys resulting from infection], a great deal

of research, both laboratory and clinical, must be undertaken before a

more effective program can be administered in the prevention of urinary

tract infections.

a. <u>Laboratory Research</u>

Laboratory research should be concentrated in these areas:

1) A relationship of viral agents to renal disease;

2) The identification and treatment of host-factors which

predispose the host to urinary tract infections;

3) The role of immunologic phenomena in bacterial and/or viral

infections of the kidney;

4) The role of vascular and metabolic diseases in urinary tract

infections;

5) The role of various chemical agents (e.g., phenacetin) in
    renal tissue infection;

6) The nature of the exudative response to renal infection;

7) The nature of connective tissue proliferation in renal
    tissue;

8) A classification of the organisms causing renal infections
    and the identification of toxins, enzymes, etc., produced
    by these organisms; and

9) The pharmacology of specific antibiotics including drug
    inhibitors affecting the viability of microorganisms in
    renal tissue.

No sound estimate can be made for the cost of each of these
basic research programs, but approximately $1,500,000 should be
made available in the form of research grants from HEW.[23/]

b. Clinical Research

Clinical research must include studies to evaluate therapeutic
programs and long-term follow-up of patients with kidney infections,
and attempts to identify crucial points in the natural history of the
disease at which therapy is most effective. Other studies would be
attempted with susceptible patients (pregnant females, persons
with obstructive uropathy, diabetics, etc.) to discover pertinent
facts in the pathogenesis of renal infection. It is estimated that
each large scale clinical study will cost approximately $500,000 per
year.[24/] This amount is based on existing cooperative studies and
does not include the cost of hospitalization or laboratory tests
which must be borne by other sources. Four cooperative studies
will be developed, each costing $500,000: one study will address

itself to a study of the natural history of renal infection; two, to therapeutic trials; and a fourth to the pathogenesis of the disease in susceptible sub-groups of patients.

An additional $500,000 will be used for detailed studies on a small group of patients with renal infection. This study would encompass the definition of changes in renal function, the effects of specific antibacterial agents on the infection, the trial of new treatments such as chronic water loading, etc.

Total clinical research expenditures will amount to $2,500,000 supported by HEW.

Total costs for research will be $5,330,000 of which HEW would contribute $4,000,000; $1,330,000 would come from other sources.

4. Training

Training includes the financial support of research fellows engaged in clinical laboratory studies, and the cost of relevant facilities. Support and laboratory facilities for approximately 12 fellows for one year would cost HEW approximately $400,000 plus $130,000 from other sources, yielding a total of $530,000.[25/]

5. Facilities

This program utilizes only existing facilities; however, laboratory and hospital space is limited at present and in order to develop an efficient program as outlined, expanded facilities would undoubtedly be required for research and for the screening of patients for urinary tract infection. Consequently, it is anticipated that about $1,000,000 would be expended by HEW and an additional $330,000 by other sources, yielding a total of $1,330,000.

A benefit-cost summary associated with this program is presented in Table I.

Table I

INFECTIOUS DISEASES OF THE URINARY TRACT, HYPOTHETICAL PROGRAM
AT CURRENT HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Screening, diagnosis and treatment of individuals in short and long-term hospitals and nursing homes as well as non-hospitalized pregnant females and diabetics.							
1. Screening	1,803	9,017					
2. Confirming test		84,457					
3. Treatment		54,931					
Sub-Total	1,803	148,405					
B. Supportive education and administration	2,000	2,670					
Sub-Total	3,803	151,075					
II. Research	4,000	5,330					
III. Training	400	530					
IV. Facilities	1,000	1,330					
TOTAL	9,203	158,265	70	3,231,260	15,962,420	1,750	25,850

C. Infectious Diseases of the Urinary Tract, Hypothetical Program
at Intermediate HEW Expenditure Level, Based on Current State
of the Art

1. Introduction

This program has four components:

1) Screening, diagnosis, treatment, and supportive education and
administration;

2) Research;

3) Training; and

4) Facilities.

As illustrated in Figure 2, the total cost for this program is
estimated to be $174,252,000, of which HEW funds would account for
$20,179,000. A discussion of the various program components follows.

2. Screening, Diagnosis, Treatment, and Supportive Education and
Administration

This program is concerned with the screening, diagnosis and treat-
ment of infections of the urinary tract similar to those described in
Section B.2. above. It has, however, been expanded to include all
females 6 to 9 years of age who can realistically be reached in a
screening program. It is felt that this group can best be reached
through screening tests applied in elementary schools.

a. Relevant Population and Program Component Costs

Because of the difficulties anticipated in attempting to reach
the entire female population 6 to 9 years of age, it is assumed
that a successful program covering a two-year span will be able
to reach about 62% of these individuals.[26/] Of 8,134,000[27/] females
in this age group, 5,040,000 will be reached every two years, and
50% (2,520,000) of these individuals will be screened each year.

Costs ($1,000,000)
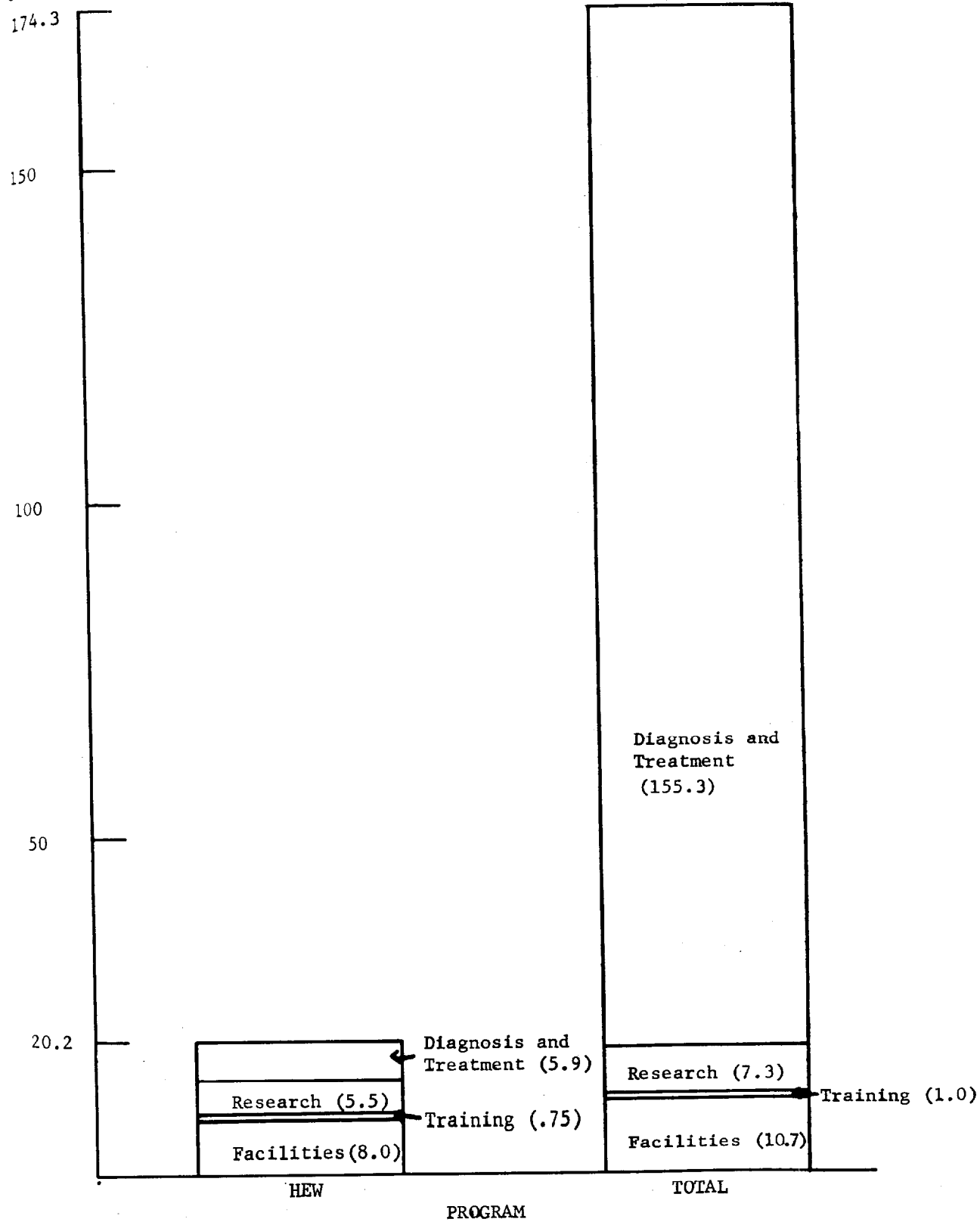
Fig. 2. Infectious Diseases of the Urinary Tract, Hypothetical Program
Costs at Intermediate HEW Expenditure Level, Based on the
Current State of the Art.

Cost of screening per individual in this additional population is estimated at $0.25 (as part of a general screening program). If 2,520,000 are screened annually, the total cost will be $630,000 ($126,000 from HEW) yearly.

Total cost for screening all the population-at-risk, reached by a general screening program, will be $9,647,000 ($1,929,000 from HEW).

It is believed that 1% of these young females (25,200) will have significant bacteriuria.[29/] It is still assumed that only 85% (21,420) of these individuals can be screened, and that the test has associated with it a 5% false positive value so that 22,491 will have positive results. Confirmatory tests will be necessary both before and after therapy; therefore, at $7.50 per test, the total cost for confirmatory tests will be $330,000. For the entire surveyed population, the cost for these confirmatory tests will amount to $84,787,000, none of which will come from HEW.

The treatment costs for each of the females 6 to 9 years of age is estimated at $10.00 for drugs and $15,00 for physicians' services, or a total cost for all of these individuals of $557,000. Total treatment costs for all groups surveyed having renal infections are $55,488,000.

The costs outlined above are minimal and are based on conservative estimates. They do not include, for example, intravenous pyelograms and other diagnostic studies necessary for complete diagnosis.

Also note that the overlap in the female population 6 to 9 years of age and the other high-risk groups (that is, the individuals in short and long-term hospitals, nursing homes and the non-

hospitalized pregnant females and diabetics) has not been taken into account and some double-counting may be present.

The supportive education and administration portions of this program component are estimated at a level of $4,000,000 from HEW and $1,330,000 from other sources.[30/] The educational program involves the extensive education of medical personnel throughout the country in the proper uses of catheters and antibiotics, the importance of follow-up studies on individuals with urinary tract infections, the natural history of pyelonephritis, the proper use of diagnostic techniques, etc. The focal centers of the educational program will be community hospitals from which information will be disseminated among appropriate personnel.

Total costs for this program component are estimated at $155,252,000 ($5,929,000 from HEW).

b. Short-Term Benefits

In addition to the short-term benefits described in Section B.2. above, the following benefits are expected to result from the screening of these young females:

1) Due to the current low mortality rate from urinary infections in females 6 to 9 years of age, no estimate on the reduction of immediate mortality is made;

2) A 50% reduction in the prevalence rate from a base of 25,200 to 12,600;[31/] and

3) A 65% reduction of 311,220 in morbid days from a base of 478,000.[32/]

Total short-term benefits for all groups surveyed are 70 prevented deaths, a reduction in prevalence by 3,243,860, and a

reduction in morbid days by 16,273,640.

c. Long-Term Benefits

(1) Annual Long-Term Benefits

Early diagnosis and treatment of urinary tract infections in this group of females 6 to 9 years of age will decrease the number of cases of renal failure by 20 per year. (A 33% reduction from a base line of 60 which would eventually have acquired end-stage uremia without this program).[33/]

There will be a reduction by 1,770 cases of end-stage uremia in all relevant groups from a base line of 8,560.[34/]

(2) Cumulative Long-Term Benefits

Approximately 5% (2,520) of the 50,400[35/] females with bacteriuria could eventually develop significant urinary tract infections. Approximately 40% (1,010)[36/] of these individuals would have developed end-stage uremia. Since the females in this age group can be reached at a very early stage of the disease, a reduction in end-stage uremia by 33% (340)[37/] is anticipated.

About 26,190 cases of eventual renal failure in all groups surveyed will be avoided.

3. Research

Again, clinical and laboratory research are the two major areas of effort. Given increased resources, it is realistic to project that two additional clinical research programs at $500,000 each could be added to the four existing ones at a total cost of $3,000,000.

Laboratory research project expenditures could feasibly be increased

to $2,000,000 (i.e., an increase of $500,000). Again, a $500,000

project designed to study susceptible sub-groups of patients is

also anticipated. The total HEW support for research is $5,500,000,

and it is anticipated that about $1,830,000 will be generated from other

sources.

4. Training

Training expenditures are estimated to be $750,000 from HEW with

an additional $250,000 from other sources.

5. Facilities

In the intermediate health program, it is estimated that HEW will

provide $8,000,000 in addition to an expected $2,670,000 from other

sources.

A benefit-cost summary associated with this program is presented in

Table II.

Table II

INFECTIOUS DISEASES OF THE URINARY TRACT, HYPOTHETICAL PROGRAM
AT INTERMEDIATE HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Screening, diagnosis and treatment of individuals in short and long-term hospitals and nursing homes as well as non-hospitalized pregnant females, diabetics and females 6 to 9 years of age.							
1. Screening	1,929	9,647					
2. Confirming		84,787					
3. Treatment		55,488					
Sub-Total	1,929	149,922					
B. Supportive education and administration	4,000	5,330					
Sub-Total	5,929	155,252					
II. Research	5,500	7,330					
III. Training	750	1,000					
IV. Facilities	8,000	10,670					
TOTAL	20,179	174,252	70	3,243,860	16,273,640	1,770	26,190

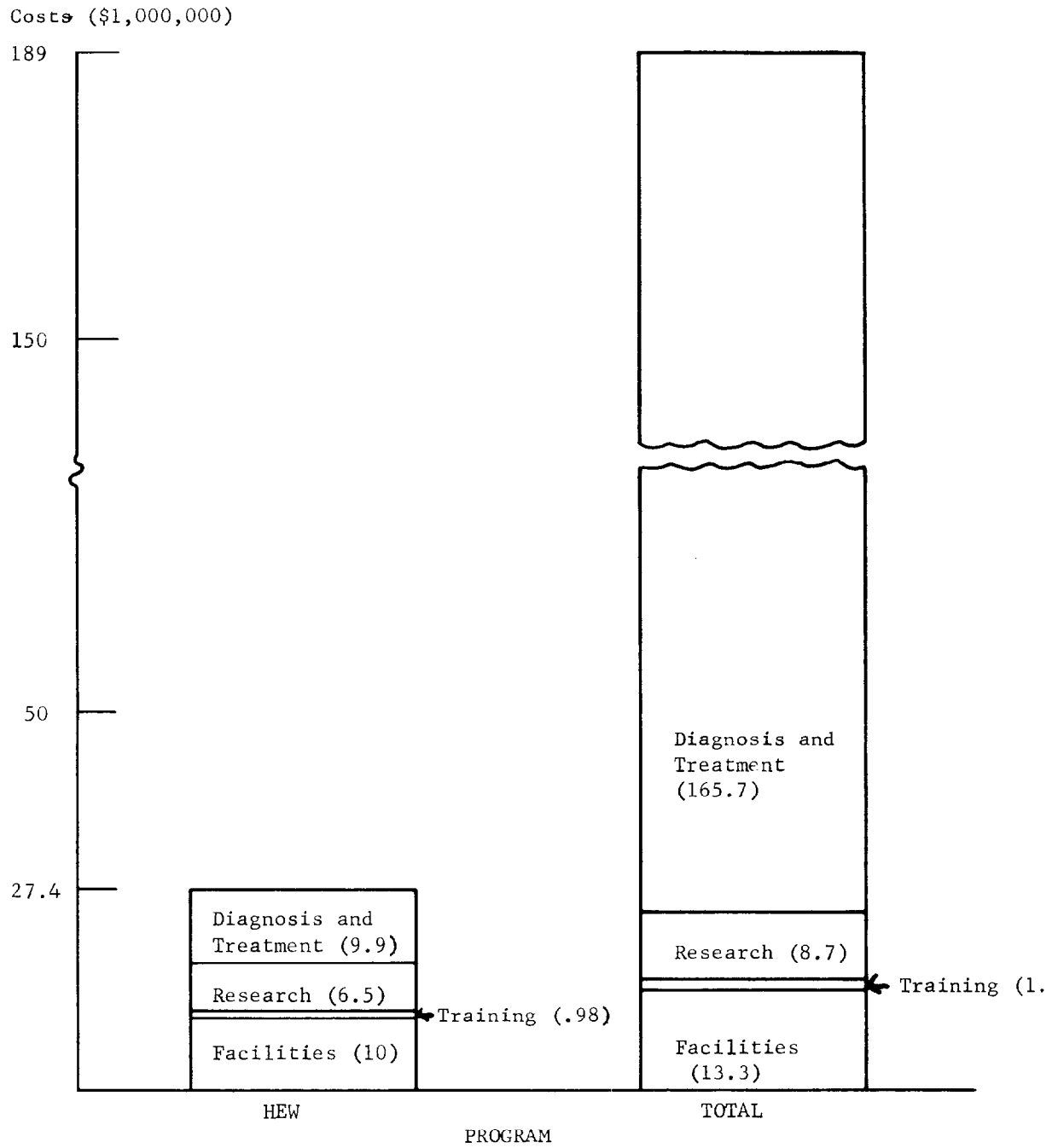D. **Infectious Diseases of the Urinary Tract, Hypothetical Program at Accelerated HEW Expenditure Level, Based on Current State of the Art**

1. **Introduction**

This program has four components:

1) Screening, diagnosis, treatment, and supportive education and administration;

2) Research;

3) Training; and

4) Facilities.

As illustrated in Figure 3, the total cost for this program is estimated at $189,013,000, of which HEW will contribute $27,394,000. A detailed discussion of the various program components follows.

2. **Screening, Diagnosis, Treatment, and Supportive Education and Administration**

In addition to the high risk groups surveyed in Section B.2., this program component has been expanded to include all females 21 years of age and under. It is again postulated that the expected rewards from controlling infectious diseases of the urinary tract in these females would be sizeable enough to merit its consideration. It is desirable to reach the majority of females in this age group through schools, colleges, and various youth programs such as Operation Headstart.

a. **Relevant Population and Program Component Costs**

A successful program will probably reach approximately 60% of the relevant female population. This program will again cover a two-year span so that one-half of this population will be screened every year. Therefore, of the 41,065,000 females 21 years of age and under in the U. S.,[38/] 12,319,500 will be screened each year

[i.e., 24,639,000 (approximately 60%) of the total will be reached in

Costs ($1,000,000)

Fig. 3. Infectious Diseases of the Urinary Tract, Hypothetical Program
Costs at Accelerated HEW Expenditure Level, Based on the
Current State of the Art.

two years, and 50% of these, or 12,319,500, will be reached every
year]. It is estimated that about 1% of the females 21 years of age
and under, 246,390, will have significant bacteriuria; therefore,
123,195 will be detected each year. It is to be emphasized that
this figure is quite conservative since it is known that females
12 to 16 years of age have a high incidence of bacteriuria,[39/] and
while no information was available regarding the incidence of
bacteriuria in college-age females, it may be even higher than that
of other school-age females.

Screening costs in this female population are estimated at $0.25
per person (as part of a general screening program). If 12,319,500
are screened annually, the total cost will be $3,080,000 ($616,000
from HEW).

Total screening costs for all the surveyed populations (includ-
ing those described in Section B.2.) will be $12,097,000 ($2,419,000
from HEW.

The number of confirmatory tests required for females 21 years
of age and under will be 109,952 pre-therapy and 104,716 post-therapy
tests,[40/] and the cost for these tests will be $1,610,000 assuming a
rate of $7.50 per test.

For all the surveyed populations (including those described in
Section B.2.) the total cost for confirmatory tests will be
$86,067,000, none of which is assumed to come from HEW.

The treatment costs for each female 21 years of age and under
with a confirmed diagnosis of renal infection is estimated at $10.00
for drugs and $15.00 for physicians' services. This means that the

total cost for these affected females is $2,618,000, all of which comes from sources other than HEW.

Total treatment costs for all population groups surveyed having renal infections are $57,549,000.

The costs outlined are minimal and do not include such items as intravenous pyelograms and other diagnostic studies which are necessary for a complete diagnosis.

Again, the overlap of the female population, 21 years of age and under, and the other high-risk groups has not been taken into account and some repetitious counting may be present.

The supportive education and administrative portion of this program component is estimated to be $7,500,000 from HEW and $2,500,000 from other sources. It is anticipated that the educational program will be intensified and similar to the one described in Section C.2.a.

The total cost for this program component is estimated at $165,713,000 ($9,919,000 from HEW).

b. Short-Term Benefits

In addition to the short-term benefits described in Section B.2.b. above, the following results can be anticipated from a screening program in females 21 years of age and under:

1) No estimates were made on the reduction of immediate mortality due to the very low mortality rates from urinary tract infection in this population;

2) A 50% reduction (61,600) in prevalence rate from a base of 123,195; [41/] and

3) A 65% reduction of 1,521,460 in morbid days from a base

of 2,340,710.[42/]

Total short-term benefits in all groups surveyed with renal infections are 70 prevented deaths, a reduction in prevalance of cases by 3,292,860, and a reduction in the number of morbid days by 17,483,880.

c. Long-Term Benefits

   (1) Annual Long-Term Benefits

As a result of the early diagnosis and administration of treatment of urinary tract infections, a 33% reduction in the number of annual cases of renal failure is anticipated. This would amount to a decrease of 120 cases from a base line of 360 cases per year.

There will be a reduction by 1,870 cases of renal failure in all relevant groups from a base line value of 8,860 cases which would have occurred without this program.[43/]

   (2) Cumulative Long-Term Benefits

Of the 246,390 females with significant bacteriuria who can be reached by this program, approximately 5% (12,320) would eventually develop significant urinary tract infection.[44/] Of this group approximately 40%, 4,930, would eventually die in renal failure.[45/] Implementation of the above program would be expected to reduce this mortality figure by 33%, or 1,630.[46/]

A total of 27,480 cases of renal failure in all groups surveyed would be avoided.

3. Research

Given the increased resources of this accelerated program, the number of clinical research projects could be doubled from the current level of 4

to 8 projects at $500,000 each for a total of $4,000,000.

Laboratory research expenditures could feasibly be set at $2,000,000, with an additional $500,000 available for projects designed to study susceptible sub-groups of patients.

Thus, the total HEW support for research would be $6,500,000. It is anticipated that an additional $2,170,000 would be contributed by other sources.

4. **Training**

Training costs are estimated to be 15% of the research expenditures i.e., $1,300,500, of which $975,000 comes from HEW, and an additional $325,500 from other sources.

5. **Facilities**

With an accelerated health program, it is estimated that HEW will expend about $10,000,000 for facilities in addition to $3,330,000 contributed by other sources.

A benefit-cost summary associated with this program is presented in Table III.

Table III

INFECTIOUS DISEASES OF THE URINARY TRACT, HYPOTHETICAL PROGRAM
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| Program | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Screening, diagnosis and treatment of individuals in short and long-term hospitals and nursing homes as well as non-hospitalized pregnant females, diabetics, and females 21 years of age and under.							
1. Screening	2,419	12,097					
2. Confirming		86,067					
3. Treatment		57,549					
Sub-Total	2,419	155,713					
B. Supportive education and administration	7,500	10,000					
Sub-Total	9,919	165,713					
II. Research	6,500	8,670					
III. Training	975	1,300					
IV. Facilities	10,000	13,330					
TOTAL	27,394	189,013	70	3,292,860	17,483,880	1,870	27,480

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E. Infectious Diseases of the Urinary Tract, Hypothetical Program for
    Fiscal Year 1975, at Accelerated HEW Expenditure Level, Based on
    Expected State of the Art in 1975

    1. Introduction

        This program has four components:

        1) Screening, diagnosis, treatment, and supportive education and
            administration;

        2) Research;

        3) Training; and

        4) Facilities.

        The total estimated cost for this program is $215,471,000 of which

        HEW will contribute $31,228,000 (see Figure 4). Under an advanced

        state of the art it is assumed that the research efforts undertaken

        have made possible 1) more effective antimicrobial therapy, and 2)

        a better understanding of the pathophysiology of urinary tract

        infection, with new treatment methods for predisposing factors which

        sometimes lead to bacteriuria. A detailed discussion of the various

        program components follows.

