MANAGING TECHNOLOGY
IN HEALTHCARE

edited by
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and
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Kluwer Academic Publishers
Boston/London/Dordrecht
FORGOTTEN PATHS IN MEDICINE:  
THE CASE OF THE LOW PROTEIN DIET  
IN CHRONIC RENAL FAILURE  

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The current high and escalating costs of medical care in the U.S. has prompted a renewed interest in how new treatments become part of established medical practice. Moreover, recent findings have raised serious questions concerning the efficacy of several commonly accepted treatments.¹ As the related disciplines of medical technology assessment and adoption are fairly new, there is much controversy concerning underlying mechanisms and approaches to studying these phenomena.² Essentially, three perspectives on treatment assessment and adoption have started to emerge.

The rational-bioscientific perspective states that treatments move along a continuum from experimental to therapeutic by progressing through a series of scientific hurdles.³ These hurdles include tests conducted at local and global sites and controlled tests conducted prospectively with a randomly chosen sample. Implicit in this perspective is a belief that new treatments become part of established medical practice simply because they work and are safe.⁴ This view represents a type of technological Darwinism, wherein the bests technologies eventually win out.⁵

A second perspective, proposed by medical economists, focuses not as much on scientific determinants, but on economic ones. This perspective asserts that there are a number of strong economic issues that encourage the acceptance of certain treatments over others. These economic issues include: (1) the extent
to which resources are available to cover any treatment modality, including medical insurance and patients' ability to pay, (2) profit motives involved in the promotion of one treatment modality over the other, and (3) the reluctance to adopt new treatments when it cannibalizes investments in earlier approaches.

A third view, from an institutional perspective, stresses the role of historical events, present assumptions and future expectations in determining which treatment modalities become a part of accepted medical practice over time. This view, in contrast to the rational-bioscientific perspective, recognizes that the "best" technology may not necessarily be the one that is eventually adopted. Instead, many social, cognitive, and political forces shape the evolution of technologies irrespective of what is economically or technologically optimal.

The institutional perspective holds that technologies develop in a path dependent, cumulative manner, and that institutionalized rules and practices surrounding the technology create a context that shapes the cognition of technology champions and proponents. For example, Powell asserts that path dependencies supported by self-reinforcing feedback mechanisms influence the development and persistence of institutional structures and practices, of which include suboptimal technological arrangements. This argument is concerned with situations in which initial choices constrain future options. That is, certain procedures and systems persevere because of path-dependent patterns of development and thus may lock out others that would have proved more effective in the long run.

People operating within well-established institutional bounds tend to conform to a series of beliefs, not simply because they are the best, but because conformance confers legitimacy. Consistent with this perspective in bioscience is the "dominant-doctor" hypothesis which suggests that medical practice in a given region tends to follow the treatment norms of the local dominant physician, not because that doctor is powerful, but because the imitating physicians will secure legitimacy for themselves. All of these factors can serve to influence what technologies are adopted.

Each of these perspectives, when considered alone, encourages a microanalytic view, downplaying or ignoring the dynamic interaction among different forces that could cause certain approaches to be favored over others. When technological, economic or institutional forces are isolated from one another, their patterns of interaction are ignored. As a consequence, the analysis of the evolution of technology becomes mired in one perspective, losing both comprehensiveness in understanding the phenomenon, and generalizability of the findings to other settings. Moreover, these three perspectives disagree on the generative force that propels new treatments toward acceptance: the rational-bioscientific perspective focuses on technological determinants; the economic perspective focuses on resources and their utilization; and the institutional perspective focuses on conformance, legitimacy and path dependencies.

This paper shows how these viewpoints are not mutually exclusive. Technological, economic and institutional forces are all important in determining technology assessment and adoption. People do choose technologies that work and that are safe, but within a "choice set" prescribed by institutional fields and influenced by path dependencies. Economic forces play a role, but only occasionally do they possess the power to dislodge entrenched trajectories. More commonly they work to reinforce existing trajectories. In this way, technological, economic and institutional forces combine to shape the rate and direction of technology selection and evolution.

Together, these forces create what has been labeled as technological trajectories. Trajectories represent paths along which technologies develop within a body of knowledge that includes beliefs about what is possible, purposes for the technology, a "set of evaluation routines and procedures", and a definition of the "relevant" problems. These trajectories are shaped as much by advances in science and technology as they are by market forces. Yet, advances along a trajectory are somewhat predictable in the long run as previous choices and future expectations shape technology evolution. Specifically, technological advances occur in a cumulative manner as initial choices dictate future opportunities; some or all of the investments are irreversible and may not be easily deployed to pursue other approaches. Moreover, trajectories are also shaped by the institutionalized practices and commonly held beliefs that constrain the development of technologies in certain directions.