    2. Screening, Diagnosis, Treatment and Supportive Education and
        Administration

        In 1975 the total U. S. population will have increased by 14%[47]

        but there are no anticipated changes in the nature of the relevant

        population.

        a. Relevant Populations and Program Component Costs

            It is estimated that of a projected 33,227,580 hospitalized

        and nursing home residents, 6,645,520 will have significant bacter-

        iuria (a 20% prevalence rate).[48] The non-hospitalized pregnant

        female population is estimated to be 5,126,580;[49] assuming a

Costs ($1,000,000)
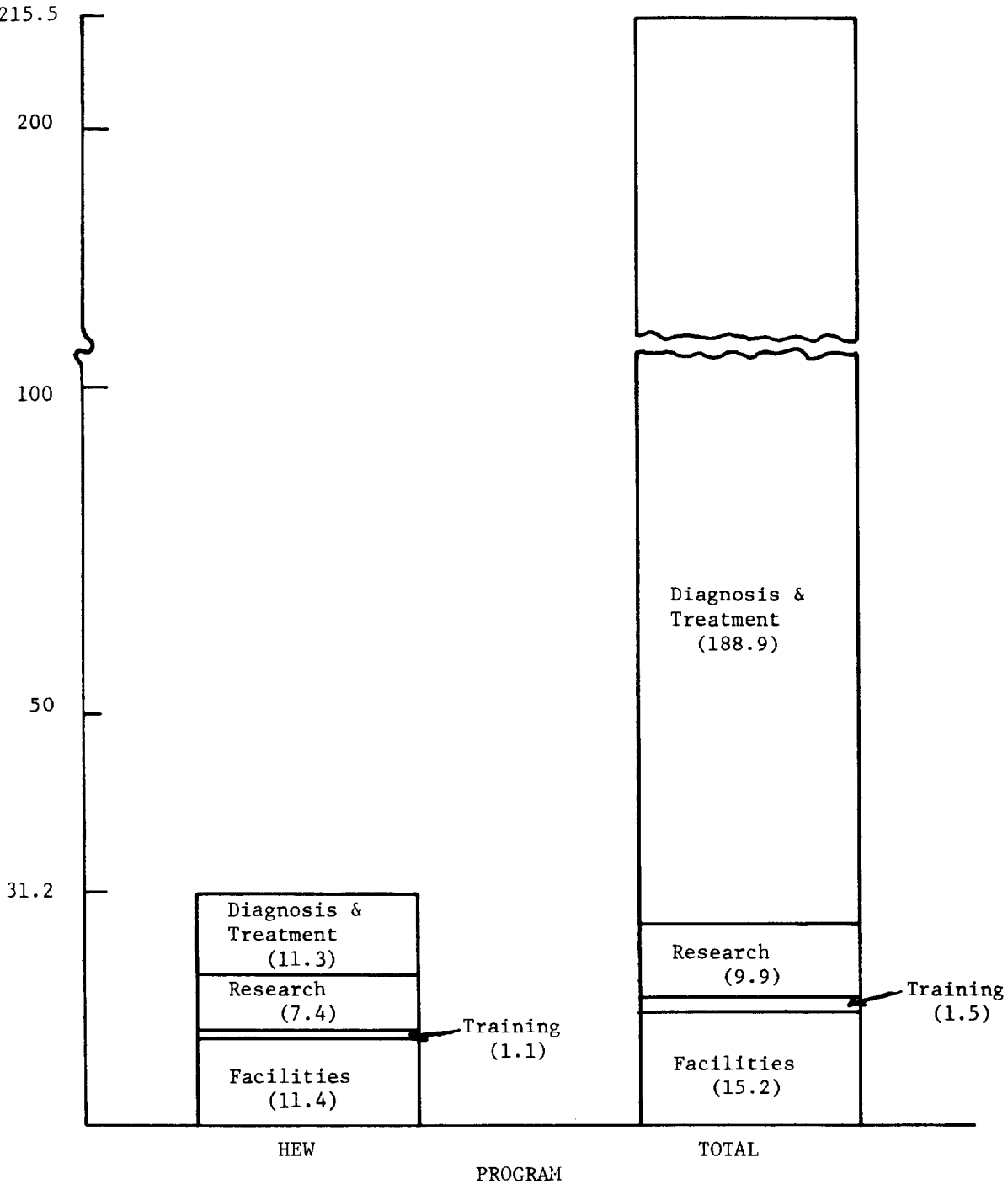
Fig. 4. Infectious Diseases of the Urinary Tract, Hypothetical Program
Costs for Fiscal Year 1975, at Accelerated HEW Expenditure Level,
Based on Expected Advanced State of the Art in 1975.

prevalence rate of 6% for bacteriuria, 307,590 persons will have

positive screening tests. The non-hospitalized diabetic population

will be 2,761,080[50]/ and approximately 414,160 will have

bacteriuria (assuming a 15% prevalence rate in the diabetic

population). While it is possible that significant improvements

in the treatment and diagnosis of diabetics will have occurred,

this assumption was not made. It is anticipated that 14,044,230

females under 21 years of age will be screened yearly; 140,440

of these women will have significant bacteriuria, assuming a 1%

prevalence rate.[51]/ (Note it is still assumed that only 60% of

the females 21 years of age and under can be reached, and that the

screening program will cover a two-year span.)

Cost of screening will be $13,790,000 ($2,758,000 to be borne

by HEW). It is still assumed that the cost per test under a general

screening program will be $0.25, and this cost is applied to the

55,159,440[52]/ individuals to be screened each year.

The cost of confirmatory tests remains at $7.50 per person.

Total cost is approximately $98,150,000, excluding a second repeat

test for false-positive patients.

Treatment costs also remain the same, i.e., $10.00 for drugs

for those individuals who are already under a physician's care. It

is estimated that there are 6,262,180 of these individuals yielding

a cost of $62,622,000. For those individuals who would not have

been under a physician's care (the female population 21 years of age

and under), $15.00 per individual for physicians' services is added.

The cost of treatment for this group is $2,984,000 (119,374 x $25).[53]/

Total cost of treatment is thus estimated to be $65,606,000.
HEW is not responsible for the cost of confirmatory tests or
treatment.

Total cost for this initial portion of the program component
is $177,511,000, of which $2,758,000 is to be borne by HEW.

Support for education and administration is estimated to cost
$8,550,000 for HEW, to include a more extensive educational program
to reach the increased population. An additional $2,850,000 will
come from outside sources.

Therefore, the total cost for this program component is
$188,911,000, of which $11,308,000 comes from HEW.

b. Short-Term Benefits

The estimated short-term benefits are as follows:

1) From a base line of 7,750 deaths in the group surveyed
    which would have occurred in the absence of any program,
    a reduction of 80 deaths is estimated;[54]

2) It is estimated that there will be an 85% reduction
    (5,630,780) in prevalence from 7,507,710 cases [35 of the 85%
    (1,876,930) can be attributed to advances in the state of
    the art];[55] and

3) It is estimated that the number of morbid days will be
    reduced by 85% (26,064,430) from a base line figure of
    30,664,040 (20 of the 85% reduction, i.e., 6,132,810 is
    attributed to advances in the state of the art).[56]

c. Long-Term Benefits

    (1) Annual Long-Term Benefits

        It is estimated that approximately 7,500 of the group

surveyed per year will have developed end-stage renal failure

without the program. Ideally this program would reduce this

number by 55%, or 4,125 per year [of which 2,250 (approximately

30 of the 55% reduction) are due to advances in the state of

the art].[57/]

(2) Cumulative Long-Term Benefits

About 5% of the individuals with bacteriuria would have

developed significant urinary tract infections in the absence

of any program. Approximately 40% of these persons would

eventually die from uremia. Within the relevant population,

there would be 7,658,160 individuals having bacteriuria.[58/]

It can then be said that some 382,400 will probably develop

significant urinary tract infections and 40%, or 153,000, of

these would eventually die from uremia. It is estimated that

the number of deaths resulting from end-stage kidney failure

can be reduced by 55% or 84,150 (approximately 30 of the 55%,

or 45,900, of the reduced number of deaths is due to advances

in the state of the art).[59/]

3. Research

Research expenditures will be increased in amount to $7,410,000

which will come from HEW, and an additional $2,470,000 to come from

other sources. It is anticipated that a cure for urinary tract

infections may be found through the development of new antibiotics and

new treatment methods for predisposing factors which sometimes lead to

bacteriuria.

4. Training

Money expended for training purposes will total $1,480,000, about

15% of that spent for research. Of this amount, $1,110,000 will come from HEW and an additional $370,000 from other sources.

5. Facilities

In an accelerated Health Program it is estimated that HEW will contribute $11,400,000 for facilities, Additional sources will contribute $3,800,000.

A benefit-cost summary associated with this program is presented in Table IV.

F. Benefits Dependent on New Research Developments [60/]

An annual reduction by 1,876,930 in the prevalence rate of renal infection and by 6,132,810 in the number of morbid days will be the short-term effects of new research developments. These statistics take into account a postulated 14% increase in the population of the U. S. from 1966 to 1975. Benefits based on 1966 population figures reveal a reduction in prevalence by 1,646,430 and in the number of morbid days by 5,379,660.

In assessing the annual long-term benefits dependent on new developments, it is estimated that there will be a reduction of 2,250 cases of end-stage kidney disease per year, (1,970 cases based on 1966 U. S. population). Cumulative long-term benefits reveal that 50,650 (44,430 based on 1966 U. S. population) cases of renal failure will be avoided with the advent of new developments and techniques concerned with chronic kidney infections.

Table IV

INFECTIOUS DISEASES OF THE URINARY TRACT, HYPOTHETICAL PROGRAM FOR FISCAL YEAR 1975
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON EXPECTED ADVANCED STATE OF THE ART IN 1975

| | | | Short-Term Beneifts | | | Long-Term Benefits | |
| | Expenditures | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	($1,000)	($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Screening, diagnosis and treatment of individuals in short and long-term hospitals and nursing homes as well as non-hospitalized pregnant females, diabetics, and females 21 years of age and under.							
1. Screening	2,758	13,790					
2. Confirming		98,115					
3. Treatment		65,606					
Sub-Total	2,758	177,511					
B. Supportive education and administration	8,550	11,400					
Sub-Total	11,308	188,911					
II. Research	7,410	9,880					
III. Training	1,110	1,480					
IV. Facilities	11,400	15,200					
TOTAL	31,228	215,471	80	5,630,780	26,064,430	4,125	84,150

III.   HYPERSENSITIVITY DISEASES OF THE KIDNEY

A. Introduction

This section describes program efforts projected to control renal disease

resulting from hypersensitivity phenomena.

In 1966, an estimated 12,719[61]deaths resulted from kidney disease associ-

ated with hypersensitivity reactions; 106,000 individuals are estimated to

have had hypersensitivity diseases of the kidney, requiring 4,074,000 days of

restricted activity, 1,834,000 days of bed disability, as well as 777,000

work-loss days.[62]

Four programs are considered in this analysis and discussed in detail

below (see Chapter 5, Research Methodology).

B. Kidney Diseases Related to Hypersensitivity Phenomena, Hypothetical
    Program at Current HEW Expenditure Level, Based on the Current State
    of the Art

1. Introduction

This program has four components:

1) Education and administration;

2) Research;

3) Training; and

4) Facilities.

The total cost for this program is estimated to be $9,975,000 of

which HEW's share is $7,480,000. Figure 5 illustrates costs for the

various program components, and they are discussed below.

2. Education and Administration

In order to bring an effective educational program to physicians,

it is necessary to supply the approximately 7,000 hospitals in the U. S.

with appropriate materials and other educational support. Estimating

a cost of $140 per hospital, approximately $1,000,000 will be needed for

Costs ($1,000,000)
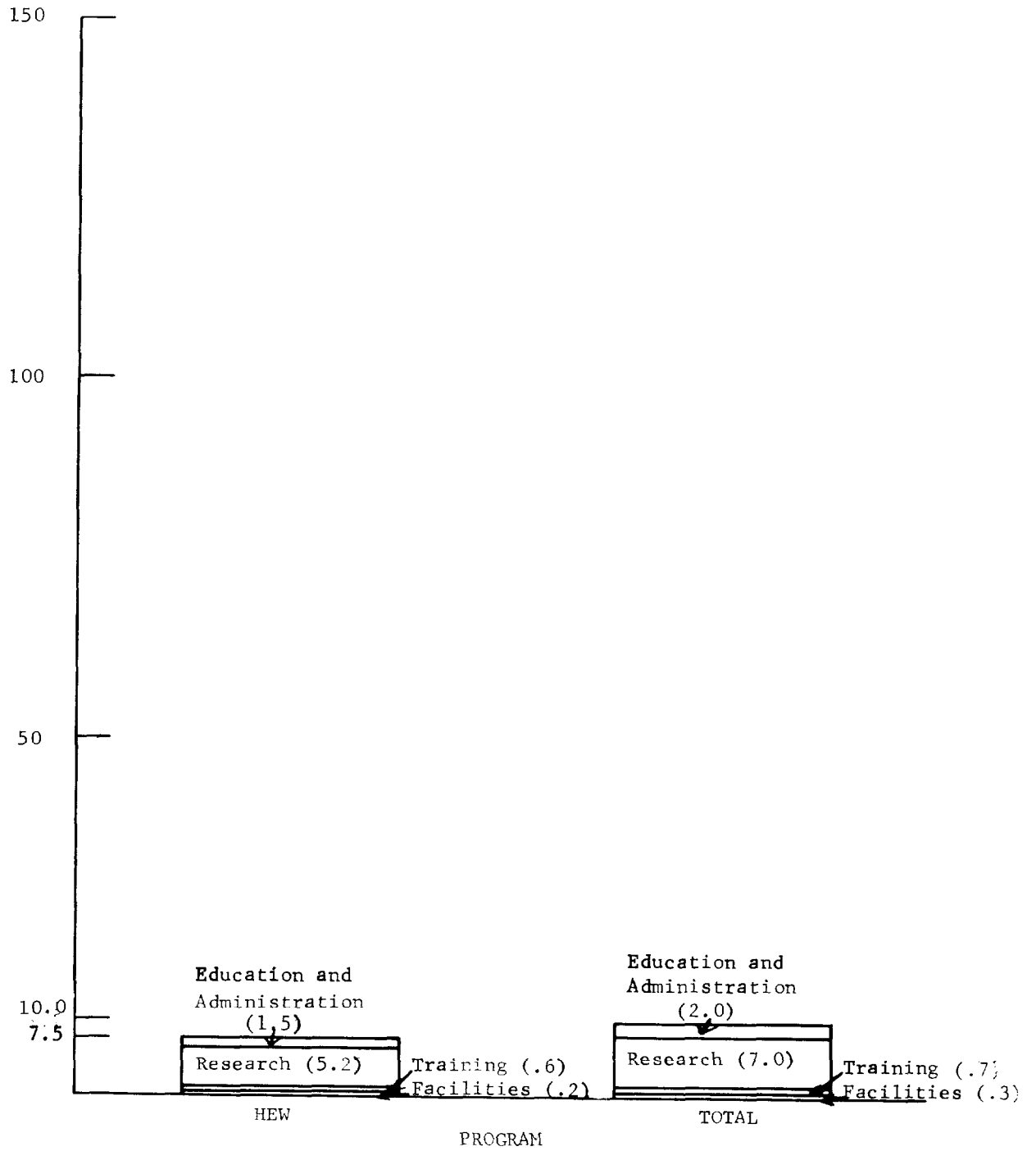
Fig. 5. Kidney Diseases Related to Hypersensitivity Phenomena,
Hypothetical Program Costs at Current HEW Expenditure
Level, Based on Current State of the Art.

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instruction in this area of kidney disease as part of a general educational program. In addition, about $500,000 will be required for the administration and implementation of this program. The total cost for HEW is then estimated at $1,500,000. An additional $500,000 is expected from other sources.

Under the current state of the art postgraduate physician education seems to be the most effective approach for achieving immediate benefits.

a. Short-Term Benefits

It is estimated that this educational program would decrease the immediate annual mortality due to hypersensitivity diseases by approximately 5% (610) from a base line of 12,719[63]/deaths per year. This figure is based on the assumption that improved understanding of diseases such as acute glomerulonephritis, and improved knowledge of fluid, electrolyte, and steroid therapy will have some impact on the immediate mortality from diseases associated with hypersensitivity phenomena.

b. Long-Term Benefits

Under the present state of the art, no long-term benefits are anticipated.

3. Research

This most important program component is separated into clinical and laboratory research efforts.

a. Clinical Research

Following are some areas of disease which need clarification and study to determine their significance in hypersensitive renal disease:

1) Minimal persistent proteinuria;

2) Orthostatic proteinuria;

3) Childhood nephrotic syndrome;

4) Adult nephrotic syndrome;

5) Acute glomerulonephritis;

6) Systemic lupus erythematosus;

7) Miscellaneous collagen diseases; and

8) Any other related hypersensitivity diseases having renal involvement.

The estimated cost for each study area is $500,000, yielding a total cost of $4,000,000 ($3,000,000 from HEW).

Following are some comments on the present status in each of the above study areas:

1) Several universities have been approached on the possibility of conducting cooperative studies on the diseases listed above and have expressed interest in them. No further progress has been made due to a shortage of funds.

2) The Air Force is currently studying orthostatic proteinuria at Lackland Air Force Base, Texas.

3) There is an international cooperative study being conducted on the childhood nephrotic syndrome under the direction of Dr. Henry Barnett of the Albert Einstein Medical Center in New York City.

4) There is no coordinated activity on the adult nephrotic syndrome at the present time in the United States. However, in Great Britain, there is a study sponsored by the British

Medical Research Council on the controlled treatment of
adult nephrotics with steroids.

5) There is a loose cooperative study on acute glomerulonephritis
under way in New York City. There is also a study being
supported on the island of Trinidad which is designed to
follow patients with acute glomerulonephritis. The re-
surgence of the Red Lake epidemic of acute glomerulonephritis
is also under study by Dr. Wanamaker's group at the University
of Minnesota.

6) There is a loose cooperative study by several university
centers emphasizing the pathology in nephritis resulting
from systemic lupus erythematosus.

7) Other disease processes that might be grouped under the
heading of hypersensitivity diseases are sub-acute glomerulo-
nephritis, chronic glomerulonephritis, serum sickness
nephritis, and nephrotoxic nephritis in animals.

b. Laboratory Research

There are at present approximately 30 immunology research units
in existence. It is estimated that approximately 15 of these units
are currently engaged in work which is applicable to hypersensitivity
diseases of the kidney. The total contribution of funds for relevant
studies to these laboratories would be approximately $1,500,000
($100,000 each) per year, of which HEW would contribute $1,125,000.
In addition, it is estimated that an additional $1,500,000 ($1,125,000
from HEW) should be made available for grant support of individual

projects in other laboratories. At an average cost of $25,000

each this amount would support the work of 60 investigators.

It is assumed that the total of $7,000,000 as described in the

above categories will come from both federal and private funds, with

the majority coming from HEW.

4. Training

It is anticipated that each of the 15 involved immunology laboratories

would provide training for two research fellows per year. The cost for

this program would be approximately $50,000 per laboratory per year,[64]/

or a total of $750,000 for the whole program ($560,000 from HEW).

5. Facilities

In order to continue expanding research capabilities and updating

the necessary equipment, it is estimated that 15% of the yearly cost of

laboratory research operations will be spent. The total cost of equip-

ment updating for 15 laboratories amounts to $225,000 per year (15% of

which, $170,000, comes from HEW).

6. Summary

The preceding discussion and estimates presume activity on a level

considerably above the current status. There is a substantial initial

cost in achieving the new elevated level of activity. Principal among

these costs is the expense of constructing and providing adequate facilities.

This amount should not be confused with the facilities estimate discussed

above which is for the improvement of equipment intended to keep research

workers supplied with the best equipment for their varied programs.

A benefit-cost summary associated with this program is found in

Table V.

Table V

KIDNEY DISEASES RELATED TO HYPERSENSITIVITY PHENOMENA, HYPOTHETICAL PROGRAM AT CURRENT HEW
EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| Program | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | HEW ($1,000) | Total ($1,000) | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
			Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I. Education and administration	1,500	2,000					
II. Research	5,250	7,000					
III. Training	560	750					
IV. Facilities	170	225					
TOTAL	7,480	9,975	610	—	—	—	—

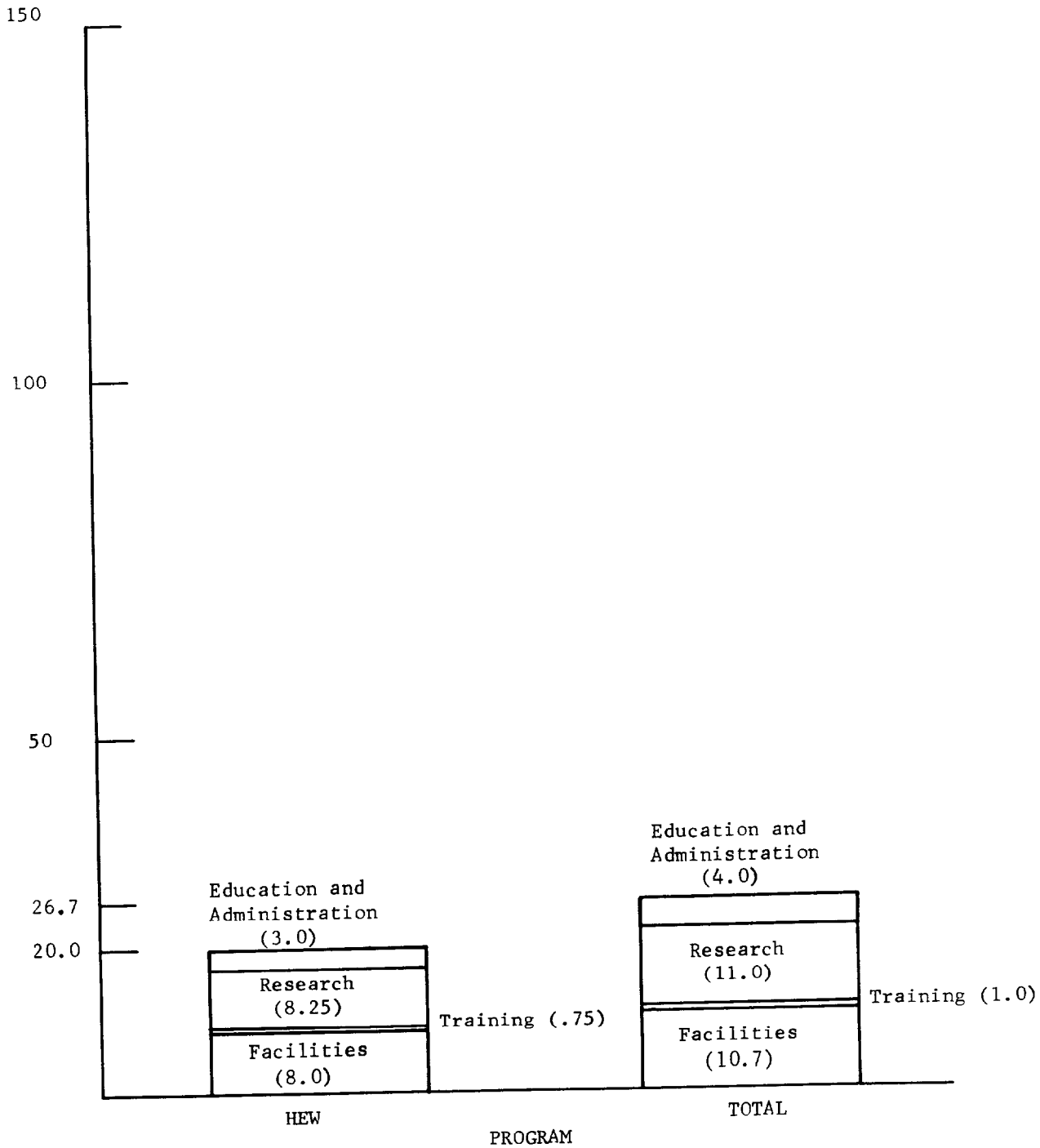C. **Kidney Diseases Related to Hypersensitivity Phenomena, Hypothetical Program at Intermediate HEW Expenditure Level, Based on the Current State of the Art**

1. **Introduction**

   This program has four components:

   1) Education and administration;

   2) Research;

   3) Training; and

   4) Facilities.

   The estimated total cost for this program is $26,670,000. HEW's share is estimated at $20,000,000. Figure 6 graphically presents the costs for this portion. A discussion of the various program components follows.

2. **Education and Administration**

   Under an intermediate, postgraduate physician education program, HEW will contribute $2,500,000, and an additional $500,000 for administrative support. An additional $1,000,000 will be needed from other sources. There are no immediate benefits expected from this new educational effort, although long-term benefits will be significant; therefore, the same mortality reduction figure of 610 (see Section B.2.) is used.

3. **Research**

   With an intermediate level of financial support, clinical research funds can be increased to $6,000,000 ($4,500,000 from HEW). This represents twelve large scale studies at $500,000 each, rather than eight as described above in Section B.3.

   To provide more rapid developments, an increase from fifteen to twenty laboratory research centers in conjunction with an increase in the amount of financial support for each of the twenty centers, will be

Costs ($1,000,000)

Fig. 6. Kidney Diseases Related to Hypersensitivity Phenomena
Hypothetical Program Costs at Intermediate HEW Expenditure
Level, Based on the Current State of the Art.

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supported by an intermediate health program. Total cost would then be $3,000,000 of which HEW would contribute $2,250,000.

Individual research grant funds would be increased from $1,500,000 to $2,000,000 per year, representing an increase in number from 60 to 70 per year at an average amount of $28,500 each. HEW's contribution would be $1,500,000.

All research efforts would total $11,000,000 with $8,250,000 coming from HEW; the remainder coming from other sources.

4. Training

Training for research would be extended to include 20 immunology research laboratory centers, which will provide for the training of two fellows per center at a cost of $50,000 per center. Total expenditures are estimated to be $1,000,000 per year ($750,000 from HEW).

5. Facilities

It is estimated that the yearly cost of expansion for the research program and the updating of equipment will require approximately $10,670,000 ($8,000,000 from HEW).

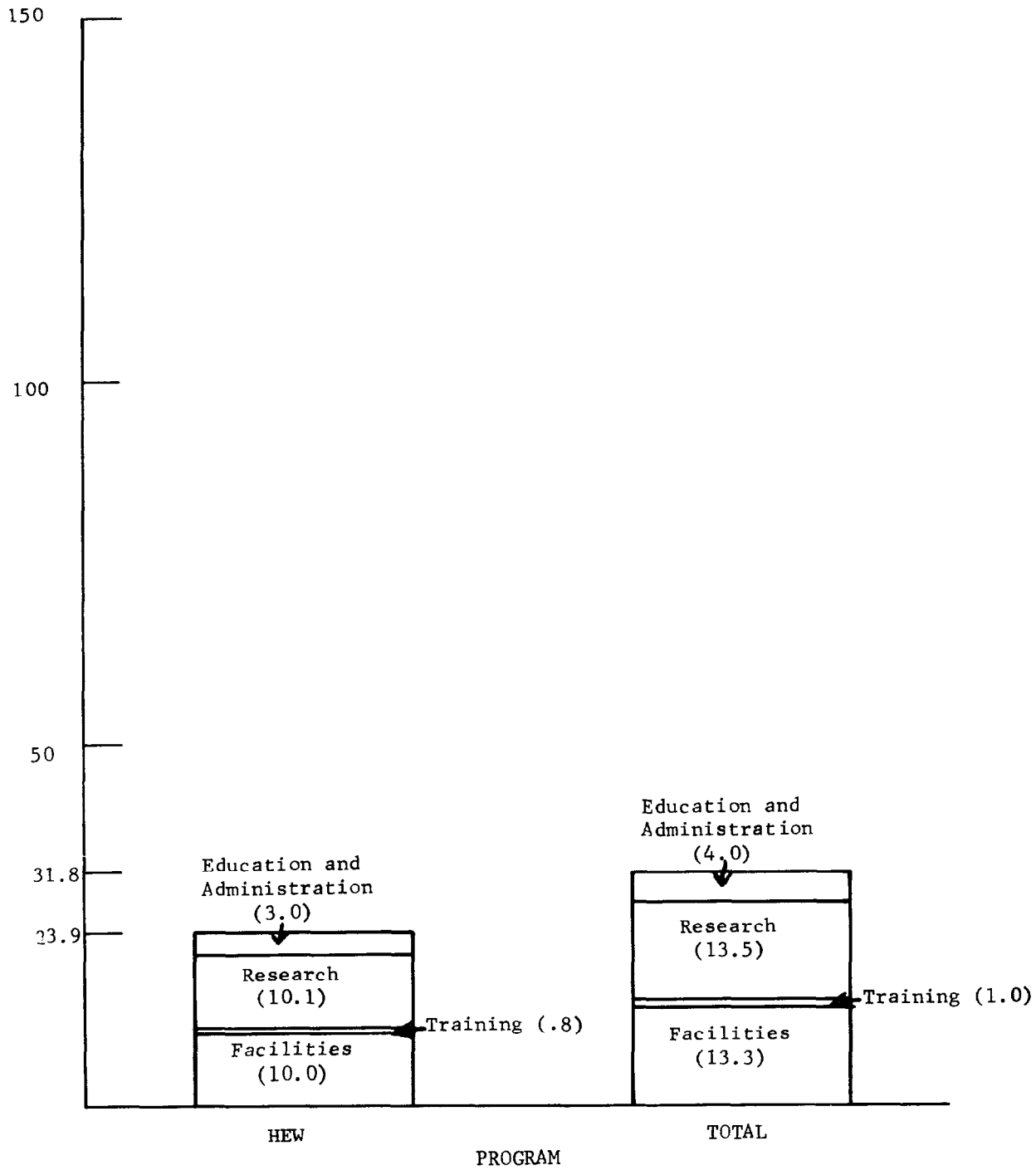A benefit-cost summary associated with this program is found in Table VI.

Table VI

KIDNEY DISEASES RELATED TO HYPERSENSITIVITY PHENOMENA, HYPOTHETICAL PROGRAM AT INTERMEDIATE
HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I. Education and administration	3,000	4,000					
II. Research	8,250	11,000					
III. Training	750	1,000					
IV. Facilities	8,000	10,670					
TOTAL	20,000	26,670	610	———	———	———	———

D. Kidney Diseases Related to Hypersensitivity Phenomena, Hypothetical
   Program at Accelerated HEW Expenditure Level, Based on the Current
   State of the Art

   1. Introduction

      This program has four components:

      1) Education and administration;

      2) Research;

      3) Training; and

      4) Facilities.

      The estimated total cost for this program is $31,830,000. HEW's

      share is estimated to be $23,875,000. Figure 7 shows the costs for this

      program and below follows a discussion of the various program components.

   2. Education and Administration

      No changes in the educational and administrative efforts are antici-

      pated under this accelerated program. HEW will provide $2,500,000 for

      educational support and an additional $500,000 for administrative support.

      Approximately $1,000,000 will be assessed to institutions other than HEW.

      No immediate benefits are expected, and the mortality reduction figure of

      610 (see Section B.2.) is used again.

   3. Research

      With ample support, clinical research funds could be increased to

      $8,000,000 ($6,000,000 from HEW). This would represent 16 large scale

      studies rather than eight as envisioned under the current HEW budget

      level.

      Laboratory research would remain at the level anticipated for an

      intermediate program at a total cost of $3,000,000 ($2,250,000 from

      HEW).

Costs ($1,000,000)

150

100

50

31.8

23.9

Education and
Administration
(3.0)

Research
(10.1)

Training (.8)

Facilities
(10.0)

Education and
Administration
(4.0)

Research
(13.5)

Training (1.0)

Facilities
(13.3)

HEW

TOTAL

PROGRAM

Fig. 7. Kidney Diseases Related to Hypersensitivity Phenomena,
Hypothetical Program Costs at Accelerated HEW Expenditure
Level, Based on the Current State of the Art.

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The number of individual research grants would be increased from 60 to 80 at an average cost of about $31,000 each and a total cost of approximately $2,500,000 per year ($1,870,000 would be HEW's responsibility).

Total efforts aimed at research would amount to $13,500,000 ($10,125,000 to come from HEW).

4. **Training**

Expenditures on research training will remain at $1,000,000 ($750,000 from HEW), the same level as anticipated for the intermediate program.

5. **Facilities**

With ample support from HEW, it is expected that $13,330,000 will be expended on facilities with $10,000,000 expected to come from HEW and $3,330,000 from other sources.

A benefit-cost summary associated with this program is found in Table VII.

Table VII

KIDNEY DISEASES RELATED TO HYPERSENSITIVITY PHENOMENA, HYPOTHETICAL PROGRAM
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I. Education and administration	3,000	4,000					
II. Research	10,125	13,500					
III. Training	750	1,000					
IV. Research	10,000	13,330					
TOTAL	23,875	31,830	610	___	___	___	___

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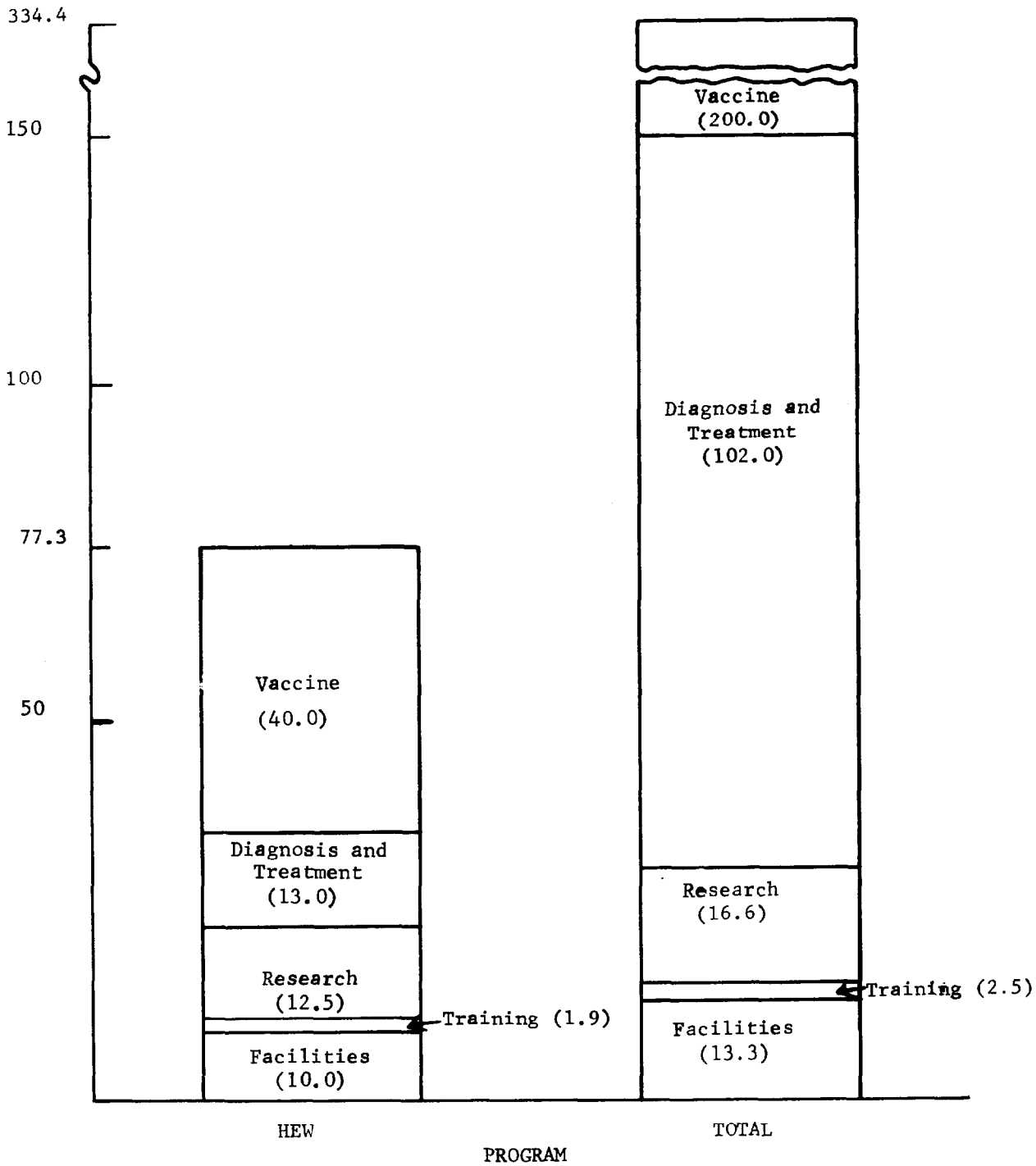E. **Kidney Diseases Related to Hypersensitivity Phenomena, Hypothetical Program for Fiscal Year 1975, at Accelerated HEW Expenditure Level, Based on Expected Advanced State of the Art in 1975**

1. **Introduction**

   This program has five components:

   1) Prevention of acute glomerulonephritis;

   2) Early detection of disease (manifested by proteinuria), treatment of diseases associated with hypersensitivity phenomena, and supportive education and administration;

   3) Research;

   4) Training; and

   5) Facilities.

   The estimated total cost for this program is $334,420,000 of which HEW will expend $77,320,000. Figure 8 illustrates costs associated with the various program components.

   Advances in the state of the art which are anticipated by 1975, have been broken down into three separate categories. They are:

   1) Acute glomerulonephritis--in which primary preventive measures will be available (e.g., a vaccine and/or effective treatment of streptococcal infections).

   2) Chronic glomerulonephritis--which is heralded by patients with proteinuria and in which secondary preventive measures may be available; and

   3) Other diseases--such as chronic sclerosing nephritis, the collagen diseases (e.g., lupus erythematosus, scleroderma, etc.) in which secondary preventive measures may be available, and a miscellaneous group of renal diseases (e.g., amyloidosis).

Costs ($1,000,000)

Fig. 8. Kidney Diseases Related to Hypersensitivity Phenomena,
Hypothetical Program Costs for Fiscal Year 1975, at
Accelerated HEW Expenditure Level, Based on Expected
Advanced State of the Art in 1975.

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No detailed analysis for the class of Other Diseases, namely collagen disorders and the miscellaneous group of renal diseases, has been undertaken.

2. Prevention of Acute Glomerulonephritis

Two possible advances in the next 10 years are analyzed in this report. These are:

1) The development of a vaccine to prevent Group A beta-hemolytic streptococcal infections (especially Type 12); and/or

2) The development of an efficient means for the early detection of beta-hemolytic streptococcal infections and the prevention of subsequent glomerulonephritis through effective therapy.

a. Development of a Vaccine to Prevent Streptococcal Infection

(1) Relevant Population and Program Component Costs

The assumption is made that 200,000,000[65]/persons would be vaccinated in 1975 at a cost of $1.00 per individual. Total cost for this vaccination program is estimated at $200,000,000 ($40,000,000 to come from HEW).

(2) Short-Term Benefits

Short-term benefits are estimated as the following:

1) From an estimated base of 650[66]/deaths resulting from acute glomerulonephritis which would have occurred without a vaccination program, a 95% reduction in mortality, i.e., 620 avoided deaths, is anticipated.

2) There will be a 95% reduction in the number of cases of acute glomerulonephritis (i.e., 52,250) from an estimated base line of 55,000 cases.

3) Assuming 40 morbid days[67]/per case of acute glomerulo-
nephritis, a base line of 2,200,000 morbid days is
calculated using 55,000 cases as a reference. Morbid
days will be reduced by 95%, or 2,090,000, with this
program.

(3) Long-Term Benefits

(a) Annual Long-Term Benefits

It is estimated that without a vaccine 5% (2,750) of
the 55,000 individuals with acute glomerulonephritis
eventually would have developed end-stage uremia. Assuming
that each new patient with acute glomerulonephritis which
progresses to the chronic stage will have a normal age-
life span, then the yearly death rate from hypersensitivity
diseases will be reduced by 2,610. The vaccine will
reduce the number of cases of acute glomerulonephritis by
95%, (i.e., 2,610 of 2,750).

(b) Cumulative Long-Term Benefits

Assuming that without a vaccine approximately
100,000[68]/of the population eventually would have developed
end-stage uremia due to acute glomerulonephritis, approx-
imately 95,000 (95% of 100,000) persons will have avoided
death resulting from end-stage uremia.

b. Alternate Detection and Treatment Program

An alternative possibility is the development of an effective
means to detect and to provide adequate treatment for immunologic

reactions in the kidney resulting from streptococcal infections. Two possibilities are presented below:

1) Early detection of streptococcal infection and immediate therapy with penicillin may prevent the serious sequelae resulting from acute glomerulonephritis; or it may succeed in interrupting an epidemic of acute streptococcal infections, thereby reducing the possible incidence of glomerulonephritis; and

2) Advances in immunosuppressive therapy could prevent cases of acute glomerulonephritis which arise from nephritogenic strains of streptococci.

This program would be directed toward a population in which an epidemic of nephritogenic beta-hemolytic streptococcal infection is in progress. Therefore, a program of close epidemiological surveillance of the population susceptible to streptococcal infections, and the rapid institution of immediate treatment procedures would be undertaken.

A 20% reduction in mortality would be expected lowering the number of mortalities due to the acute disease process by 130 per year.[69/] A reduction in prevalence rates by 30% would decrease the number of cases by 16,500 per year from a base line of 55,000; the number of morbid days would be decreased by 30%, or 660,000 days per year, from a base line of 2,200,000.[70/] The total effect on the 2,750 individuals who would have developed end-stage uremia each would be a reduction by 30%, i.e., 830 cases, with this program.[71/] Cumulative long-term benefits would be 30,000 avoided cases of

end-stage uremia (30% of the estimated 100,000 who would have developed kidney failure eventually)[72/] These alternative benefits have not been included in the summation of the program analysis.

3. Proteinuria

A second approach in preventing renal hypersensitivity disease would be an attempt at the early detection of persistent proteinuria. It is assumed that this phenomenon represents an early stage of renal disease in which the filtering apparatus of the nephron is malfunctioning, giving some indication of impending chronic nephritis. The major objective of the program is to develop an effective means for the early detection of persistent proteinuria, to identify those cases in which proteinuria signifies renal disease, and to devise adequate therapy which will interrupt the disease process, thereby preventing progression to a state of renal failure. It will be assumed that under this advanced state of the art, a means of therapy has been developed which is effective in 50% of those cases treated.

a. Relevant Population and Program Component Cost

Assuming that 150,000,000 people can be screened each year via periodic physical examinations, multiphasic screening programs, etc., 2% (3,000,000 of these) will have a positive test for proteinuria.[73/]

Of 3,000,000 patients with a positive test, approximately 20%, 600,000, will be expected to have confirmed proteinuria as shown by more refined and more expensive tests. The confirmatory test costs $1.00; therefore, the total cost is $3,000,000 since each individual with a positive screening test must have a confirmatory test.[74/]

Of the 600,000 confirmed positive patients having proteinuria, it is anticipated that additional studies will establish 20% (120,000) as having <u>persistent</u> proteinuria[75/] The estimated cost for these additional studies is $5.00 per test for a total cost of $3,000,000 ($5.00 x 600,000).

For each of these 120,000 individuals a complete diagnostic work-up including: urine analysis, amount of total protein excretion, studies of renal functions such as clearance and concentrating abilities, roentgen studies (to include a flat film of the abdomen, intravenous pyelograms, and possibly retrograde pyelograms if necessary), and in some instances a renal biopsy to be examined under the electron microscope is necessary to establish a definite cause of proteinuria. The estimated cost is $500 per individual study for a total cost of $60,000,000.

Total costs for confirming tests amount to $66,000,000, none of which is expected to come from HEW.

One-third of the 120,000 individuals with confirmed persistent proteinuria (i.e., 40,000), could potentially develop debilitating renal disease[76/] Of this number about 50% (20,000) are estimated to have renal disease associated with hypersensitivity phenomena. It is estimated that a single therapeutic course would cost $100 per patient for a total of $2,000,000.

Total costs for this program component are $98,000,000 ($2,000,000 of which is to be borne by HEW).

Support for education and administration is estimated to cost HEW $3,000,000 with $1,000,000 coming from other sources.

b. <u>Short-Term Benefits</u>

Short-term benefits for individuals having diagnosed renal

disease with hypersensitive origin followed by some form of

treatment are:

1) A reduction of 1%, or approximately 150 deaths, from a

base line of 14,500[77] expected annual deaths in patients

with hypersensitivity diseases of the kidney;

2) A reduction of 50%, or 10,000 cases, from a base line of

20,000 cases diagnosed as hypersensitivity disease of the

kidney;[78] and

3) A reduction of 65%, 520,000 days, from an estimated

800,000 morbid days.[79]

c. <u>Long-Term Benefits</u>

(1) <u>Annual Long-Term Benefits</u>

The annual death rate could be reduced by 50% based on the

assumption that new cases are diagnosed each year and that therapy

is effective in one-half of the individuals. The therapeutic

results should improve as cases can be detected earlier; and

ultimately a decrease of 6,000 from a base line of 12,000[80]

cases of fatal end-stage uremia per year could be effected.

(2) <u>Cumulative Long-Term Benefits</u>

From an expected base of 450,000 individuals[81] having

confirmed persistent proteinuria who would have developed

end-stage uremia eventually, a reduction of 50%, or 225,000,

is anticipated in an accelerated HEW health program.

4. <u>Total Screening, Diagnosis and Treatment Costs</u>

Total costs for screening, diagnosis, and treatment are estimated

to be $102,000,000 ($13,000,000 from HEW).

5. Total Short-Term Benefits

   Total short-term benefits resulting from the control of acute glomerulonephritis using a vaccine and from the detection and control of proteinuria are as follows:

   1) A reduction in immediate mortality by 770 per year;

   2) A reduction in the number of cases by 62,250; and

   3) A reduction in the number of morbid days by 2,610,000.

6. Total Long-Term Benefits

   Total long-term benefits resulting from the control of acute glomerulonephritis using a vaccine and from the detection and control of proteinuria are an annual reduction of 8,610 cases of fatal end-stage uremia and cumulative long-term reduction of 320,000.

7. Research

   Research programs under the advanced state of the art are anticipated to increase so that HEW's expected level of effort will be $12,450,000; $4,150,000 will come from other sources.

8. Training

   Funds needed for training will approximate 15% of the amount spent on research, i.e., $2,493,000, of which $1,870,000 will come from HEW and $620,000 will come from other sources.

9. Facilities

   HEW will expend about $10,000,000 for facilities and an additional $3,330,000 will come from other sources.

10. Estimated Benefits Dependent Upon Research

   Benefits dependent on new disease control techniques are;

   a) Short-Term Benefits:

1) A reduction in immediate mortality by 770 deaths (680 based on 1966 U. S. population);[82/]

2) A reduction in the number of cases by 62,250 (54,610 based on 1966 U. S. population); and

3) A reduction in the number of morbid days by 2,610,000 (2,289,470 based on 1966 U. S. population).

b) Long-Term Benefits:

1) An annual reduction of fatal end-stage uremia by 8,610 cases (7,550 based on 1966 U. S. population); and

2) A cumulative reduction of fatal end-stage uremia by 320,000 cases (based on 1966 U. S. population).

A benefit-cost summary associated with this program is found in Table VIII.

Table VIII

KIDNEY DISEASES RELATED TO HYPERSENSITIVITY PHENOMENA, HYPOTHETICAL PROGRAM FOR FISCAL YEAR 1975
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON EXPECTED ADVANCED STATE OF THE ART IN 1975

| | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I. Attack on acute glomerulonephritis streptococcal vaccine	40,000	200,000					
II. Proteinuria, screening, diagnosis and treatment, and supportive education and administration:							
1. Screening	10,000	30,000					
2. Confirming test for persistent proteinuria		6,000					
3. Confirming test for renal complications		60,000					
4. Treatment for renal complications		2,000					
Sub-Total	10,000	98,000					
5. Education and administration	3,000	4,000					
Sub-Total	13,000	102,000					
III. Research	12,450	16,600					
IV. Training	1,870	2,490					
V. Facilities	10,000	13,330					
TOTAL	77,320	334,420	770	62,250	2,610,000	8,610	320,000

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IV. KIDNEY DISEASES RELATED TO HYPERTENSIVE VASCULAR DISEASES

A. Introduction

This section pertains to programs needed to control renal diseases

associated with hypertension. It is assumed throughout the discussion that

the amelioration of hypertension will result in a significant reduction in

associated renal disease.[83]

In 1966, 71,347 deaths[84] are estimated to have had hypertensive vascu-

lar disease as the underlying cause of death. Of this group it is estimated

that about 30%[85] were caused at least partially by serious renal sequelae.

In 1966, some 11,430,000 individuals are estimated to have had hyper-

tensive vascular disease; associated with these were 181,280,000 days of

restricted activity, 68,580,000 days of bed disability, and 11,330,000

work-loss days resulted.[86]

Three programs are considered in this analysis (see Chapter 5, Research
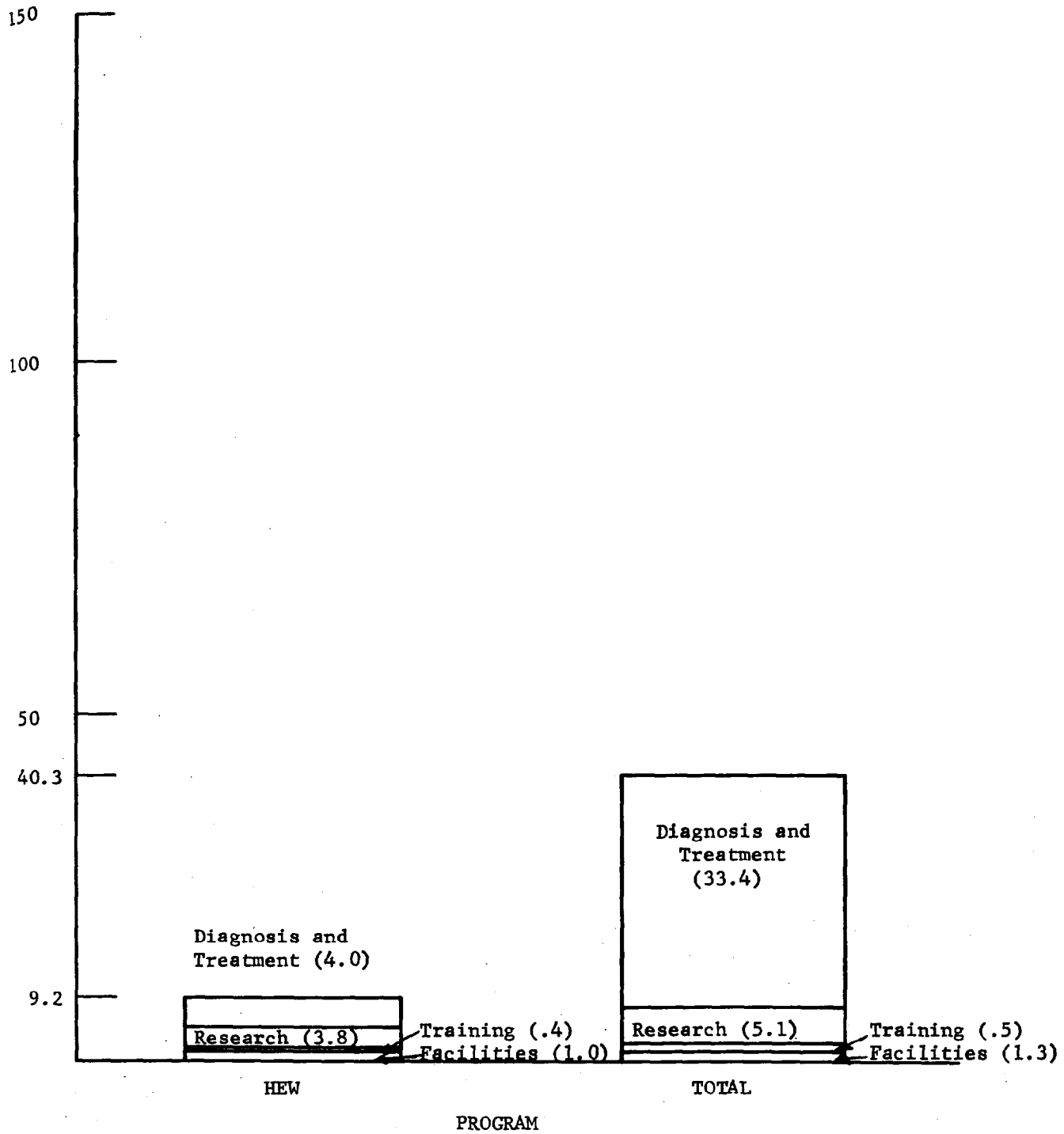
Methodology) and are described in detail below.

B. Kidney Diseases Related to Hypertensive Vascular Diseases, Hypothetical
    Program at Current HEW Expenditure Level, Based on the Current State of
    the Art

1. Introduction

This program has four components:

1) Diagnosis, treatment, supportive education and administration;

2) Research;

3) Training; and

4) Facilities.

The total estimated cost for this program is $419,440,000 ($40,272,000

specifically for associated renal problems). HEW would account for

$9,180,000, all of which would be used to control the renal complications

of hypertension. Figure 9 illustrates the program expenditures for associated renal problems. A discussion of the various program components follows.

2. <u>Diagnosis, Treatment and Supportive Education and Administration</u>

Screening, diagnosis and treatment are aimed at individuals 17 years of age and over who have potentially curable (non-essential) hypertension or currently non-curable (essential) hypertension.

   a. <u>Relevant Population and Program Component Costs</u>

This program component provides for the extension of complete care to individuals with known hypertension. HEW would provide financial support for education and administration of this program.

Various studies have shown that between 10-20% of all hypertensive patients have potentially curable hypertension.[87/] It is estimated that approximately 15%, 1,450,000, of the known total hypertensive population (9,330,000 in 1966) have curable (non-essential) hypertension. Of this number, it is estimated that about 450,000 are presently receiving adequate treatment. With this program, an additional 450,000 would receive adequate treatment over a five-year period. This program would provide treatment for 90,000 of these patients each year.

Since this is a population of known hypertensives and no screening test would be necessary, the cost for definite diagnosis and treatment of a specific type of hypertensive vascular disease would be $1,000 per patient per year. The total cost is then $90,000,000 per year, and an estimated 10% ($9,000,000)[88/] of this amount is to be used to treat associated renal hypertensive disease.

Fig. 9. Kidney Diseases Related to Hypertensive Vascular Diseases,
Hypothetical Program Costs at Current HEW Expenditure Level,
Based on the Current State of the Art.

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No screening test is required for the currently known non-curable hypertensives. The treatment cost for each of these individuals is estimated at $200.00 per year.[89/] In addition, it is anticipated that this program will provide for an increase of 20% (1,586,000)[90/] in the number of patients being adequately treated. Therefore, total treatment costs for these individuals would be $317,200,000. Approximately 6%[91/] of this amount, $19,032,000 would be used for the treatment of associated renal disease.

Total cost for the above program is $407,200,000 ($28,032,000 of which is for associated renal problems). These costs are not to be borne by HEW.

The supportive education and administration component involves the postgraduate education of physicians as well as the community on kidney malfunction as it is related to hypertensive disease. Technical support as well as some financial support is also included. It is estimated that $4,000,000 is the minimum amount needed under the 1966 HEW funding level to activate this program component. Approximately $1,330,000 will be generated by institutions and sources other than HEW.

Total cost for this program component is $419,440,000 ($40,272,000 used for associated renal disease). Total HEW expenditure for program component 2.a. is $4,000,000, all of which is employed for treatment of kidney disease.

b. Short-Term Benefits

The following are estimated short-term benefits:

(1) Known Potentially Curable (non-essential) Hypertensive Patients:

1) Of a total population of 90,000[92/] having non-essential
   hypertension, a 60% reduction in the immediate mortality
   rate is expected (i.e., 340 of the estimated 570 normally
   occurring deaths will be prevented).[93/] Approximately 50%
   (170) of these prevented deaths would have resulted from
   associated renal dysfunction.[94/]

2) A similar 60% decrease in the number of cases in the
   same population is expected (i.e., 54,000 out of 90,000).
   About 50% of this reduced number would be associated with
   renal hypertensive changes.[95/]

3) It is estimated that each patient with hypertensive
   vascular disease suffers an average of 16 morbid days per
   year;[96/] the total for all affected patients in this
   population would be 1,440,000 morbid days (90,000 x 16).
   Implementation of this program would effectively decrease
   the number of morbid days by 864,000, or 60% (50% of
   this number, 432,000 would involve patients with
   associated renal problems).[97/]

(2) Known Currently Non-Curable (essential) Hypertensive
Patients:

1) It is estimated that a 15% decrease of 7,490 in mortality
   from a total of 49,940 deaths[98/] will result (27%, or
   2,020, of which will have renal complications); and

2) It is estimated that a 20% reduction in the number of
   morbid days from a base line of 25,376,000[99/] will
   result in 5,075,200 additional healthy days (27%, or
   1,370,300 associated renal problems).

There is no change in prevalence rate or number of new cases.

(3) <u>Total for Known Hypertensive Patients</u>:

Total short-term benefits for the surveyed high-risk groups are the prevention of 7,830 deaths (2,190 having associated renal problems), a reduction of 54,000 cases (27,000 with associated renal problems), and a reduced number of morbid days by 5,939,200 (1,802,230 resulting from associated renal disease).

c. <u>Long-Term Benefits</u>

   (1) <u>Annual Long-Term Benefits</u>

It is anticipated that the number of patients in end-stage renal failure resulting from non-essential hypertension will be reduced by 2,940 each year (a 60% reduction rate from an estimated base of 4,900)[100] At the same time, it is estimated that there would be 13,880[101] patients suffering from essential hypertension who would have developed end-stage uremia each year. This number is expected to be reduced by 10%, or 1,390, by the implementation of this program.

The total annual long-term benefits will amount to a reduction in the number of patients developing end-stage uremia by 4,330.

   (2) <u>Cumulative Long-Term Benefits</u>

It is felt that 7% or 98,000,[102] of all potentially curable known hypertensives (1,400,000) would eventually develop chronic renal failure. With this program a reduction of this number by

60% (i.e., 58,800) is expected. An additional 3.5%, or 277,550,

of the presently non-curable known hypertensives (7,930,000)

would eventually have developed fatal end-stage uremia.

Development of this program is designed to reduce this figure

by 10%, or 27,760. [103/]

Therefore, total cumulative long-term benefits amount to

a prevention of 86,560 cases of fatal end-stage uremia.

3. Research

This research program will consist of a number of problem-focussed

clinical and laboratory research studies as well as of individual grants

for wholly independent study in the pertinent areas.

The clinical research programs would be carried out in 20 separate

study groups, and laboratory research programs would also be carried out

in 20 separate study groups. [104/] Fifteen of these study groups would be

combined in the same geographic location, leaving 5 groups to accomplish

basic laboratory research independently and 5 groups to accomplish clinical

research independently.

The laboratory research would be funded with approximately $40,000

per group, [105/] for a total of $800,000. The clinical research would be

funded with approximately $50,000 [106/] per group, or approximately

$1,000,000. Since 15 of these groups will be concerned with both

laboratory and clinical research, the level of support to these centers

would be $90,000 each.

The remaining area of research would consist of approximately 50

individual grants, at $40,000 each, for a total grant cost of $2,000,000.

The total amount for research equals $1,800,000 for laboratory and

clinical research and $2,000,000 for individual grants yielding a total

of $3,800,000 supported by HEW. An additional $1,270,000 is expected to be generated by other sources.

The clinical studies mentioned above will consist of long-term studies of the natural history and treatment of hypertensive vascular disease, especially as it relates to renal disease. Both the laboratory and clinical studies will result in additional benefits to disease areas other than renal disease such as hypertensive heart disease, arteriosclerosis, etc. The basic research programs would be directed towards the discovery of the etiology of hypertension, the identification of facets and factors in the disease process which affect renal function, and the development of novel treatment methods.

4. Training

The training of physicians and allied personnel would cost HEW approximately $380,000. An additional $130,000 would be obtained from other sources.

5. Facilities

The expenditures for facilities is estimated at $1,000,000 with an additional $330,000 to come from other agencies.

A benefit-cost summary associated with this program is found in Table IX.

Table IX

KIDNEY DISEASES RELATED TO HYPERTENSIVE VASCULAR DISEASES, HYPOTHETICAL PROGRAM
AT CURRENT HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Diagnosis and treatment of individuals 17 years of age and over with known curable (non-essential) hypertension and non-curable hypertension		407,200 (28,032)[1]					
B. Supportive education and administration	4,000 (4,000)	5,330 (5,330)					
Sub-Total	4,000 (4,000)	412,530 (33,362)					
II. Research	3,800 (3,800)	5,070 (5,070)					
III. Training	380 (380)	510 (510)					
IV. Facilities	1,000 (1,000)	1,330 (1,330)					
TOTAL	9,180 (9,180)	419,440 (40,272)	7,830 (2,190)	54,000 (27,000)	5,959,200 (1,802,230)	(4,330)	(86,560)

[1] Figures in parenthesis refer to statistics attributable to renal complications.

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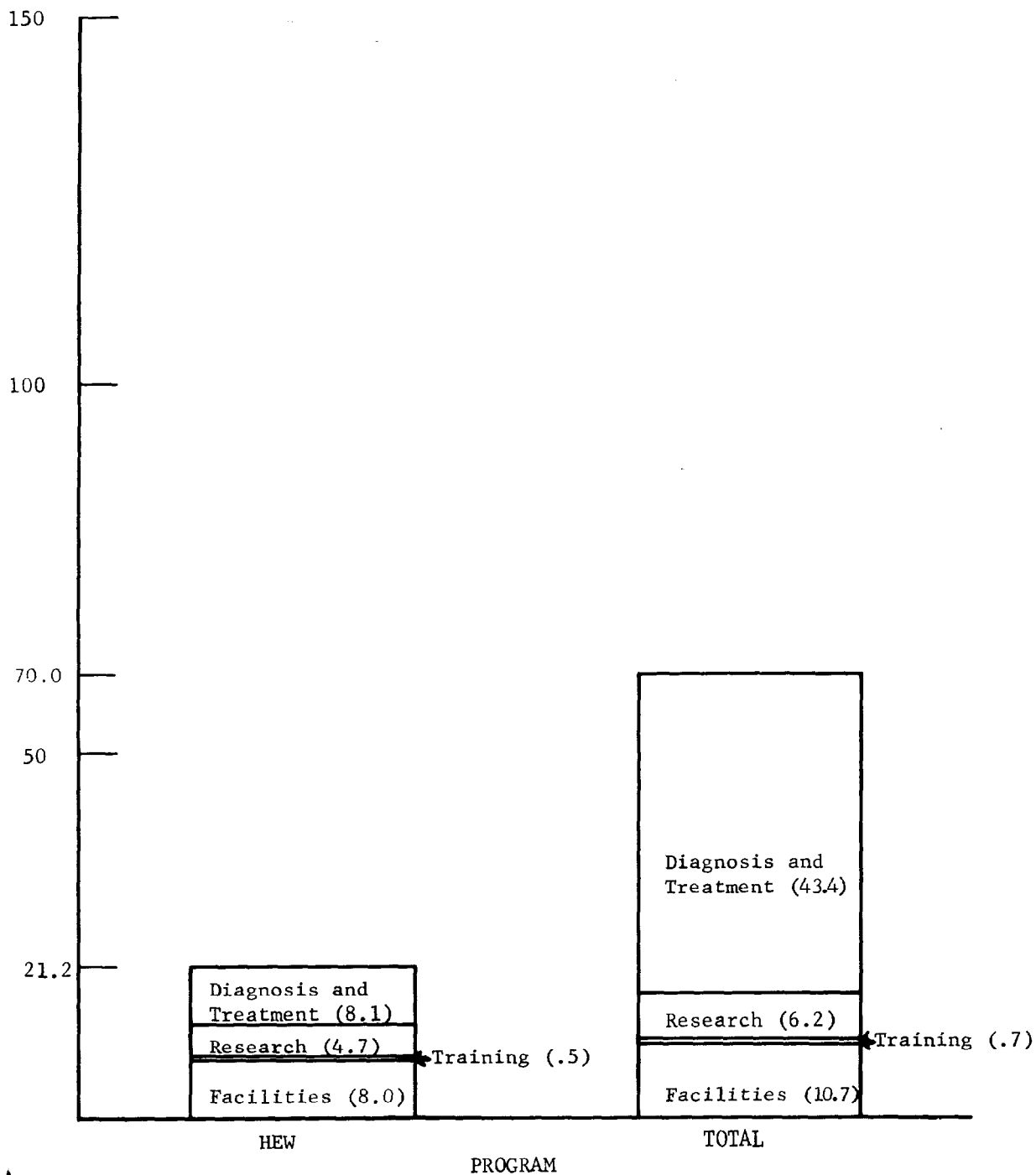C. **Kidney Diseases Related to Hypertensive Vascular Diseases, Hypothetical Program at Intermediate HEW Expenditure Level, Based on the Current State of the Art**

1. **Introduction**

This program has four components:

1) Screening, diagnosis, treatment, and supportive education and administration;

2) Research;

3) Training; and

4) Facilities.

The estimated total cost for this program is $496,150,000 ($6,936,000 will be used for associated renal problems). HEW will account for $22,098,000 ($21,207,000 for associated renal complications). Figure 10 illustrates the total program expenditures by components. A discussion of the various program components follows.

2. **Screening, Diagnosis, Treatment, and Supportive Education and Administration**

This program is designed to cover a six-year period in order to attain maximum effectiveness under an intermediate budget constraint. In the intermediate program level, an additional risk group must be considered. This group is comprised of individuals who have not been examined by a physician during the preceding year. In this population, there are an estimated 43,500,000 persons 17 years of age and over in the U. S.,[107] 2,100,000 with undiagnosed hypertension.[108] Over a 6 year period, 50% (21,750,000) of these individuals could realistically be screened. This means that each year 3,792,000 persons would be subjected to a screening test.[109] If only 50% of the total population at risk is randomly screened, then it can be assumed that 50% of the individuals with hypertension will be detected, i.e., 1,050,000. Since

Fig. 10. Kidney Diseases Related to Hypertensive Vascular Diseases, Hypothetical
Program Costs at Intermediate HEW Expenditure Level, Based on the
Current State of the Art.

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the program covers a 6 year period, 175,000 individuals will have a
positive screening test for hypertension each year. The cost per test
is $1.25, thus, the total cost for a general screening test is
$4,740,000 ($1.25 x 3,792,000). $240,000 of this amount can be
attributed to renal involvement. HEW will support 20% of the total
or $948,000 ($57,000 of which is attributed to renal disease).

In addition to the cost of screening, expenses for treatment and
confirming diagnosis will be incurred.

Approximately 15%, 26,500, of the 175,000 diagnosed hypertensives
are assumed to have curable hypertension. At a cost of $1,000 per year,
total treatment and confirming diagnosis costs will be $26,250,000
($2,625,000 for associated renal complications).

Approximately 85% (148,750) of the 175,000 have non-curable hyper-
tension. At an estimated treatment cost of $200 per individual per
year, total costs will be $29,750,000 ($1,785,000 for associated renal
complications). Treatment costs will be borne by sources other than
HEW.

Total costs for this part of the program are $467,940,000
($32,726,000 for associated renal complications). HEW's share of the
total is $948,000 ($57,000 for associated renal complications).

The supportive educational and administrative funds needed to
implement the screening, diagnosis and treatment for these hypertensive
patients is estimated to be $8,000,000 from HEW with an expected additional
$2,670,000 from other sources. These funds are to be used for the
postgraduate education of physicians and allied medical personnel, as
well as for technical and administrative support by HEW.

The total cost for this program component is estimated to be $478,610,000 ($43,396,000 for associated renal complications). HEW's share is $8,948,000 ($8,057,000 for associated renal complications).

a. Short-Term Benefits:

The following are estimated short-term benefits.

(1) Newly Detected Potentially Curable (non-essential) Hypertensives:

1) Of the total population of 26,250 having the disease, 140 deaths would have occurred without this program; a reduction of 80 (60%) is anticipated (50% of which reflect those deaths avoided in cases having associated renal problems).$\underline{110/}$

2) A 60% reduction in prevalence is also expected, accounting for 15,750 (50% or 7,880 with associated renal problems).$\underline{111/}$

3) From a base line of 420,000 morbid days$\underline{112/}$ a 60% reduction is expected, i.e., 252,000 days (126,000 in patients with associated renal problems).

(2) Newly Detected Currently Non-Curable (essential) Hypertensives

Short-term benefits associated with the currently non-curable hypertensives, 17 years of age and over, are as follows:

1) An estimated 15% decrease of 160 in immediate mortality from a base line of 1,070 deaths$\underline{113/}$ which would have occurred without this program (27% of the avoided deaths, or 40, are attributed to cases with associated renal problems).

2) There is no change in prevalence rate.

3) An estimated 20% reduction, 476,000, in the number
of morbid days from a base line of 2,380,000[114]
(128,520 as a result of associated renal problems).

(3) All Hypertensives

Total short-term benefits for the surveyed high-risk
groups are

1) A reduction of 8,070 deaths (2,270 with associated
renal problems);

2) A reduction in prevalence of 69,750 (34,880 with
associated renal problems); and

3) A reduction in morbid days of 6,193,720 (2,056,820 in
patients with associated renal problems).

b. Long-Term Benefits

The following are estimated long-term benefits:

(1) Annual Long-Term Benefits

It is estimated that of a total of 550 deaths which would
have occurred in the newly detected non-essential hypertensives
annually, 60%, or 330 per year, would be prevented by this
program.[115]

In the population with newly diagnosed essential hypertension,
a 10% reduction of 156 in the number of cases of fatal end-
stage uremia is expected from a base line of 1,560.[116]

Total (annual) long-term benefits for all groups surveyed
equal 4,820 prevented cases of fatal end-stage uremia each
year.

(2) Cumulative Long-Term Benefits

It is anticipated that this program will result in a 60% reduction in the number of cumulative cases of fatal end-stage uremia in patients with newly detected non-essential hypertension. This would be a reduction of 6,720 from a base line of 11,025. [117/]

It is also expected that 3,120 (10% of the total 31,240) [118/] potential cases of fatal end-stage uremia will be prevented in patients with essential hypertension.

Total cumulative long-term benefits for all the surveyed high-risk groups, including those discussed above in Section B.2.c., amount to a reduction of 96,300 cases of fatal end-stage uremia.

3. Research

The research program would be expanded in the following manner: clinical research will be expanded to include 25 separate groups at a cost of $50,000 per group for a total of $1,250,000.

Laboratory research projects will also be expanded to include 25 separate study groups at a cost of $40,000 per group for a total of $1,000,000.

The number of individual grants will be increased from 50 to 60 at a cost of approximately $40,000 each for a total of $2,400,000.

Total support for research efforts from HEW would amount to $4,650,000. An additional $1,550,000 would be generated by other sources.

4. Training

The training of physicians and allied personnel will cost HEW

approximately $500,000. An additional $170,000 would be obtained from other sources.

5. Facilities

HEW's expenditures for facilities is anticipated to be $8,000,000 plus an additional $2,670,000 from other sources.

A summary of the benefits and costs associated with this program is found in Table X.

KIDNEY DISEASES RELATED TO HYPERTENSIVE VASCULAR DISEASES, HYPOTHETICAL PROGRAM
AT INTERMEDIATE HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

Program	Expenditures		Short-Term Benefits			Long-Term Benefits	
			Reduction Per Year In			Reduction In End-Stage Uremia	
	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Screening, diagnosis and treatment of individuals 17 years of age and over with known curable (non-essential) hypertension and non-curable hypertension and individuals who would have had undetected hypertension without the initiation of the program component							
1. Screening	948 (57)	4,740 (284) 1/					
2. Diagnosis and treatment	— —	463,200 (32,442)					
Sub-Total	948 (57)	467,940 (32,726)					
B. Supportive education and administration	8,000 (8,000)	10,670 (10,670)					
Sub-Total	8,948 (8,057)	478,610 (43,396)					
II. Research	4,650 (4,650)	6,200 (6,200)					
III. Training	500 (500)	670 (670)					
IV. Facilities	8,000 (8,000)	10,670 (10,670)					
TOTAL	22,098 (21,207)	496,150 (60,936)	8,070 (2,270)	69,750 (34,880)	6,193,720 (2,056,820)	(4,820)	(96,300)

1/ Figures in parenthesis refer to statistics attributable to renal complications

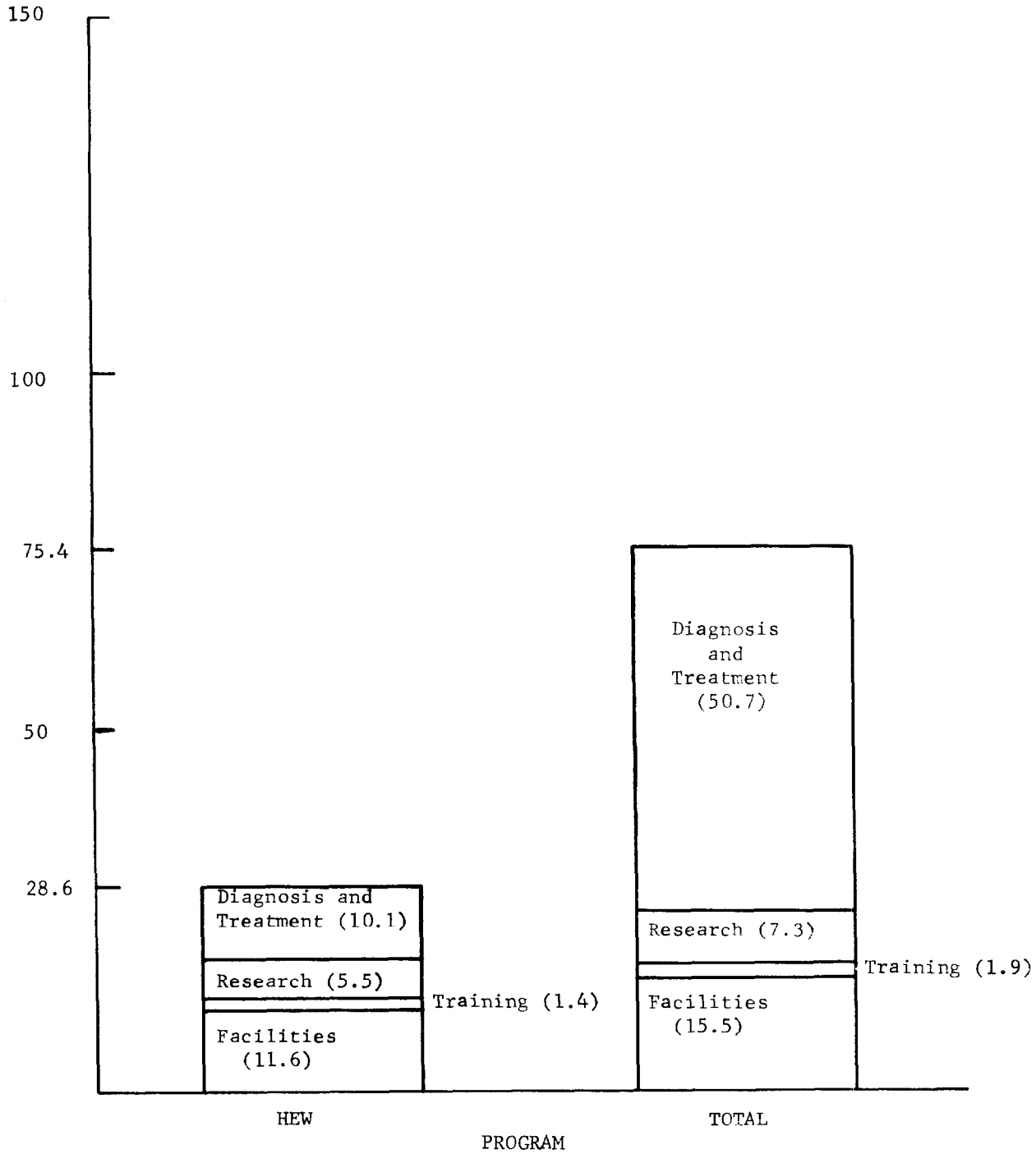**D.** Kidney Diseases Related to Hypertensive Vascular Diseases, Hypothetical Program at Accelerated HEW Expenditure Level, Based on the Current State of the Art

1. Introduction

   This program has four components:

   1) Screening, diagnosis, treatment, and supportive education and

      administration;

   2) Research;

   3) Training; and

   4) Facilities.

   The estimated total cost for this program is $566,700,000 ($75,441,000

for associated renal complications). HEW will account for $30,421,000

($28,639,000 for associated renal problems). Figure 11 illustrates the

total program expenditures by components. A discussion of these various

program components follows.

2. Screening, Diagnosis, Treatment, and Supportive Education and Administration

   With an accelerated program there is no expected change in the

target populations.

   a. Relevant Population and Program Component Costs

   The screening program for undetected hypertensive patients

will be accelerated so that rather than taking six years to reach

50% of the 43,500,000 individuals at risk, three years would be

sufficient to complete the task.

   An average of 7,580,000 individuals are expected to be screened

per year. Of these, 350,000 will have hypertension.[119/]

Screening costs are estimated at $1.25 per individual (as part of

a general screening program). Total screening cost is $9,480,000

Costs ($1,000,000)

Fig. 11.   Kidney Diseases Related to Hypertensive Vascular Disease,
            Hypothetical Program Costs at Accelerated HEW Expediture Level,
            Based on the Current State of the Art.

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per year ($569,000 attributed to associated renal problems). HEW
will contribute to this program an estimated $1,896,000 ($114,000
for associated renal problems).

If 15% of the 350,000 patients with positive screening tests
have curable hypertension (i.e., 52,500 and if the yearly treat-
ment and confirming diagnosis cost per individual is $1,000, then
total treatment costs for this group are $52,500,000 per year
(10% or $5,250,000 for associated renal complications).

If 85% of the 350,000 have currently non-curable hypertension
(i.e., 297,500), and if the estimated cost of treatment is $200 per
individual per year, total treatment costs for these individuals
are estimated at $59,500,000 per year ($3,570,000 for associated
renal disease).

Total costs for this component (and for all the surveyed popu-
lation) is now estimated at $528,680,000 ($37,421,000 for associated
renal complications). HEW's contribution is $1,896,000 ($114,000
for associated renal disease).

Financial support for education and administration in the
accelerated program is $10,000,000 to come from HEW with an additional
$3,330,000 anticipated from outside sources.

The total cost for this program component is $542,010,000
($50,751,000 for associated renal complications), of which HEW will
contribute $11,896,000 ($10,114,000 for associated renal complica-
tions).

b. Short-Term Benefits

The following are estimated short-term benefits:

(1) Newly Detected Potentially Curable (non-essential) Hypertensives:

   1) A 60% decrease in the immediate mortality of the individuals with curable hypertension is anticipated. From a base line of 290[120/] deaths occurring without this health program, there would be 170 prevented deaths (50% or approximately 90 reflect deaths avoided in patients having associated renal problems).

   2) A 60% reduction in prevalence of 31,500 from the base line of 52,500 cases is expected (50%, or 15,750, with associated renal problems).[121/]

   3) Morbid days are also expected to be reduced by 60% from a base line of 840,000[122/] to 504,000 (252,000 attributed to associated renal disease).

(2) Newly Detected Currently Non-Curable (essential) Hypertensives:

   1) An estimated 15% decrease in mortality from a base line of 2,140[123/] deaths to 320 (27% or 90 patients having associated renal disease).

   2) An estimated 20% reduction in the number of morbid days is anticipated, i.e., a decrease of 952,000 from a base line of 4,760,000[124/] (27% or 257,040 due to associated renal problems).

(3) All Surveyed Hypertensives:

   Total short-term benefits for the surveyed high-risk groups are 10,260 prevented deaths (2,370 with associated renal problems), a reduction in the number of cases by 85,500 (42,750 with associated renal problems), and a reduction in morbid days

by 7,395,200 (2,311,340 in patients with associated renal problems).

c. Long-Term Benefits

The following are estimated long-term benefits:

(1) Annual Long-Term Benefits

Under an accelerated program, there will be no change in the number of currently undiagnosed hypertensives who can be reached compared to the number reached in the intermediate program. Therefore, the annual long-term benefits will be identical with that group: an annual reduction of fatal end-stage uremia by 330 in currently non-curable hypertensives.

Total annual long-term benefits for all the surveyed high risk groups equal a reduction in fatal end-stage renal failure by 4,820 each year.

(2) Cumulative Long-Term Benefits

No changes from the intermediate program are anticipated. A reduction of 3,120 in the number of cases of fatal end-stage uremia will occur.

Total cumulative long-term benefits for all of the surveyed high-risk groups are 96,300 prevented cases of fatal end-stage uremia.

3. Research

Under an accelerated HEW funding program, an additional increase in the number of research projects is anticipated to encompass a total of 30 laboratory research study groups costing $40,000 per group, for a total cost of $1,200,000. Thirty clinical research study groups costing $50,000 per group will also be in progress yielding a total of $1,500,000.

Approximately $2,800,000 will be expended on 70 individual research

grants, averaging $40,000 per grant. Total HEW support for research is

expected to be $5,500,000. An additional $1,830,000 is anticipated

from outside sources.

4. Training

The training of physicians and allied medical personnel would cost

HEW approximately $1,425,000 with an additional $475,000 from other

sources.

5. Facilities

Under an accelerated HEW health program, $11,600,000 would be

expended on facilities. An additional $3,860,000 would come from other

sources.

A summary of the benefits and costs associated with this program is

found in Table XI.

Table XI

KIDNEY DISEASES RELATED TO HYPERTENSIVE VASCULAR DISEASES, HYPOTHETICAL PROGRAM
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | | | Long-Term Benefits | |
| | | | Reduction Per Year In | | | Reduction In End-Stage Uremia | |
Program	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Screening, diagnosis and treatment of individuals 17 years of age and over with known curable (non-essential) hypertension and non-curable hypertension and individuals who would have had undetected hypertension without the initiation of the program component.							
1. Screening	1,896 (114)	9,480 (569) 1/					
2. Diagnosis and treatment	———	519,200 (36,852)					
Sub-Total	1,896 (114)	528,680 (37,421)					
B. Education and administration for I.A.	10,000 (10,000)	13,330 (13,330)					
Sub-Total	11,896 (10,114)	542,010 (50,751)					
II. Research	5,500	7,330					
III. Training	1,425	1,900					
IV. Facilities	11,600	15,460					
TOTAL	30,421 (28,639	566,700 (75,441)	10,260 (2,380)	85,500 (42,750)	7,395,220 (2,311,340)	(4,820)	(96,300)

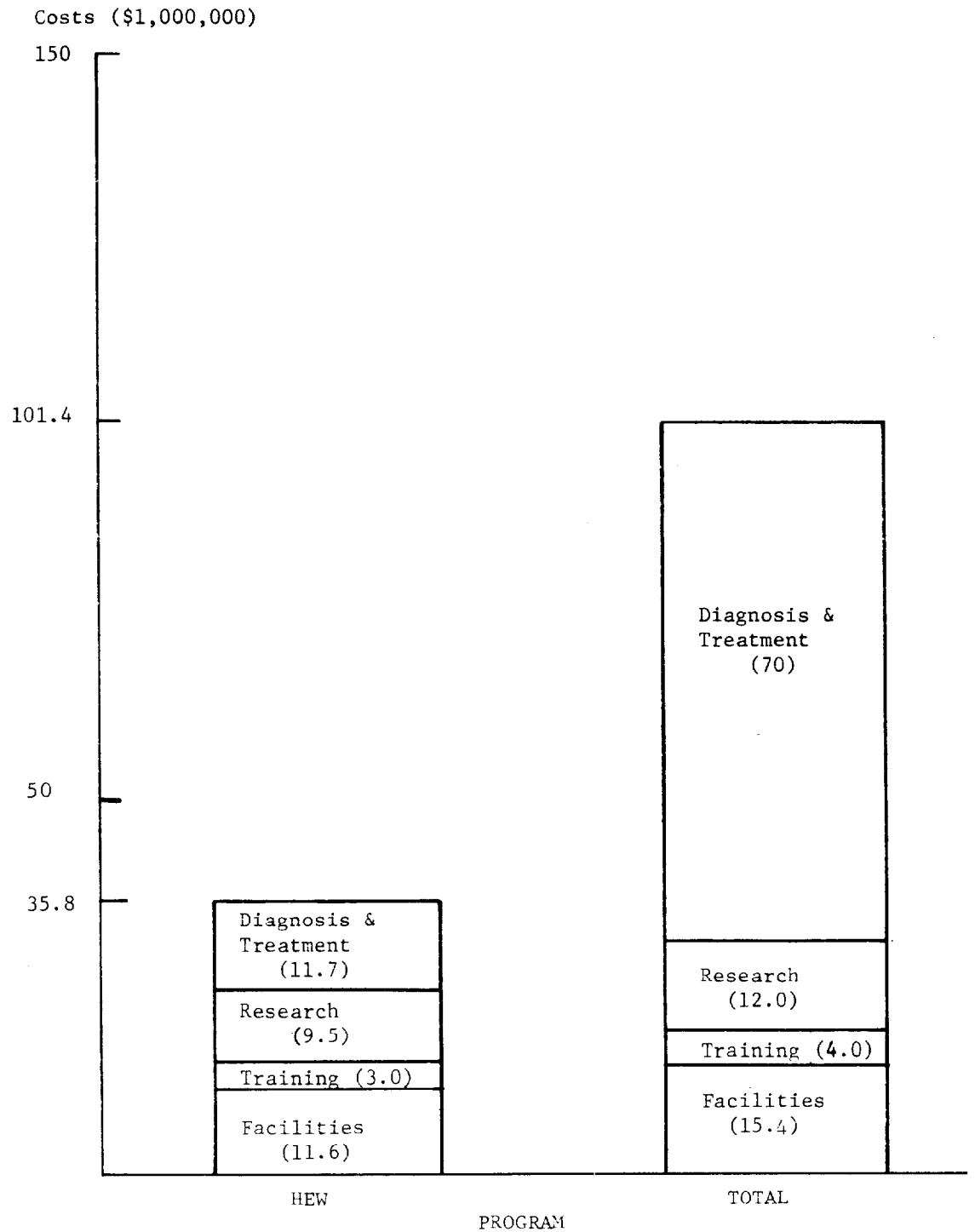1/ Figures in parenthesis refer to statistics attributable to renal complications.

E. Kidney Diseases Related to Hypertensive Vascular Diseases, Hypothetical
    Program for Fiscal Year 1975, at Accelerated HEW Expenditure Level,
    Based on the Expected Advanced State of the Art in 1975

1. Introduction

    This program has four components:

    1) Screening, diagnosis, treatment and supportive education and

        administration;

    2) Research;

    3) Training; and

    4) Facilities.

    The estimated total cost for this program is $878,675,000

    ($101,438,000 for associated renal problems). HEW will account for

    $37,899,000 ($35,832,000 for associated renal problems).

    Anticipated advances in the state of the art include:

    1) Advances in the knowledge concerning the underlying causes of

        hypertension, e.g., an appreciation of the renin-angiotensin

        mechanism;

    2) Specific therapy directed toward the underlying causes of hyper-

        tension, e.g., an anti-renin substance in a situation in which

        renin could be a cause of hypertension;

    3) Improved diagnostic tests for detecting hypertension, e.g.,

        advanced use of radio-isotopes, improved split renal function

        tests, implementation of photo-electric methods for determining

        high blood pressure, etc.; and

    4) Advances in the art of treatment of surgically treatable hyper-

        tension, e.g., improved vascular prostheses, etc.

    Figure 12 illustrates the total program expenditures by components

Fig. 12.   Kidney Diseases Related to Hypertensive Vascular Diseases,
          Hypothetical Program Costs for Fiscal Year 1975, at
          Accelerated HEW Expenditure Level, Based on Expected
          Advanced State of the Art in 1975.

including associated renal disease. A detailed discussion of the various

program components follows.

2. Screening, Diagnosis, Treatment, and Supportive Education and
   Administration

In 1975, the accelerated program activity reflects changes in the

population. The ratio of the 1975 population of individuals 17 years of

age and over to that of 1966 is estimated at 1.16.$\underline{125/}$ No changes in the

number of target population groups are anticipated.

a. Relevant Population and Program Component Costs

It is estimated that there will be about 104,400 patients with

non-essential hypertension from among currently known hypertensives

receiving more adequate treatment. At an estimated cost of $1,000

per individual treated per year, a cost figure of $104,400,000 (10%,

or $10,440,000, for those having associated renal disease) is arrived

at.

In 1975, there will be approximately 9,198,800 individuals with

essential hypertension among those currently known to be hypertensives.

This accelerated program is designed to affect 20% of these individuals.

As a result of improved treatment programs and further advances in

the state of the art, it is estimated that the treatment costs for

these individuals per year is $300.$\underline{126/}$ Assuming no additional expense

for screening, the cost for treatment and differential diagnosis for

the affected individuals is now estimated at $551,928,000 (6%, or

$31,116,000, attributed to associated renal problems).

In 1975, assuming no change in the current health services

system, there will be 50,460,000 individuals 17 years of age and

over who have not been seen by a physician in the previous year.

Again, it is assumed that the program will be able to reach 50%

of these patients (26,390,000) over a three-year period. With an

accelerated program effort, approximately 33% (8,797,440) of these

persons will be reached each year. Screening costs per individual

per year remain at $1.25 (as part of a general screening program).

The total cost for screening is estimated at $10,997,000 ($660,000

for associated renal dysfunction).$\underline{127/}$ HEW's share in this program

is estimated to be $2,199,000 ($132,000 for associated renal disease).

Of the anticipated 2,436,000 individuals who will have hyper-

tension detectable in these screening tests, it is assumed that 50%

will be detected over a period of three years; 406,000 will be

reached each year. Of this group, 15% or 60,900 individuals will

have non-essential hypertension. At a cost of $1,000 per year per

individual for treatment and differential diagnosis, the total cost

in this group is $60,900,000 (10% or $6,090,000 for patients with

associated renal problems).

Approximately 85% of the 406,000 hypertensive patients, or 345,100,

will have essential hypertension. At a cost of $300 per year per

individual for treatment, the total cost is estimated to be

$103,530,000 (6%, or $6,212,000, attributed to associated renal

diseases).

Total treatment costs for all groups are estimated at $820,758,000

($53,858,000 for associated renal problems). These costs are not

expected to be borne by HEW.

Total cost for this entire component (screening, diagnosis, and

treatment) is $831,755,000 ($54,518,000 for associated renal problems).

HEW will contribute $2,199,000 ($132,000 for associated renal problems).

The educational and administrative support for this program component is estimated to cost $15,460,000 of which $11,600,000 would come from HEW and an anticipated $3,860,000 would come from other sources.

Total cost for the entire program component is $847,215,000 ($69,978,000 for associated renal problems). HEW's contribution is $13,799,000 ($11,732,000 for associated renal problems).

b. Short-Term Benefits 128/

The following are estimated short-term benefits:

(1) Known Hypertensives with Potentially Curable (non-essential) Hypertension:

   1) A 65% reduction in immediate mortality is expected from a base line of 660 expected deaths (i.e., 430 prevented deaths of which 220 have associated renal problems). About 5 of the 65%, or 30 (20 from renal involvement), can be attributed to the advanced state of the art;

   2) A reduction of 65% in prevalence is anticipated, or 67,860, from a base line of 104,400 (33,930 with renal problems). About 5 of the 65% or 5,220 prevented cases can be attributed to advances in the state of the art (2,610 with renal problems); and

   3) A 65% reduction in the number of morbid days from a base line of 1,670,400, or a reduction of 1,085,760 days (542,880 of the reduction in morbid days would have associated renal problems). About 5 of the 65% reduction in morbid days, or 83,520, is attributed to advances in

the state of the art (41,760 are in patients with renal problems).

(2) Known Hypertensives with Essential Hypertension

    1) Mortality will be reduced by 55%, or by 31,860, from a base line of 57,930 (8,600 with associated renal problems). Forty of the 55% decrease, or 23,170, is attributed to advances in the state of the art (6,260 represent patients with associated renal problems);

    2) It is estimated that a 40% reduction of 735,900 in the number of cases from a base line of 1,133,760 will occur (198,690 with renal complications) all of which is attributed to advances in the state of the art; and

    3) A 50% reduction in morbid days, or 14,718,050, is anticipated from a base line of 29,436,160 (3,973,880 in patients with associated renal problems). Thirty of the 50% reduction, or 8,830,850 days are attributed to the advances in the state of the art (2,384,330 in patients with associated renal disease).

(3) Undiagnosed Individuals with Non-Essential Hypertension

    1) An estimated reduction in immediate mortality by 65%, or by 220, from a base line of 340 (110 with associated renal problems). About 5 of the 65% reduction, or 20, is attributed to advances in the state of the art (10 represent patients with associated renal problems);

    2) A 65% reduction, 39,590, in prevalence is also anticipated

from a base line of 60,900 (19,800 are patients with

associated renal problems). About 5 of the 65%

reduction, or 3,050 controlled cases are attributable

to advances in the state of the art (1,530 of these

would have had associated renal problems); and

3) Morbid days will be reduced by 65%, or 633,360, from a

base line of 974,400 (316,680 of these in patients with

associated renal problems). Five of the 65% reduction,

or 48,720 days are attributable to advances in the

state of the art (24,360 in patients with associated

renal problems).

(4) Undiagnosed Individuals with Essential Hypertension

1) A 55% reduction in immediate mortality, or 1,360, is

anticipated from a base line of 2,480 deaths (370 of the

prevented deaths would have been associated with renal

failure). Forty of the 55% reduction, or 990 deaths

avoided are attributed to advances in the state of

the art (270 in patients with associated renal problems);

2) Prevalence will decrease by 40%, or by 138,040, cases,

from a base line of 345,100 (37,270 would be cases

with associated renal disorders) all of which is

attributable to advances in the state of the art; and

3) A 50% reduction in morbid days, or 2,760,800, is

anticipated from a base line of 5,521,600 (745,420 in

patients with associated renal problems). Thirty of the

50% reduction, or 1,656,480 morbid days avoided may be

attributed to advances in the state of the art (447,250

of these in patients with associated renal disease).

(5) All Surveyed Hypertensive Patients

1) Immediate mortality will be reduced by 33,870 cases

(9,300 would have been patients with associated renal

problems). Approximately 24,210 of these are attributed

to advances in the state of the art (6,560 of these

would have been patients with associated renal problems);

2) Prevalence will be reduced by 981,390 cases (289,690

with associated renal problems). 882,210 of the total

reduction in prevalence is attributed to advances in the

state of the art (240,100 would have been patients with

associated renal problems); and

3) Morbid days will be reduced by 19,198,000 (5,578,860 in

patients with associated renal problems). Approximately

10,619,570 of the total reduction is attributed to

advances in the state of the art (2,897,700 in patients

with associated renal problems).

c. Long-Term Benefits[129/]

(1) Annual Long-Term Benefits

It is anticipated that 3,690 out of 5,680 individuals with

known non-essential hypertension (who would normally progress

to renal failure), can be prevented from developing end-stage

kidney failure each year. Approximately 5 of this 65% reduction

(a reduction of 280 cases/year) is attributed to advances in the

state of the art.

For the group of known patients with essential hypertension, it is expected that 4,830, or 30% of 16,100 individuals (who would develop renal failure), can be prevented from progressing to end-stage renal failure each year. About 20 of the 30% reduction (a reduction of 3,220 cases/year is attributed to advances in the state of the art.

In the group of individuals with undetected non-essential hypertension it is anticipated that a 65% reduction in end-stage uremia will occur from the base line of 640 (420 such cases averted each year). About 5 of the 65% reduction, or 30 cases of prevented end-stage uremia per year are attributed to advances in the state of the art.

In the group of individuals with undetected essential hypertension it is anticipated that a 30% reduction (540 cases) in end-stage uremia will occur from a base line of 1,810 cases of renal failure which would normally occur each year. About 20 of the 30% reduction, or 360 cases averted can be attributed to advances in the state of the art.

For all surveyed hypertensive groups the reduction in end-stage uremia is estimated at 9,480 per year. Approximately 3,890 of these cases are attributed to advances in the state of the art.

(2) Cumulative Long-Term Benefits

In the group of patients with known non-essential hypertension a 65% reduction in cumulative long-term cases of end-stage uremia is anticipated. This will amount to a reduction of 73,890

cases from a base line of 113,680. Approximately 5 of the 65%
reduction, or a reduction of 5,680 cases of end-stage uremia
can be attributed to advances in the state of the art.

In the group of patients with known essential hypertension
a 30% reduction in cumulative long-term end-stage uremia is
anticipated. This amounts to 96,590 cases avoided from a
base line of 321,960. About 20 of the 30% reduction, or 64,390
cases of end-stage uremia avoided, are attributed to advances
in the state of the art.

In the group of individuals with undetected non-essential
hypertension it is estimated that a 65% reduction in end-stage
uremia will occur. This will amount to 8,310 cases avoided
from a base line of 12,790 (5 of the 65% reduction, or a reduc-
tion of 640 cases, is attributed to advances in the state of the
art).

In the group of individuals with undetected essential hyper-
tension it is anticipated that a 30% reduction of 10,870 in
the number of cases of end-stage uremia will occur from a
base line of 36,240. About 20 of the 30% reduction, or a
reduction of 7,250 cases is attributed to advances in the
state of the art.

Total cumulative long-term benefits for all groups surveyed
are the prevention of 189,660 cases of end-stage uremia, 77,960
of which are attributable to advances in the state of the art.

3. Research

It is anticipated that in this hypothetical situation an estimated
$9,500,000 would be required from HEW and an additional $2,500,000 from

other institutions to support the various research programs.

4. Training

With the advanced state of the art, it is anticipated that there will be an additional requirement for the training of physicians and allied medical personnel requiring increased financial support amounting to $3,000,000 from HEW with an additional $1,000,000 to come from other agencies.

5. Facilities

Expenditures for facilities are estimated to be $15,460,000 of which $11,600,000 will come from HEW and an additional $3,860,000 will come from other sources.

A benefit-cost summary associated with this program is presented in ible XII.

6. Estimated Benefits Dependent on Research and Development 130/

Advances in the state of the art would produce a further 5% decrease in short-term mortality, prevalence, and morbid days for known patients with non-essential hypertension. A 5% long-term reduction in end-stage uremia is also anticipated.

A further 40% decrease in immediate mortality and prevalence is estimated for the group of patients with known essential hypertension. Also anticipated is an additional 30% decrease in morbid days and an additional 20% reduction in end-stage renal failure.

A summary of the short-term benefits dependent on research and development follows:

Table XII

KIDNEY DISEASES RELATED TO HYPERTENSIVE VASCULAR DISEASES, HYPOTHETICAL PROGRAM FOR FISCAL YEAR 1975
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON EXPECTED ADVANCED STATE OF THE ART IN 1975

Program	Expenditures		Short-Term Benefits			Long-Term Benefits	
			Reduction Per Year In			Reduction In End-Stage Uremia	
	HEW ($1,000)	Total ($1,000)	Mortality	Prevalence	Morbid Days	Per Year	Cumulative
I.A. Screening, Diagnosis and treatment of individuals 17 years of age and over with known curable (non-essential) hypertension and non-curable hypertension and individuals who would have had undetected hypertension without the initiation of the program component							
1. Screening	2,199 (132)[1]	10,997 (660)					
2. Diagnosis and treatment	— —	820,758 (53,858)					
Sub-Total	2,199 (132)	831,755 (54,518)					
B. Supportive education and administration	11,600 (11,600)	15,460 (15,460)					
Sub-Total	13,799 (11,732)	847,215 (69,978)					
II. Research	9,500 (9,500)	12,000 (12,000)					
III. Training	3,000 (3,000)	4,000 (4,000)					
IV. Facilities	11,600 (11,600)	15,460 (15,460)					
TOTAL	37,899 (35,832)	878,675 (101,438)	33,870 (9,300)	981,390 (289,690)	19,198,000 (5,578,860)	(9,480)	(189,660)

1/ Figures in parenthesis refer to statisti...

1) 24,210 prevented deaths (6,560 in patients with associated renal
   problems);

2) A reduction in prevalence by 882,210 (240,100 cases with
   associated renal problems); and

3) A reduction in morbid days by 10,619,570 (2,897,700 in patients
   with renal problems).

A summary of the long-term benefits includes:

1) An annual reduction in cases of end-stage kidney disease of
   3,890; and

2) A cumulative reduction in the cases of end-stage kidney disease
   of approximately 77,960.

All of these benefits have been based on the projected 1975 population
of individuals 17 years of age and over, which is estimated to be 16%
greater than the 1966 population. Disregarding the effects of population
changes, it is estimated that the following short-term benefits are the
result of research and development advances (using 1966 population figures):

1) Approximately 20,870 prevented deaths (5,660 in patients with
   associated renal problems);

2) A reduction in prevalence by 760,530 (206,980 cases with associated
   renal problems); and

3) A reduction in morbid days by 9,154,800 (2,498,020 in patients
   with associated renal problems).

Long-term benefits dependent on research and development are estimated
as follows:

1) An annual reduction in the cases of end-stage kidney disease of
   3,350; and

2) A cumulative reduction in the cases of end-stage kidney disease of
   67,210.

V. END-STAGE KIDNEY DISEASE

A. Introduction

This section describes programs which are concerned with alleviating the
effects of end-stage kidney disease--the result of a natural progression of
the infectious, hypersensitivity, hypertensive, and other kidney disease
processes. End-stage kidney disease is currently treated by two procedures,
chronic intermittent hemodialysis and kidney transplantation.

Approximately 50,000 people die as a result of uremia each year.[131]
Of these 50,000 about 79% are in the age group above 55, about 19% are in
the age group 15-54, and about 2% are in the age group 0-14. It has been
estimated that of the 50,000 annual end-stage uremia victims, about 8,000[132]
are ideally suited for dialysis therapy. While published estimates of
transplant candidates are not available, it is assumed for the purposes of
this report that about 6,000 of the ideal dialysis candidates are also ideal
transplant candidates. It is also assumed that an additional 2,000 persons
would be suited for transplantation but not for chronic dialysis.[133] Most
patients suitable for either procedure are within the 15-54 age group.

A schematic representing the progression of a patient into a hemodialysis
and/or transplant program is presented in Figure 13. With the development of
end-stage uremia, the patient becomes a candidate for chronic intermittent
dialysis or renal transplantation. Following the transplant procedure
(especially if a cadaver kidney has been used), the patient may require
temporary dialysis until the transplanted kidney is functioning normally.
If the transplant has been successful, the patient exits from the program.
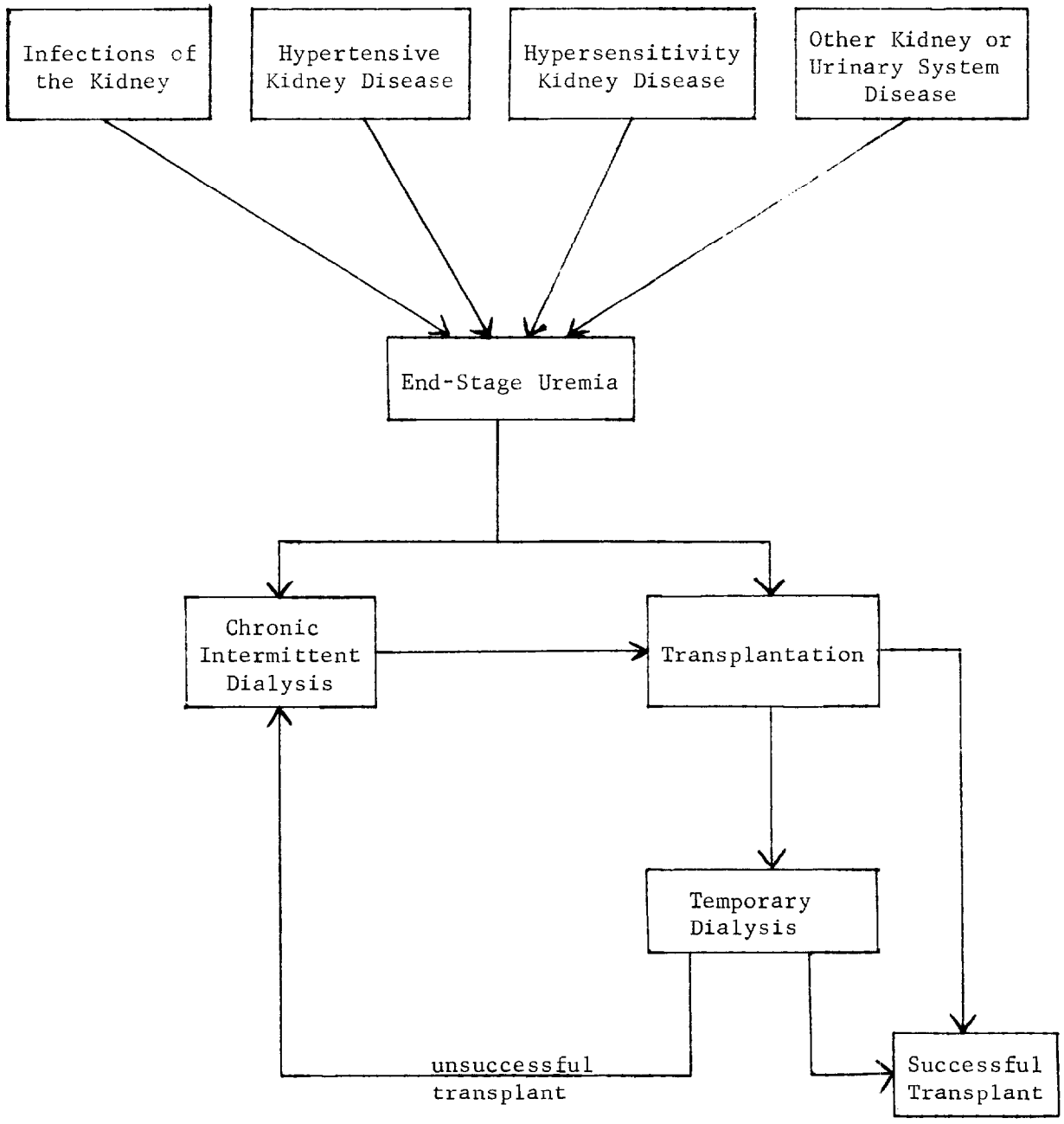If the transplant is unsuccessful, the patient is returned to the chronic

Fig. 13. Schematic of Transplant and Dialysis Patients.

intermittent dialysis program either for life or to await a second attempt of transplantation. Certain patients undergoing chronic intermittent dialysis therapy are suitable for transplantation and may be dialysed only until a matching donor kidney is available. Death, of course, can occur at any stage in the schematic.

Benefits attributable to the various dialysis programs presented in this section are measured in terms of reduction in mortality (lives prolonged) for the year in which the program is active.

In contrast to transplantation, which--if successful--is a one-time treatment, chronic dialysis is an ongoing type of treatment. All patients on dialysis who survive the first year must be treated in successive years. Thus, if during year x, there are 1,000 patients who are being maintained on hemodialysis, all of these patients less those dying during the year must be treated in subsequent years. If the mortality rate among these 1,000 dialysis patients is 20%, only facilities for some 200 new patients would be available for the 8,000 ideal dialysis candidates who will develop end-stage uremia during the next year. This situation is further complicated by the addition of those persons with unsuccessful transplants who require subsequently chronic dialysis treatment in order to survive.

The benefits attributed to transplantation are measured in terms of a reduction in mortality (patients cured). As is shown in Figure 14, the patient undergoing transplantation may, as a result of the procedure, a) be cured, b) die, or c) have an unsuccessful transplant subsequently he will enter a chronic dialysis program or be retransplanted. The benefits, as measured here take into account only those who are cured by the transplant procedure. Those persons not successfully transplanted who survive will, of course, become part of the chronic dialysis patient population or will be retransplanted.

Four specific programs have been postulated in this analysis. (See

Chapter 4, Research Methodology.) These are described in detail in the

following sections.

B. **End-Stage Uremia Program, Hypothetical Program at Current HEW Expenditure Level, Based on Current State of the Art**

1. **Introduction**

This program has five components consisting of:

1) Treatment by dialysis,

2) Treatment by transplantation,

3) Research,

4) Training, and

5) Facilities.

HEW costs and total costs of this program are presented in Figure 14.

As can be seen, total program costs are about $33,000,000 with HEW

expenditures at approximately $21,000,000. This hypothetical program is

essentially a reflection of the current allocation of funds for end-stage

uremia programs. A discussion of the various components of the program

follows.

2. **Dialysis Treatment**

As was indicated earlier, with the present operational state, only

about 8,000 of the 50,000 annual uremic victims are ideal candidates for

life-long chronic hemodialysis. Of these 8,000 annual dialysis candi-

dates about 750[134]/ are currently receiving treatment. Treatment costs

for some 225 of these treated patients can be attributed to HEW funding,[135]/

about 175, to the Veterans Administration[136]/ and the remainder to other
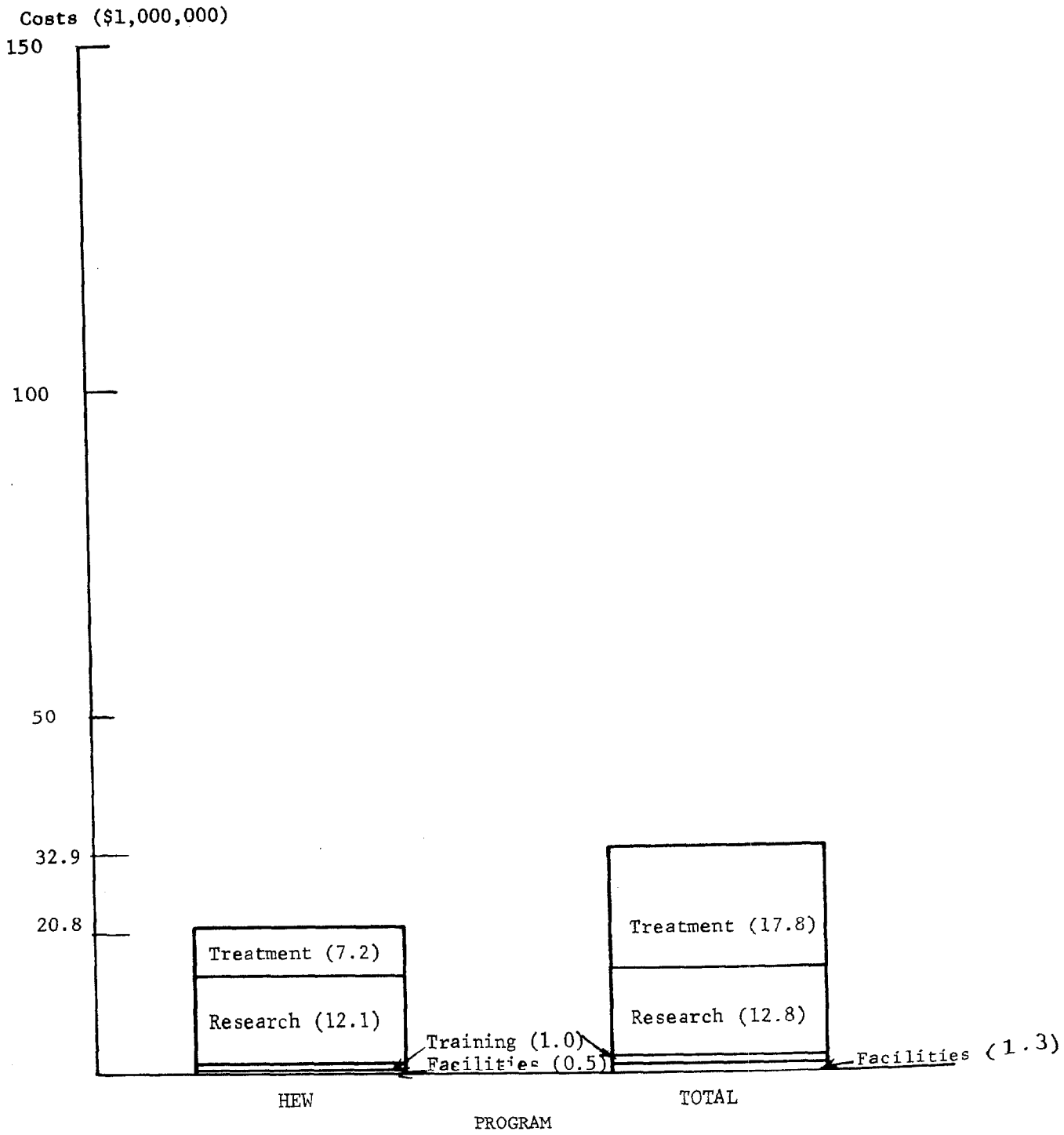
sources.

Fig. 14. End-Stage Uremia, Hypothetical Program Costs at Current HEW
Expenditure Level, Based on the Current State of the Art.

The present cost of chronic dialysis is approximately $15,000 per year per patient.[137/] The cost of dialysis as used here is derived from the cost in organized hospital dialysis centers supported by Government funds. If such a treatment were to be undertaken independently, private costs would run considerably higher. It has been estimated for the purposes of this study that the cost of private dialysis is on the order of $20,000 per year per patient. Current total expenditures for chronic dialysis therapy for the year are approximately $13,000,000 of which about $3,400,000 can be attributed to HEW.[138/]

In determining the benefits associated with this dialysis program, (see Section A above), it is assumed that treated patients suffer an annual 20% overall mortality.[139/] Approximately 600 lives are saved due to the total current program efforts. Of these, about 180 lives saved can be attributed to HEW funding.

3. Transplantation Treatment

As indicated above, approximately 8,000 individuals of the 50,000 who die annually from end-stage uremia are ideally suited for transplantation. Of these, approximately 300 patients per year are now being treated by transplantation. About 240 of these can be attributed to HEW funding.[140/] Those individuals who are not cured by transplantation and who survive, usually must revert to chronic intermittent dialysis in order to survive.

The cost of transplantation is estimated to be approximately $16,000 per patient per year.[141/] A total of $4,800,000 is spent in transplant treatments of which about $3,800,000 can be attributed to HEW.[142/]

Benefits associated with this transplant program are measured in terms of a reduction in mortality (patients cured, see Section A above). The average mortality rate among patients undergoing transplantation (with kidneys from living donors or utilizing "cadaver kidneys") is estimated to be about 40%.[143] Among the 60% who survive, about one-half are cured.[144] The remainder must revert to chronic hemodialysis therapy or adjunctive dialysis pending retransplantation. The number of patients cured as a result of the total program was found to be 90 of which 72 can be attributed to HEW funding.

4. Research

Expenditures in dialysis and transplant research totaled about $12,800,000 of which $12,100,000 was expended by HEW. Current HEW programs include intra- and extramural laboratory and clinical research and demonstration grants involving about 188 projects.[145]

5. Training

It is estimated that about $1,000,000 is being expended by HEW in the area of training and education of personnel to work in dialysis and transplant operations and related research programs. This value also reflects total U. S. training expenditures.[146]

6. Facilities

Expenditures for facility construction, expansion and remodeling are estimated to be about $1,300,000,[147] of which $500,000 is being expended by HEW.

No benefits were estimated for research, training and facility expenditures although quite obviously these funds will provide long-term benefits.

7. Summary

HEW expenditures for this program are about $21,000,000 with total program expenditures estimated at about $33,000,000. Total benefits derived from these expenditures are about 690 lives saved of which about 250 can be attributed to HEW.

A summary of benefits and costs attributed to this program are presented in Table XIII.

Table XIII

END-STAGE UREMIA, HYPOTHETICAL PROGRAM
AT CURRENT HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | |
| | | | Reduction in Mortality for 1966 | |
Programs	HEW ($ 1,000)	Total ($ 1,000)	HEW Program (No. of Lives)	Total Program (No. of Lives)
Dialysis	3,400	13,025	180	600
Transplant	3,840	4,800	72	90,
Research	12,100	12,800		
Training	1,000	1,000		
Facilities	500	1,300		
Totals	20,840	32,925	252	690

173a

**End-Stage Uremia, Hypothetical Program at Intermediate HEW
Expenditure Level, Based on Current State of the Art**

1. Introduction

This program describes what could be accomplished in an end-stage

uremia program with an "intermediate" funding level (i.e., two to

three times greater than the current level), and no change in the

current state of the art. There are five components in this program

including:

1) Dialysis treatment,

2) Transplantation treatment,

3) Research,

4) Training, and

5) Facilities.

The total cost of this intermediate program would be about

$70,500,000 of which HEW would contribute about $56,000,000. Figure 15

graphically presents the expenditures under this program. A description

of the program components follows.

2. Dialysis Treatment

There are now a total of 1,430 persons undergoing chronic dialysis

therapy due to the increase in funds supporting treatment. Of these,

about 880 can be attributed to HEW support. It is estimated that

because of the general availability of HEW funds, the VA will have about

200 chronic dialysis patients (an increase of 25 over the current level

program), and that there will still be about 350 patients being treated

through other resources.

It is anticipated that the annual cost of chronic dialysis will

remain at about $15,000 per year for patients supported by HEW and VA

funds, and that treatment by private resources will remain at about

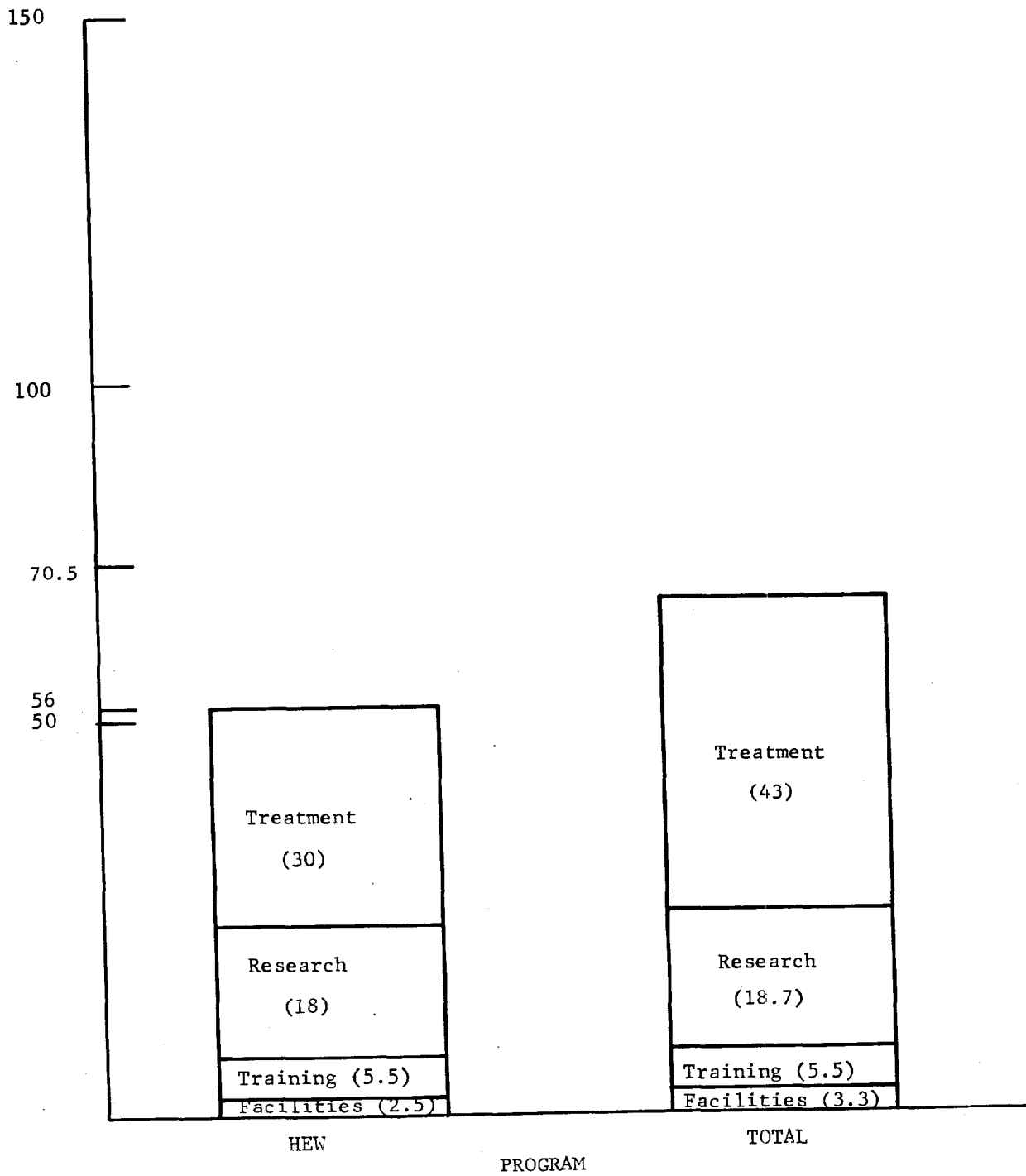$20,000. A total of $21,000,000 will be expended for dialysis treatment.

Costs ($1,000,000)

Fig. 15. End-Stage Uremia, Hypothetical Program Costs at Intermediate.
HEW Expenditure Level, Based on the Current State of the Art.

174a

It is assumed that there is no change in the 20% annual overall

mortality rate associated with chronic dialysis therapy. Total

benefits derived from this program are about 1,144 lives prolonged

of which about 704 can be attributed to HEW funding.

3. Transplant Treatment

This program provides financial support for 1,387 persons undergoing

kidney transplantations on an annual basis. Of these, about 1,187 can

be attributed to HEW funding. It is assumed that the cost of trans-

plantation will remain at $16,000, which as indicated previously,

includes the actual transplant procedure and pre- and post-operative

supportive therapy. The total cost of the transplant program is about

$22,200,000 of which HEW contributes about $19,000,000.

The benefits associated with this program are measured in terms of

a reduction in mortality (patients cured). It is assumed that the

general increase in funding has not markedly affected either the

mortality rate associated with this procedure (about 40%) or the cure

rate among surviving transplantees (about 50%). About 416 patients

are cured as a result of this program of which 356 can be attributed

to HEW funding.

4. Research

It is anticipated that research expenditures will increase to about

$18,000,000. While no specific research plans for dialysis and trans-

plantation will be outlined, it is anticipated that the existing 188

intra- and extramural research projects (please see previous program)

will increase in number and in some instances, in scope. Research

efforts to reduce the costs of chronic dialysis therapy and to improve immunosuppression and organ matching techniques will be intensified. It is estimated that an additional $700,000 will be expended by voluntary health agencies in dialysis and transplant research.

5. Training

HEW training expenditures for basic and on-the-job education for staff to work in dialysis and transplant therapy will increase to about $5,500,000 to measure up to the additional needs. No other expenditures in this area are anticipated from outside sources.

6. Facilities

HEW facility expenditures are expected to increase to about $2,500,000 with outside funding estimated to be about $800,000. This increase reflects the need for additional facilities for treatment of end-stage uremia patients.

7. Summary

HEW expenditures for this program are estimated to be about $56,000,000 with total program expenditures estimated at about $71,000,000. Total benefits in terms of reduction in mortality derived from the program are about 1,560 lives of which 1,060 can be attributed to HEW funding.

A summary of the benefits and costs of this program is presented in Table XIV.

Table XIV

END-STAGE UREMIA, HYPOTHETICAL PROGRAM
AT INTERMEDIATE HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | |
| | | | Reduction in Mortality for 1966 | |
Program	HEW ($ 1,000)	Total ($ 1,000)	HEW Program (No. of Lives)	Total Program (No. of Lives)
Dialysis	11,000	21,000	704	1,144
Transplant	19,000	22,200	356	416
Research	18,000	18,700		
Training	5,500	5,500		
Facilities	2,500	3,300		
	56,000	70,700	1,060	1,560

D. End-Stage Uremia, Hypothetical Program at an Accelerated HEW
   Expenditure Level, Based on Current State of the Art

   1. Introduction

   This program describes what could be accomplished in an end-stage

   uremia program with a funding level about 10 times that of the current

   program and with no changes in the state of the art, that is, assuming

   no significant technological or research advances. There are five

   program components including:

   1) Dialysis treatment;

   2) Transplantation treatment;

   3) Research;

   4) Training; and

   5) Facilities.

   The costs of this accelerated HEW program will be approximately ten

   times the cost of the current program, or about $210,000,000. Total

   program costs will be approximately $230,000,000 and take into account

   expenditures by other federal agencies and the private sector of the

   economy. Figure 16 graphically presents the costs of the accelerated

   kidney disease program assuming the current state of the art. Based

   on the nature of the two specific types of treatment, their results,

   the nature of the patient population available, and time and facility

   requirements, the assumption is made that about 30% of the patients

   will be treated by chronic dialysis therapy and the remainder by a

   transplant-dialysis therapy program. Descriptions of specific components

   of the total program and their associated benefits follow.
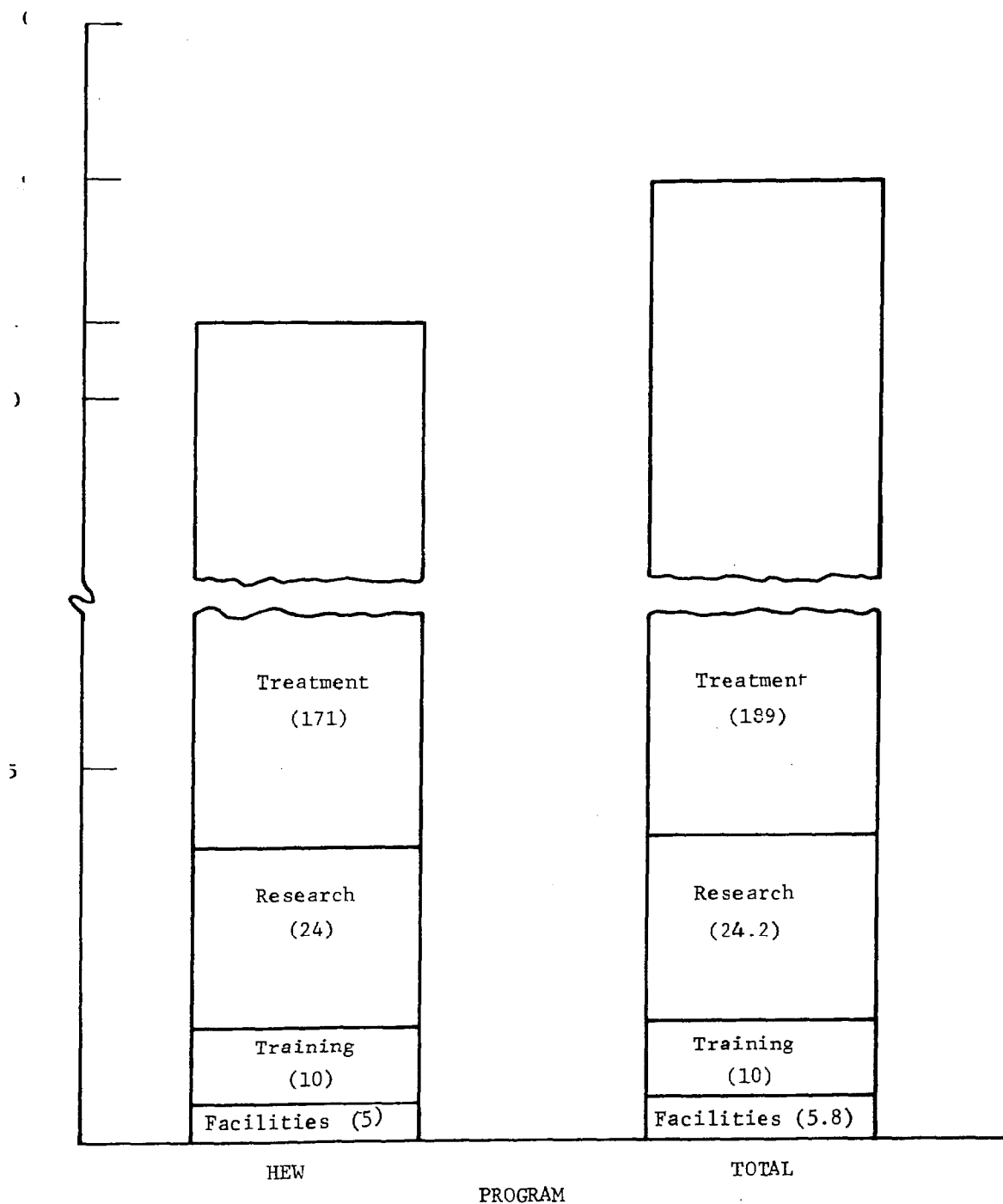
($1,000,000)

Fig. 16. End-Stage Uremia, Hypothetical Program Costs at Accelerated
HEW Expenditure Level, Based on the Current State of the Art.

2. Dialysis Program

A total of about 5,100 patients will undergo chronic dialysis therapy; 4,500 of these can be attributed to HEW funding. It is estimated that the Veterans Administration is now treating about 225 patients and that the cost of 350 patients is borne by private and other sources.

Under the circumstances of greater efficiency associated with mass treatment, it is assumed that dialysis costs have decreased to $10,000 per year per patient. HEW expenditures for dialysis treatment total approximately $45,000,000. As indicated above, it is assumed that because of the availability of HEW money, private and VA funding for dialysis will not change materially. The total costs for dialysis treatment are now estimated at approximately $55,000,000.

It is assumed that the overall annual mortality of 20% among dialysis patients has not changed. Applying this mortality factor to the patients undergoing therapy, it can be surmised that 3,600 lives will be prolonged by HEW funds. The benefits associated with the total program are about 4,100 lives prolonged. As indicated previously, these benefits are anticipated during the first year the program is in effect.

3. Transplant Program

Because of the availability of funds about 11,000 patients will now be treated on an annual basis. Of these, approximately 10,500 are attributed to HEW funding.

Under circumstances of more efficient mass treatment and utilization
of facilities an assumption is made that transplant costs per patient
have decreased from $16,000 to $12,000. Transplant costs for individual
non-HEW supported patients will remain at about $16,000. HEW expenditures
in support of transplantation treatment now total approximately $126,000,000.
Total expenditures in support of transplantation treatment are approximately
$134,000,000.

It is assumed that the mortality among the transplantees will be
decreased from 40% to about 35% due to the improved kidney:patient
matching which is possible under circumstances of a large program. Among
the 65% who survive about one-half are cured; the remainder return to
chronic dialysis therapy or adjunctive dialysis pending retransplantation

The number of patients cured as a result of the accelerated transplant
program is 3,575 of which 3,412 can be attributed to HEW support.

4. **Research**

While no specific research plans will be outlined, it is assumed
that HEW research expenditures have increased to a total of about
$24,700,000 in order to provide support for accelerated laboratory and
clinical research in dialysis and transplantation. Non-HEW research
expenditures primarily from voluntary health agencies are expected to
be slight in comparison, i.e., approximately $700,000.

5. **Training**

HEW training costs will increase to about $10,000,000 to provide
the necessary training and experience for support of professional
personnel involved in dialysis and transplant therapy. This training

will range from formal education in the form of postgraduate fellowships
to on-the-job training. It is estimated that HEW expenditures will reflect
the total costs in the area of training.

6. Facilities

Facility expenditures by HEW will increase to $5,000,000 and will
be used to aid in the construction of new treatment facilities and
expansion and modification of existing treatment facilities. Non-HEW
expenditures for facilities are expected to be no more than $800,000.

7. Summary

HEW expenditures for the entire program are about $210,000,000 with
total costs estimated at $230,000,000. It is estimated that the total
program benefits in terms of mortality avoided will be 7,675 lives
saved of which about 7,000 can be attributed to HEW funding. A total
of about 16,000 patients can be treated under this program. Of these,
about 4,900 will die as a combined result of either treatment. Of
those surviving, about 3,600 are cured of kidney disease; because of
transplantation, and about 4,100 are being maintained on chronic
dialysis.

A summary of the benefits and costs of the program are presented in
Table XV.

Table XV

END-STAGE UREMIA, HYPOTHETICAL PROGRAM
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON THE CURRENT STATE OF THE ART

| | Expenditures | | Short-Term Benefits | |
| | | | Reduction in Mortality for 1966 | |
Programs	HEW ($ 1,000)	Total ($ 1,000)	HEW Program (No. of Lives)	Total Program (No. of Lives)
Dialysis	45,000	55,375	3,600	4,100
Transplant	126,000	134,000	3,412	3,575
Research	24,000	24,700		
Training	10,000	10,000		
Facilities	5,000	5,800		
Totals	210,000	229,875	7,012	7,675

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E. **End-Stage Uremia, Hypothetical Program for 1975, Accelerated Funding Level and Advanced State of the Art**

1. **Introduction**

This program has five components consisting of:

1) Treatment by dialysis,

2) Treatment by transplantation,

3) Research,

4) Training, and

5) Facilities.

This program assumes that a number of advances have been made in the state of the art in dialysis and transplantation (see below). It is also assumed that progress in research and development in the primary kidney disease areas has not reduced the annual number of uremic deaths significantly because of implementation lag time. The major emphasis in this program is on transplantation since this procedure requires only a single treatment, thus about 60% of all patients are being transplanted. Total program costs are approximately $162,000,000 of which about $149,000,000 is being expended by HEW. A summary of program costs is presented graphically in Figure 17. A discussion of the various program components follows.

2. **Dialysis Treatment**

It is assumed that a simplified dialysis treatment has been developed which can be performed by the patient essentially independent of hospital or clinic facilities. Because of advances in the state of the art, the debilitating side effects of dialysis therapy have been largely eliminated. It is estimated that the annual overall mortality among chronic dialysis patients has been reduced to 5%. A total of about 12,000 patients are

;ts ($1,000,000)

Treatment

(132)

Treatment

(145)

(1.5)   ← Research →   (1.5)

Training (5)   Training (5.5)

Facilities   Facilities
(10)   (10)

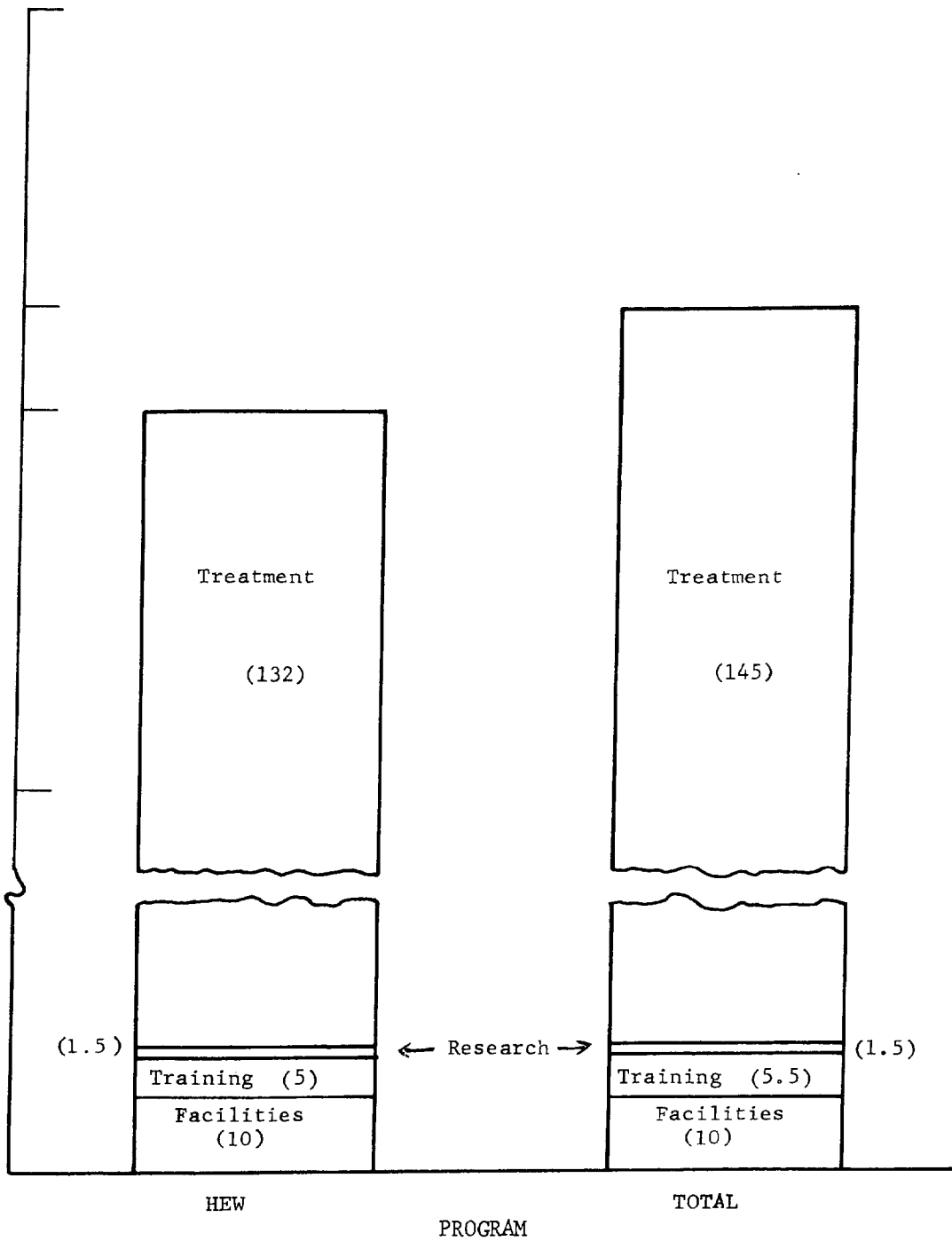HEW   TOTAL
PROGRAM

Fig. 17. End-Stage Uremia, Hypothetical Program Costs for Fiscal Year
1975, At Accelerated HEW Expenditure Level, Based on Expected
Advanced State of the Art in 1975.

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now being treated. Because of the availability of ample HEW funds only about 650 patients are being supported by other (VA and private) funds. The majority of these patients are "carry-overs" from previous years.

The cost to HEW and VA for maintaining dialysis patients has decreased to an absolute minimum of about $3,000 per patient per year largely due to advances in technology and supplies, including disposable materials. Costs for private patients are estimated to be about $5,000 annually. About $34,000,000 will be expended by HEW for dialysis treatment during the first year this program is in effect. Total costs for dialysis treatment are estimated to be about $37,000,000.

The total mortality avoided (lives prolonged) as a result of this program is about 11,400 of which some 10,800 can be attributed to HEW funding. Please note that these benefits are only for the first year that the program is in effect.

3. Transplant Treatment

Because of advances in the state of the art, the transplant program encompasses a highly effective organ matching and organ preservation system. Immunosuppressive techniques have become highly developed and successful. The procedure can now be carried out in most of the general hospitals in the United States. Overall annual survival among transplantees has increased from 65 to 90% and it is assumed that all survivors of the transplant procedure are cured. A total of about 17,750 kidney transplant procedures are being performed annually of which HEW supports about 16,350.

The cost of total patient management by transplantation within Federal programs has been reduced to about $6,000 because of easier matching of organs, a decrease in graft-rejection reactions, and a decreased need for adjunctive dialysis. Non-Federal transplantation costs are about $8,000 per patient.

The number of patients cured due to the total transplant program efforts is approximately 16,000 of which about 15,000 can be attributed to HEW funding.

4. Research

Because of previous research achievements, HEW research expenditures have decreased considerably to an annual level of $1,500,000. It is anticipated that there will be no support for research by other sources.

5. Training

HEW training expenditures are estimated to be $5,000,000 to provide for the necessary professional and allied personnel required in the treatment program. It is anticipated that because of the availability of HEW funds, there will be no expenditures from other sources for training.

6. Facilities

Facilities expenditures are estimated to be $10,000,000 and are used in establishing or maintaining the complex of treatment facilities required for this program. An additional $800,000 is estimated to be spent by other sources.

7. Summary

HEW expenditures for this program are estimated at about $148,000,000. Total program costs are estimated to be about $102,000,000. Total mortality

avoided because of this program will be about 27,000 lives of which about 26,000 will be attributed to HEW.

The above program sustains about 11,400 dialysis patients and about 16,000 transplantees during the first year the program goes into effect. The majority of the dialysis patients (about 90%) would be carry-over patients from previous years. These patients include transplant rejects as well as uremic patients unsuitable for transplantation.

A summary of the benefits and costs of this program is presented in Table XVI.

END-STAGE UREMIA, HYPOTHETICAL PROGRAM FOR FISCAL YEAR 1975
AT ACCELERATED HEW EXPENDITURE LEVEL, BASED ON EXPECTED ADVANCED STATE OF THE ART IN 1975

| Programs | Expenditures | | Short-Term Benefits | |
| | | | Reduction in Mortality for 1966 | |
	HEW ($ 1,000)	Total ($ 1,000)	HEW Program (No. of Lives)	Total Program (No. of Lives)
Dialysis	34,125	36,775	10,806	11,424
Transplant	98,100	108,100	14,715	15,975
Research	1,500	1,500		
Training	5,000	5,000		
Facilities	10,000	10,800		
Totals	148,725	162,175	25,521	27,399

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REFERENCES AND FOOTNOTES

1/ In 1964 there were 10,297 deaths recorded under ICD codes 600, 605, 607, and 640 (United States Department of Health, Education, and Welfare, Vital Statistics of the United States, Vol. II – Mortality Part A, Washington, D. C.: U. S. Government Printing Office, 1966, p. 1-68). The 1966 estimates were derived by multiplying the 1964 deaths by the ratio of the total United States population in 1966 versus 1964 (1.0246). Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex; July 1, 1960 to 1965," Population Estimates, Series P-25, No. 321, November 30, 1965, p. 11 and Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex; July 1, 1966, "Population Estimates, Series P-25, No. 352, Nov. 18, 1966, p. 1.

2/ It is estimated from the Division of Health Interview Statistics, National Center for Health Statistics, U. S. Department of Health, Education, and Welfare, report (unpublished), that in fiscal year 1965 the civilian non-institutional population had an estimated prevalence of 1,933,000 cases of infectious diseases of the kidney with an associated 37,535,000 days of restricted activity (an average of 19 days per case), 17,012,000 days of bed disability, and 4,121,000 work-loss days.

In order to take into account population changes for 1965 to 1966, the above morbidity statistics were corrected by a factor of 1.0156. This reflects the increase in population--Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex; July 1, 1966," Population Estimates, Series P-25, No. 352 (November 18, 1966), p. 1 and Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex; July 1, 1960 to 1965," Population Estimates, Series P-25, No. 324, (November 11, 1965), p. 11.

The corrected statistics yielded an estimated prevalence of 1,963,000 with an associated 38,197,000 days of restricted activity, 17,277,000 days of bed disability, and 4,185,000 work-loss days.

3/ Edward H. Kass, "Asymptomatic Infections of the Urinary Tract," Transactions of the Association of American Physicians, Vol. 69, 1956, p. 56-64.

4/ Alan L. Kaitz, and Elizabeth J. Williams, "Bacteriuria and Urinary-Tract Infections in Hospitalized Patients," The New England Journal of Medicine, Vol. 262, No. 9, (March 3, 1960), pp. 425-430.

Edward H. Kass, "Bacteriuria and Pyelonephritis of Pregnancy," Archives of Internal Medicine, Vol. 105 (1960), pp. 257-264.

Ruth Osterby Hansen, "Bacteriuria in Diabetic and Non-Diabetic Out-Patients," Acta Medica Scandinevica, Vol. 176, No. 6 (1964), pp. 721-730.

5/ Admissions to non-federal long-term general hospitals, non-federal short-term general hospitals and federal general hospitals were used to derive the hospitalized population. In 1965 these totalled 28,184,957. Hospitals, Vol. 40, Part 2 (August 1, 1966), p. 442.

In order to take into account population changes and to provide estimates for 1966, we corrected the 1965 hospital admissions by a factor of 1.56% (see Footnote 2 above) for a total of 28,625,000.

The resident population in nursing homes was derived from National Center for Health Statistics, "Characteristics of Residents in Institutions for the Aged and Chronically Ill in United States, April-June 1963," Vital and Health Statistics, Series 12, No. 2, p. 19, and amounted to 505,242 residents in 1963.

The Nursing Home population was corrected for increases in the population 65 years and over from 1963 to 1966 by a factor of 3.37% (the sources for this factor are the same as the ones described above for the hospital admissions). The new estimate is 522,000 residents in nursing homes.

The total relevant population for 1966 is estimated at 29,147,000.

6/ The number of pregnant females for fiscal year 1965 was taken from National Center of Health Statistics, "Current Estimates from the National Health Interview Survey, United States, July 1964 - June 1965," Vital and Health Statistics, Series 10, No. 25, November 1965, p. 5. The published number of 4,472,000 was corrected for the increase in population for females between 20 and 45 years of age. The correction factor was .57% (Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex; July 1, 1966," Population Estimates, Series P-25 No. 352 (November 18, 1966), p. 15, Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex; July 1, 1960-1965," Population Estimates, Series P-25, No. 324 (November 11, 1965), p. 11. The new estimate is 4,497,000.

7/ The estimated number of non-hospitalized diabetics was obtained from unpublished data from the National Center of Health Statistics. The unpublished estimates showed a prevalence of 2,385,000. Taking into the account the increase in population from 1965 to 1966 of 1.56% (see Footnote 2) we arrived at a new estimate of 2,422,000.

8/ See Footnote 4.

9/ 36,066,000 individuals divided by 6,462,520 cases of significant bacteriuria.

10/ Based on informed medical judgment.

11/ The estimate of 5% false positives was based on informed medical judgment.

12/ A "best estimate."

13/ 36,066,000 individuals in the target population times $0.25.

14/ Based on patient charges from Duke University Hospital, Durham, N.C.

15/ A "best estimate."

16/ A "best estimate."

17/ It was felt that 65% of the deaths could be attributed to the relevant population, or 6,800 from a base of 10,550 (see Footnote 1).

18/ Based on informed medical judgment.

19/ It is estimated that of the 19 average morbid days per individual (see Footnote 2), only 20% should be attributed to infections of the kidney because all of the high-risk groups have other primary diagnoses. The prevalence was multiplied by 19 days and then corrected by the 20% factor.

19A/ The specific relationship between infections of the urinary tract and end-stage kidney disease due to chronic pyelonephritis is still subject to conjecture. The estimates made here are based on the assumption of a cause and effect relationship between bacteriuria and chronic pyelonephritis.

20/ Based on informed medical judgment.

21/ Based on informed medical judgment.

22/ All the estimates in this paragraph were based on informed medical judgment.

23/ A "best estimate."

24/ A "best estimate."

25/ A "best estimate."

26/ Based on informed medical judgment.

27/ Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex, July 1, 1966," Population Estimates, Series P-25 No. 352 (November 18, 1966), p. 17.

28/ A "best estimate."

29/ C. Kunin, T. Southall, and A. J. Paquin, "Epidemiology of Urinary-Tract Infections. A Pilot Study of 3,057 School Children," New England Journal of Medicine, Vol. 203 (1960), p. 817.

30/ A "best estimate."

31/ The prevalence base used is the one derived from the 1% or 25,200 detected cases with significant bacteriuria among females 6 to 9 years of age.

32/ See Footnote 19.

33/ Based on informed medical judgment.

34/ Based on informed medical judgment.

35/ The estimated total number of detected cases of significant bacteriuria in the 6 to 9 years of age female group.

36/ Based on informed medical judgment.

37/ Based on informed medical judgment.

38/ See Footnote 27.

39/ S. Switzer, "Bacteriuria in a Healthy Population and Its Relation to Hypertension and Pyelonephritis," New England Journal of Medicine, Vol. 264 (1961), p. 7.

40/ Since 12,319,500 are expected to be screened each year and 1% or 123,195 are estimated to have significant bacteriuria, then if 85% (104,716) will be detected, 109,952 (104,716 x 105%) will show a positive screening test result.

41/ It was felt that about 60% of the 41,065 females 21 years of age and under can be reached. Of these 24,639,000 females, the screening program would reach one-half each year or 12,319,500. One percent of these or 123,195 would have bacteriuria.

42/ From a prevalence base of 123,195, 2,340,710 morbid days were calculated by using an average of 19 morbid days per individual (unpublished data from National Center of Health Statistics).

43/ Based on informed medical judgment.

44/ Based on informed medical judgment.

45/ Based on informed medical judgment.

46/ Based on informed medical judgment.

47/ Bureau of the Census, "Estimates of the Population of the United States by Age, Color, and Sex; July 1, 1960 to 1965," Population Estimates, Series P-25, No. 352 (November 18, 1966), p. 1, and Bureau of the Census, "Projections of the Population of the United States by Age, Sex and Color to 1990, with Extensions of Total Population to 2015," Population Estimates, Series P-25, No. 359 (February 20, 1967), p. 14.

48/ See Footnote 4.

49/ See Footnote 4.

50/ See Footnote 4.

51/ See Footnote 39.

52/ These include all high-risk groups adjusted for population changes.

53/ A "best estimate."

54/ Based on informed medical judgment.

55/ Based on informed medical judgment.

56/ Based on informed medical judgment.

57/ Based on informed medical judgment.

58/ Based on informed medical judgment.

59/ Based on informed medical judgment.

60/ Based on informed medical judgment.

61/ In 1964 there were 12,414 deaths recorded under ICD codes 590-594
(U. S. Department of Health, Education, and Welfare, Vital Statistics
of the United States, Vol. II - Mortality Part A, Washington, D. C.:
U. S. Government Printing Office, 1966, pp. 1-68). The 1966 estimates
were derived by multiplying the 1964 deaths by the ratio of the total
United States population in 1966 versus 1964 (1.0246).
(See Footnote 1.)

62/ It is estimated based on data from the Division of Health Interview Statistics,
National Center for Health Statistics, U. S. Department of Health,
Education, and Welfare report (unpublished), that in fiscal year 1965
the civilian non-institutional population had an estimated prevalence
of 104,000 cases of hypersensitivity diseases of the kidney with an
associated 4,011,000 days of restricted activity (an average of 40
days per case), 1,806,000 days of bed disability, and 765,000 work-loss
days. Taking into account the population increase from 1965 to
1966 (correction factor of 1.0156; see Footnote 2), the prevalence
is estimated at 106,000 with an associated 4,074,000 days of
restricted activity and 1,834,000 days bed disability as well as
777,000 work-loss days.

63/ See Footnote 61.

64/ A "best estimate."

65/ Based on informed medical judgment.

66/ Based on informed medical judgment.

67/ Estimated from unpublished data from the National Center for Health
Statistics.

68/ Based on informed medical judgment.

69/ Based on informed medical judgment.

70/ Based on informed medical judgment.

71/ Based on informed medical judgment.

72/ Based on informed medical judgment.

73/ John I. Levit, "The Prognostic Significance of Proteinuria in Young College Students." Annals of Internal Medicine, Vol. 66, No. 4, (April 1967), pp. 685-698, and Maurice B. Strauss and Louis G. Welt, ed., Diseases of the Kidney, Boston: Little, Brown and Company, 1963, pp. 80-88.

74/ Ibid.

75/ Ibid.

76/ Ibid.

77/ The estimate of 1966 deaths of 12,719 (see Footnote 61), was corrected by the change in population factor of 1.14% (see Footnote 46).

78/ Based on informed medical judgment.

79/ The 20,000 cases with hypersensitivity diseases were multiplied by 40 morbid days (unpublished data from the National Center for Health Statistics) to arrive at 800,000 morbid days.

80/ Based on informed medical judgment.

81/ Based on informed medical judgment.

82/ See Footnote 47.

83/ Maurice B. Strauss and Louis G. Welt, ed., Diseases of the Kidney, Boston: Little Brown, and Company, 1963, p. 505.

84/ In 1964 there were 69,634 deaths recorded under ICD codes 440-447 (U. S. Department of Health, Education, and Welfare, Vital Statistics of the United States, Vol. II – Mortality Part A, Washington, D. C.: U. S. Government Printing Office (1966), pp. 1-68). The 1966 estimates were derived by multiplying the 1964 deaths by the ratio of the total United States population in 1966 versus 1964 (1.0246). (See Footnote 1.)

85/ Based on informed medical judgment.

86/ It is estimated based on data from the Division of Health Interview Statistics, National Center for Health Statistics, U. S. Department of Health, Education, and Welfare report (unpublished), that in fiscal year 1965 the civilian non-institutional population had an estimated prevalence of 9,187,000 cases of hypertension with an associated 147,126,000 days of restricted activity (an average of 16 days per case), 54,638,000 days of bed disability (an average of 6 days per case), and 7,948,000 work-loss days (an average of 1 day per case). Taking into account the population increase from 1965 to 1966 of 1.0156 (see Footnote 2), the prevalence is estimated at 9,330,000 in 1966. To this is added an estimated 2,100,000 cases which are undiagnosed for a total of 11,430,000 hypertensives in 1966. Applying the same correction factors to the different classifications of morbid days and taking into account the undiagnosed cases, estimates of 181,280,000 days of restricted activity, 68,580,000 days of bed disability and 11,330,000 work-loss days are derived.

87/ H. Brainerd, et al., Current Diagnosis and Treatment, Los Altos, Calif.: Lange Medical Publication, 1966, p. 201.

Paul B. Beeson, and Walsh McDermot, Textbook of Medicine, Philadelphia: W. B. Saunders Co., 1963, p. 712.

88/ It is estimated that 20% of the costs of curing those currently curable hypertensives who have renal complications (50% of these hypertensives) is attributable to renal causes, or 10% of the total cost.

89/ A "best estimate."

90/ Twenty percent of the 85% (7,930,000) with currently non-curable hypertension.

91/ It is estimated that 20% of the costs of curing those currently non-curable hypertensives who have renal complications (27% of these hypertensives) is attributable to renal causes, or 6% of the total cost.

92/ See Chapter 6, Section B.a.

93/ Based on informed medical judgment.

94/ Since only .8% of the hypertensives are being considered it is assumed that they would account for .8% of the hypertensive deaths in 1966 or 570.

95/ Based on informed medical judgment.

96/ Estimated from unpublished data from the Division of Health Interview Statistics, National Center for Health Statistics, U. S. Department of Health, Education, and Welfare.

97/ Based on informed medical judgment.

98/ Since approximately 70% of the hypertensives are being considered in this group, it is assumed that these would account for 70% of the estimated deaths in 1966, or 49,940.

99/ Morbid days were obtained by multiplying the affected prevalence of 1,586,000 (see Footnote 86) by 16 days, the average number of days of restricted activity for each case (see Footnote 84).

100/ It was assumed that the average remaining life span of each hypertensive was 20 years, Henry Brainerd, et al., op. cit., p. 207, and the expected cumulative number of cases of end-stage uremia, 98,000, see Chapter 6 Section B.2.c.(2), was divided by 20.

101/ Again, assuming that the average life span of hypertensives is 20 years, the expected number of cumulative cases of end-stage uremia, 277,550, see Chapter 6, Section B.2.c.(2), was divided by 20.

102/ Based on informed medical judgment.

103/ Based on informed medical judgment.

104/ These estimates are derived from the present level of effort in the renal hypertension program of NIH.

105/ These estimates are derived from the present level of effort in the renal hypertension program of NIH.

106/ These estimates are derived from the present level of effort in the renal hypertension program of NIH.

107/ Two-thirds of the population has been estimated to have seen a physician within a year prior to interview. (National Center for Health Statistics, "Age Patterns in Medical Care, Illness, and Disability, United States - July 1963 - June 1965," Vital and Health Statistics, Series 10, No. 32, June 1966, p. 12.) The estimated population of the United States in 1966, 17 years of age and over is 130,640,750. (Bureau of the Census, "Estimates of the Population of the United States, by Age, Color, and Sex: July 1, 1966," Population Estimates, Series P-25, No. 352, Nov. 18, 1966, p. 14.) Applying a factor of one-third to the population, we arrive at a rounded estimate of 43,500,000.

108/ Based on informed medical judgment.

109/ A "best estimate" taking into account intermediate program level budgetary constraints.

110/ Since approximately 0.2% of the total hypertensives is affected each year by this program sub-component, 0.2% of the 71,347 estimated deaths or 140 deaths are expected to occur yearly without the new program effort.

111/ Prevalence was derived by taking 15% (see Footnote 85) of the expected 175,000 newly detected hypertensives, or 26,250.

112/ The prevalence of 26,250 was multiplied by the average 16 days of restricted activity per case of hypertension (see Footnote 86).

113/ Since approximately 1.5% of the total hypertensives is affected by this program sub-component, 1.5% of the 71,347 estimated deaths, or 1,070 deaths are expected to occur yearly without the new program effort.

114/ The prevalence of 148,750 [85% (see Footnote 85) of the expected 175,000 newly detected hypertensives] was multiplied by the average 16 days of restricted activity per case of hypertension (see Footnote 86).

115/ Assuming that the average life span of hypertensives is 20 years, the expected number of cumulative cases of end-stage uremia, 11,025, (see Footnote 117), was divided by 20.

116/ Again, assuming that the average life-span of hypertensives is 20 years the expected number of cumulative cases of end-stage uremia, 31,240, was divided by 20.

117/ Seven percent, of the 157,500 (15% of the 1,050,000 newly detected hypertensives), or 11,025 patients with currently curable hypertension are estimated to progress eventually to end-stage uremia without this program sub-component.

118/ 3.5% of the 892,500 (85% of the 1,050,000 newly detected hypertensives), or 31,240 patients with currently non-curable hypertension are estimated to progress eventually to end-stage uremia without this program sub-component.

119/ Based on informed medical judgment.

120/ Since approximately 0.4% of all hypertensives are affected each year by this program sub-component, 0.4% of the 71,347 estimated deaths or 290 deaths are expected to occur yearly without this new program effort.

121/ The prevalence was derived by taking 15% (see Footnote 87) of the expected 350,000 newly detected hypertensives.

122/ The prevalence of 52,500 was multiplied by the average 16 days of restricted activity (see Footnote 86).

12_/ Since approximately 3% of all hypertensives are affected each year by this program sub-component, 3% of the 71,347 estimated deaths, or 2,140 deaths are expected to occur yearly without this new program effort.

124/ The prevalence of 297,500 [85% (see Footnote 87) of the expected 350,000 newly detected hypertensives] was multiplied by the average 16 days of restricted activity per case of hypertension (see Footnote 86).

125/ The estimated population 17 years of age and over in 1975 is 150,554,000 (Bureau of the Census, "Projections of the Population of the United States by Age, Sex, and Color to 1990, with Extensions of Total Population to 2015," Population Estimates, Series P-25, No. 359, February 20, 1967, p. 14). The estimated population of 17 and over in 1966 is 129,746,000 (Bureau of the Census, "Estimates of the Population of the United States, by Age, Color, and Sex: July 1, 1966," Population Estimates, Series P-25, No. 352, November 18, 1966, p. 14). The ratio of the 1975 to 1966 population 17 years of age and over is 1.16.

126/ A "best estimate."

127/ It was assumed that approximately 30% of all hypertensives would have some associated renal problem and that 20% of their total treatment costs would be attributed to the treatment of the renal complication; therefore, 6% of $10,997,000, or $660,000, was attributed to renal complications.

128/ The vital statistics bases are derived in the same way as those in the 1966 accelerated program with the addition of 16% for anticipated increases in the population 17 years of age and over in 1975. Expected benefits take into account probable advances in the state of the art (see Chapter 6, Section E.6.).

129/ See Footnote 127.

130/ The benefits are the sum for all high-risk groups described and take into account 1) the 1975 population 17 years of age and over, and 2) the change in benefit rates due to advances in the control of the diseases discussed.

131/ The number of uremic deaths is based on conservative estimates from unpublished data gathered during a study conducted by the Research Triangle Institute, Research Triangle Park, North Carolina, entitled: Estimation of a Chronic Hemodialysis Population, March 1967.

132/ Ibid.

133/ The estimate of ideal transplant candidates was based on informed medical judgment.

134/ Unpublished data from the ongoing study, Socio-Economic Status of Dialysis Patients, Berkeley, California, University of California Medical Center.

135/ Ibid.

136/ U. S. Veterans Administration, unpublished data on Inpatient Mortality, Morbidity, and Treatment Costs, April 1967.

137/ B. H. Scribner, "Hemodialysis in the Treatment of Chronic Uremia," Abstracts, III International Congress of Nephrology, Vol. I: General Sessions--Symposia, Washington, D. C.: 1966, pp. 43-44.

138/ The total and HEW end-stage uremia programs costs for dialysis treatment were calculated on the basis of average annual costs of dialysis per patient.

139/ The dialysis-mortality estimate was based on informed medical judgment and unpublished data from the Kidney Disease Control Program, National Center for Chronic Disease Control.

140/ Public Health Service, U. S. Department of Health, Education, and Welfare, Kidney Diseases: 1968 Issue Paper and Appendices, Washington, D. C.: U. S. Government Printing Office, July 1966.

141/ Transplantation costs are based on informed medical judgment.

142/ The total and HEW end-stage uremia program costs for transplantation treatment are based on the average annual costs of transplantation per patient.

143/ Based on recent unpublished report "Fifth Report of the Human Kidney Transplant Registry," Department of Surgery, Harvard Medical School, the Peter Bent Bingham Hospital, the Massachusetts General Hospital, and the Harvard Computing Center.

144/ The transplant cure rate is based on informed medical judgment.

145/ Kidney Disease Issue Paper, op. cit.

146/ Training expenditures were based on unpublished data and expert opinion.

147/ Facility expenditures were based on unpublished data and expert opinion.

Chapter 6

The Cost of Treating All Patients with Chronic Kidney Failure

I. INTRODUCTION

Whenever consideration is given to the problem of kidney diseases, including end-stage kidney disease or progressive, ultimately fatal chronic renal failure, the question arises of the overall cost of treating all patients threatened by a uremic death, either with the aid of lifelong maintenance on dialysis or through an attempt at kidney transplantation whenever donor kidneys may be available. Although the original mission of the Kidney Disease Analysis Group did not include the preparation of an answer to this question it was felt that an analysis of this cost would be a natural corollary to the preceding analyses of costs and benefits of optimal programs aimed at the major primary kidney diseases and at end-stage kidney disease. In any consideration of possible programs for the amelioration of the kidney disease problem, the overall expense of treating all patients threatened with a uremic death regardless of the possible costs, for humanitarian reasons, represents one extreme in a broad spectrum of possible programs. It should therefore be ascertained to serve as a maximal bench mark for any intensive attempt at program analysis or planning.

II. APPROACH TO THE TOTAL TREATMENT OF END-STAGE KIDNEY DISEASE

A. General Assumptions

In this particular hypothetical situation it is assumed that a population of 50,000 individuals exists who are threatened by death from end-stage

kidney disease during the first year of the projected program. It is
known that approximately three-fourths of this population is above the
age of 60. The available modes of treatment are primarily lifelong dialysis
and transplantation.

For the purposes of this analysis an assumption is made that the
change in population size during the following few years can be disregarded.
Likewise this analysis assumes that any existing programs aimed at the
amelioration of primary kidney diseases do not affect to a significant
extent the figure of the vulnerable end-stage kidney disease population,
at this point. This analysis assumes that there are no restraints on the
availability of well-trained, competent physicians and other necessary
personnel to administer the available treatments and on facilities needed
for dialysis and transplantation. In reality such a "total push" program
could not be undertaken all at once because of the above restraints,
particularly because of the lack of sufficient qualified and willing physi-
cians.

B. Treatment Modalities

1. Conservative Treatment

Conservative treatment, primarily by diet and symptomatic therapy
will be reserved for a certain proportion of the vulnerable population,
namely those extremely old and beset with other intercurrent complicating
diseases which would make them unacceptable for major surgery and
extremely poor risks for prolonged dialysis. (Also included in this
list would be those individuals who, for a variety of other reasons are
not suitable for chronic dialysis, or who refuse either treatment.) It
is assumed that about 10,000 individuals out of the total vulnerable
population of 50,000 belong in this category. A more conservative view
may place the former figure at 15,000 to 20,000.

2. Transplantation

Projections for this treatment are based on the present state of the art. However, to make such a large-scale treatment program by transplantation possible at all it is assumed that efficient methods for collection of cadaver kidneys are in force and that existing legal barriers to tissue taking have been overcome. In addition, it is assumed that donation of kidneys upon death has become a popularly accepted procedure. In the subsequent calculation it is taken for granted that generally there will be no transplantation in patients over the age of 60 because of the highly increased operative risk and the many concurrent secondary disorders or complications found in this age group.

Of the 50,000 vulnerable patients, 10,000 will be treated by conservative means only (please see above). Of the remaining 40,000 candidates, 2,000 would meet ideal criteria for transplantation. Such criteria include not only optimal state of the patient's health (aside from his renal defect) but also the changes of optimal tissue matching with available kidneys. An additional 9,000 individuals would meet satisfactory criteria for transplantation.

In the group of ideal candidates it is expected that about 80 percent would be cured, and that approximately an additional 10 percent would survive but their transplanted kidneys would fail and they would require chronic dialysis for survival; an additional 10 percent would probably die directly due to the surgery or due to the sequellae of their operation or because of eventual immunosuppression therapy which makes them susceptible to overwhelming infections. In the group of satisfactory candidates the respective figures would be approximately

30 percent, 30 percent, and 40 percent.

On the average, it can be assumed that among the 11,000 patients in whom transplantation would be attempted, about 30 to 35 percent will be cured, an additional 30 to 35 percent would survive but would have to be returned to dialysis because of eventual failure of the transplanted kidney, and about 35 percent would die.

A small number of eventual secondary kidney failures may be expected among patients who were originally thought to be cured by transplantation. Most of these cases would probably represent development of glomerulonephritis in the transplanted kidney in patients in whom this disease was the original cause of renal failure. The assumption is made in the calculations to follow that these patients would be counted in the general reservoir of 50,000 vulnerable individuals who present themselves each year in need of treatment because of end-stage chronic kidney failure.

Based on the considerations and percentages mentioned above, of the 11,000 patients treated by transplantation each year, about 3,575 would be cured, an additional approximate 3,575 patients will have to be returned, eventually, to dialysis treatment, and approximately 3,850 will die during that year or soon thereafter.

3. Chronic Dialysis

Projections for this treatment are based on the current state of the art.

Of the 50,000 vulnerable patients, 10,000 will be treated by conservative means only, and of the remaining 40,000 candidates, 11,000 will be subject to transplantation (please see above). Thus, in any

one year there remain 29,000 patients who would be placed on chronic

dialysis. In reality, conservative medical opinion may hold that many

of these patients are not promising candidates for chronic dialysis. In

addition there will be a group of about 3,575 patients each year who would

be placed on chronic dialysis treatment because of eventual failure of

their transplanted kidney (see above).

Among the large group of individuals who are candidates for

chronic dialysis treatment there is a small group of highly suitable

patients for dialysis. Based on current experience in the United

States there is a yearly survival rate of 90 percent among such

individuals on chronic dialysis. The majority of vulnerable individuals,

however, cannot be considered good risks for chronic dialysis treatment

under present conditions. At present, such patients would not be

acceptable to the small number of existing dialysis programs in the

United States. On the other hand, there has been considerable experi-

ence with such patients in many European centers who are accepting

patients for chronic dialysis not on the basis of strict medical,

psychological and socioeconomic admission criteria, but on the basis

of patient need. The yearly survival rate for such patients is only

about 50 percent during the first year and varies from 50 to 90 percent

in subsequent years.

There is a great overlap in the groups which are considered ideal

for transplantation and ideal for chronic dialysis and since trans-

plantation will be attempted in those ideal or near-ideal for this

purpose, the majority of patients in the chronic dialysis program will at

best be satisfactory or high-risk patients. Based on the above considera-

tions and percentages, the overall assumption was made that the survival

rate in chronic dialysis for the first year of treatment will be 50

percent and that the survival rate in subsequent years among the remaining

patients will be 90 percent.

Thus, on the average it can be assumed that of the 29,000 new
patients treated by chronic dialysis each year, about 14,500 will
survive and 14,500 will not survive the first year of treatment.
The 14,500 survivors (now depleted of the poorest risks) will sub-
sequently have a 90 percent survival rate in the ensuing years.
In addition, of the approximate 3,575 brought into the dialysis
program each year after an initial unsuccessful attempt at trans-
plantation, approximately 3,218 will survive the first year because
they were derived from a strongly overlapping group of highly suitable
patients for either treatment.

III. CALCULATION OF COSTS

A. <u>Yearly Costs</u>

It is obvious that the mere calculation of the cost of the <u>first</u> year
of such a "total push" program would leave a misleading impression as to
the true long-term expense involved if such an approach is chosen. Because
of the significant rate of survival from year to year among the patients
treated by chronic dialysis the cost of extending treatment to all those
needing it in subsequent years will increase considerably with the passage of
time. It was therefore decided to calculate the actual cost of the treatment
of <u>all</u> individuals requiring it (the new group of vulnerable uremic patients
presenting itself each year and the patients on lifelong dialysis who are
survivors from previous years) for as many years as needed after the start of
the program until a year was reached which could be considered characteristic
of a "steady state." At this particular point in time the number of new
patients included each year in this program would equal the number of patients

dying in the same year, and in this situation a constant or near-constant yearly cost of the program would be reached.

Calculations to find a year in which a steady state would be reached showed that under the conditions of this program its yearly cost would increase greatly each year during the first 15 years, that the subsequent yearly increases in cost would be of a somewhat lesser magnitude but still highly significant, and that an asymptotic curve approach would show that the steady state would not yet be reached by the twenty-fifth year. Obviously one can expect research advances to occur well within the first 10 or 15 years (provided that current Federal research support will not be diminished because of the institution of a "total push" treatment program) and that these advances would modify greatly the respective efficacies of transplantation and hemodialysis and their costs. It was therefore decided that it would be unrealistic to report the cost of the hypothetical total push treatment program for end-stage kidney disease in terms of the eventual yearly cost of the steady state after 25 years. Rather, it was felt that it would be sufficiently indicative of the true costs to be expected to report the cost of the first year of such a program (the lowest yearly cost), the cost of the fifth year (a realistically foreseeable sum which is not likely to be influenced significantly by changes in the state of the art), and the cost of the fifteenth year (which is considerably higher than the cost of the fifth year and begins to approach the markedly higher eventual cost of the steady state year).

Based on the conditions in II A and II B, above, the yearly costs for this program were calculated for each of the first 15 years. As expected, the total cost of this treatment program rose considerably and progressively with each year because of the significant carry-over, from the preceding years, of surviving patients on chronic dialysis.

B. Present and Future Per Capita Costs

To obtain a realistic range of cost the calculations were done on the basis of two cost assumptions for each treatment modality:

1) A "present cost" figure of $16,000 per patient for transplantation, and a "present cost" figure of $15,000 per year per patient for chronic dialysis. The latter figure reflects as accurately as possible the present cost of chronic dialysis in a specialized dialysis center setting. (Dialysis at home was not yet considered well enough developed to be proposed for this large population. Moreover, it was recognized that the majority of patients to be treated by dialysis did not have the proper home setting, a vigorous and capable spouse, or other family conditions which are a prerequisite for successful home dialysis).

In the case of transplantation, the cost of $16,000 includes all medical and surgical expenses for the year in which the transplantation takes place, such as the necessary preliminary dialysis regimen and tissue matching, the surgery and all postsurgical treatments--dialysis, immunosuppression, and others--averaged out per patient (since some patients would require more and some less of these after-treatments).

2) An estimated "future cost" figure for each treatment modality which should reflect the decrease in cost of these treatments due to the mass operation effect, such as cost decrements due to greater efficiency of a large scale, well organized operation in dialysis, and savings due to more efficient large scale organization of the necessary preoperative, operative and postoperative activities and treatments in the case of transplantation, including greater efficiency in matching available kidneys to a large tissue-typed panel of recipients. The "future cost" figure for transplantation was thus set at $12,000 per patient and, in the case of dialysis, at $10,000 per patient per year.

As has been mentioned before, this hypothetical program could not be started in the intended scale since neither the necessary facilities nor a sufficient number of specially trained (and willing) physicians, surgeons, and paramedical personnel is available. The present analysis is carried out, nevertheless, in order to delineate the costs one must expect for such a total push endeavor.

The "present cost" figures are considered here to hold true for the first year of this hypothetical program, and may continue to influence costs in the early years until the gradual, improved organization and integration of the evolving mass effort permit the eventual cost reductions foreseen. The considerably lower "future cost" figures would become representative progressively during the subsequent years. To allow for all possibilities, the cost of the various years is reported in terms of a range between the higher "present cost" figure and the lower "future cost" figure.

It was decided not to charge the cost of conservative treatment to this total push program on the basis that the nature of the expenses of conservative treatment are not much different from those of other semi-terminal and terminal disease conditions, and that such costs would therefore not be borne by the Federal Government.

IV. RESULTS

The following results were obtained on the basis of the previously explained assumptions and calculations:

A. First Year

Based on "present cost" figures, the cost of treating 40,000 patients out of the total vulnerable population of 50,000 during the first year of this hypothetical program, by means of chronic dialysis or kidney transplantation, would be $611,000,000.

Note: If an attempt is made to treat all 50,000 vulnerable patients, the cost of this program during the first year will be $761,000,000.

If the calculation for the first year is based on the less likely "future cost" rate, the respective figures would be $422,000,000 and $522,000,000.

B. Fifth Year

The cost of this program in the fifth year of its existence will range between $1,043,600,000 (based on the low, "future cost" figure) and $1,543,415,000 (based on the higher, "present cost" figure). In this year, 102,161 patients will be treated under the program by transplantation or chronic dialysis.

C. Fifteenth Year

The cost of this program in the 15th year of its existence will range between $1,816,000,000 (based on the low "future cost" figure) and $2,702,000,000 (based on the higher "present cost" figure). In this year, 179,401 patients will be treated under this program, by transplantation or chronic dialysis.

In view of the fact that it is anticipated that research advances evolving during and after the first fifteen years of the program would introduce considerable improvements into both treatment modalities and would influence true costs significantly, projected expenses for the twentieth and twenty-fifth year of the program are not given. It should be noted, however, that the population which would require treatment during each year of this program will continue to grow and thus the yearly costs will increase, until a point beyond the twenty-fifth year at which a steady state will be reached.

V. DISCUSSION

The cost figures cited in the foregoing section are likely to be discouraging to any but the most determined advocates of a total push program. In reality, however, other factors which are more compelling than dollars are even more important in consideration of attempts at large scale treatment of end-stage kidney failure. Among these are 1) the nature of the population of 50,000 who present themselves each year with end-stage kidney failure, 2) the availability of trained and qualified physicians for the dialysis component of such a program, and of surgeons and physicians for its transplantation component, 3) the availability of the necessary competent and well-trained paramedical staff, and 4) the availability of necessary facilities for large scale chronic dialysis, be it in a hospital setting or in specialized dialysis centers associated with existing hospitals.

Assuming that one well-trained and willing physician is necessary for every 10 to 20 patients in a chronic dialysis program, the treatment of 40,000 patients would require the availability of 2-4,000 physicians for such an organized effort. The financial inducement would have to be high enough to attract this number of physicians to a new type of special medical activity which, on the whole, appears less attractive to most well-trained men because of the expected limitations and monotony of the treatment of a single, circumscribed disease condition.

The training of specialized paramedical personnel in sufficient

quantities may possibly represent less of a problem although, here too,

we face the spectre of robbing Peter to pay Paul--of withdrawing significant

numbers of veteran nurses from a field of action which is already badly

undermanned at present.

In either case, acquisition of the necessary new personnel could only

come about very gradually over a period of several years.

Provided that the necessary funds are available, construction,acquisition

and organization of relevant facilities may not be as forbidding a problem

as that of personnel; here too, however, considerable lead time will be

required until all the necessary facilities would be ready for operation.

The greatest obstacle to a total push attempt at treating all of the

50,000 yearly patients in chronic progressive renal failure is the medical

nature of this group. About three-quarters of this group are known to be

above the age of 60. A large proportion have many other concurrent dis-

orders (chronic heart disease, advanced atherosclerosis, hypertension,

diabetes, and others) which make them poor risks for kidney transplantation

and less than optimal patients for chronic dialysis. In addition, chronic

dialysis, to be successful, places large demands on the patient for emotional

stability, and experience has shown that only a portion of those who are

medically suitable for chronic dialysis possess the necessary emotional

(or minimal intellectual) prerequisites.

VI. FEASIBLE APPROACHES FOR END-STAGE
KIDNEY DISEASE TREATMENT

The elements for the planning of feasible approaches for end-stage

kidney disease treatment are contained in Chapter 5, which details

hypothetical programs for dealing with the problem of treatment for end-

stage kidney failure. For the purposes in Chapter 5, the assumption was

made, in these programs, that there had been no problem in recruiting the

necessary medical and paramedical staff, and that the necessary facilities

and funding were available. Every one of these problems exists, however,

and limits the speed in which either the "intermediate level" or "accelerated

level" programs can be translated into reality. Thus, any feasible program

for the near future must be envisioned within the confines of the following

existing restraints:

About 6,000 to 8,000 individuals in chronic renal failure are ideally

suited for chronic dialysis. About a similar number of patients are assumed

generally to be well suited for kidney transplantation. About 6,000

individuals in each of these groups overlap (i.e. about 2,000 individuals

in each of these groups is ideally suited for one treatment modality but

not for the other). Most patients suitable for either procedure are

within the 15 to 54 age group. Since it is self-evident that a number of

years is required for the training and organization of facilities for a

large scale chronic dialysis program, only the most suitable patients can

be considered as serious candidates for such a program in the near future.

In the case of transplantation, the availability of matching kidneys for

the suitable patients in the group of patients maintained by chronic

dialysis will determine the actual number of transplants attempted. Thus

the total number of individuals involved in a program feasible for

activation within the next few years will probably be in the neighborhood of 8,000 and certainly not more than 10,000.

For the chronic dialysis component of the program, a conservative assumption should be made, based on present experience, that in the beginning about one physician, two nurses and three to four technicians and aides would be required for every ten patients. This means that a going program for 8,000 patients would require 800 specialized physicians, 1600 specially trained nurses, and 4,000 specially trained technicians and aides. Because of this heavy demand for personnel the first year of such a program probably could not accommodate more than 800 new patients. Additional patients would have to be admitted to the program as additional personnel is trained and becomes available.

Since it appears that personnel is more of a critical factor than facilities, the availability of personnel (rather than facilities) is more likely to govern the number of patients included in this program during each of the subsequent years.

To reduce cost to a minimum, and based on experience obtained in dialysis centers and home dialysis programs thus far, it would probably be desirable to start new patients in full-time dialysis centers and to "graduate" subsequently those patients whose personality, family situation and home conditions are most suitable to home dialysis. Thus, eventually, the dialysis centers would harbor at any one time three types of patients: 1) new patients who are being stabilized and trained for home dialysis, 2) patients who have graduated from the center but who have gotten into trouble during home dialysis and who require, at this point, medically well supervised treatment, and 3) a hard core of patients who must be

dialyzed in a center setting since they or their family/home conditions are not conducive to home dialysis, or who have tried home dialysis and this attempt was not successful in the long run. In addition, at all times, each center would harbor a number of patients on a temporary basis who are having cannulae placed in their arteries and veins, or whose cannulae are being declotted, or who are suffering from other intercurrent disorders or complications.

Since the majority of dialysis patients would also be suitable candidates for transplantation an attempt would be made to transplant every patient for whom a matching kidney can be obtained. Thus, each center facility would embrace both treatment modalities and would consist of a combination of a chronic dialysis and dialysis training center, and a center for kidney transplantation and tissue matching activities. The transplantation staff would consist primarily of surgical teams and tissue matching laboratory staff; in addition, the internist/nephrologist staff responsible for the patients who are being dialyzed will serve for the medical backup of the transplantation staff.

With this general framework in mind and utilizing the elements and computations in Section V. of Chapter 5, it is possible to arrive at practical and feasible predictions concerning the cost of such a program and the overall number of patients which could be accommodated by it during each of the first few years, the number of patients who are likely to graduate from this program permanently each year because of successful transplantation, the number of individuals who would have to be maintained permanently with the aid of chronic dialysis, and the number of new patients which such a program could accommodate each year.

Assuming that the first year could not accommodate more than 800

patients, the subsequent yearly growth of this effort would depend on the

availability of the necessary personnel. Thus, the number of years required

until such a program could encompass 8,000 top (ideally suitable) candidates

from among the 50,000 new vulnerable individuals each year, will depend on

the availability of the requisite funds, manpower and facilities available

for expansion.