The concept of technological trajectories is particularly useful to examine a puzzling facet of renal failure treatment in the U.S. Specifically, there is little emphasis on low-technology alleviative approaches such as dietary protein restriction (DPR) to postpone the onset of end-stage renal failure. Instead, there is far greater emphasis on research attention and treatment resources on high-technology end-stage intervention techniques such as dialysis and renal transplantation -- treatments that can cost over one hundred thousand of dollars per patient over the life of the treatment. This emphasis is puzzling as many physicians in other countries, notably Italy, have demonstrated the benefits of DPR, either as an independent approach to treat chronic renal failure, or as a complement to other end-stage intervention approaches. Diet therapy for renal failure is a safe and inexpensive way to treat many kidney patients and may postpone or even prevent the need for more aggressive invasive techniques such as dialysis or renal transplantation. Despite these potential benefits, DPR has not been extensively pursued in the U.S.

Paul David's work showed how it is possible to be stuck to an "inferior" technology even though a new and "better" technology might be available. This article explores a symmetrically flip side of this observation. Specifically, we explore how and why it is possible for us to have forgotten old but "useful" technologies as advances are made at the frontiers of science and technology and why it is difficult to return to neglected technologies once these newer technologies have been adopted. We accomplish this by identifying the forces that constitute and sustain dialysis and transplantation over DPR. Through our description of the approaches to deal with renal failure, we will illustrate two aspects of trajectories that are salient to this issue. First, our description of the development of each treatment trajectory for renal failure will illustrate how they are interrelated with one another: dialysis and transplantation have demonstrated a complementary relationship with one another and a conflicting relationship with
DPR. Second, we want to offer the concept of technological interiors in contradistinction to the concept of technological frontiers. Technological interiors, for us, represent paths that were initially explored but not developed while progress was being made out on the frontiers. We will argue that DPR lies in the interiors of renal failure treatment technologies while dialysis and transplantation lie at its frontiers. We will also explore some of the forces that have kept this field at the frontiers and away from the interiors leading to the neglect of DPR by examining the historical development of kidney treatment trajectories in the U.S.23

The paper is organized as follows. First, we provide an historical description of the development of renal failure treatment trajectories in the U.S. To understand why DPR has not been adopted more widely in the U.S., we focus on forces that have reinforced one trajectory in comparison to another. Wherever appropriate, we compare practices in the U.S. with those in Italy where DPR is more prevalent. This discussion sets the stage for an analysis of relationships between trajectories and an exploration of technological interiors. Finally, we discuss the implications of the emerging theory for clues on how we might curtail escalating health care costs in the U.S.

AN HISTORICAL DESCRIPTION OF CHRONIC RENAL DISEASE TREATMENTS: COMPLETE AND PARTIAL CARE

Chronic renal failure is a progressive disease that is thought to be initiated by prolonged hypertension or some other insult to the nephrons. Somewhat similar to atherosclerosis, once initiated, the disease will usually progress inexorably towards its end-stage where kidney failure is imminent (see Figure 1). Chronic renal failure may not produce many severe symptoms until its end-stage, although it is common for patients with declining kidney function to experience symptoms such as edema, muscle cramps, nausea, and fatigue.24

Before 1960, little could be done for patients suffering from chronic renal failure, though there were physicians that reported some success with a low protein diet. After 1960, three main approaches to treat chronic renal failure started to develop more rapidly. These are dialysis, renal transplantation and dietary protein restriction (DPR). The treatments are discussed below.

Dialysis, the removal of toxic solutes from the body through an artificial kidney machine, is the most commonly used treatment in the U.S. The focus is on using a machine that is capable of performing much (but not all) of the kidneys’ function. Although there is no denying that dialysis saves lives, it has come under criticism. It has been called a "halfway technology" meaning that dialysis does not actually cure renal failure, rather it treats it by eliminating nitrogenous wastes and maintaining blood chemistry, albeit imperfectly.25 It is also an expensive treatment, generally costing over $30,000 annually.26

The primary alternative to dialysis in the U.S. is renal transplantation. Transplantation is theoretically superior to dialysis in that it cures chronic renal failure by replacing damaged kidneys with a functioning one. In practice however, transplants are plagued by technical problems and the body’s immune system. Difficulties with immunosuppressive drugs and their side effects have proved particularly vexing to transplant surgeons and their patients.27 Like dialysis, transplantation is very expensive, cost estimates range from a low of $50,000 to well over $100,000 for one surgery and follow-up care.

FIGURE 1

HOW DOCTORS EXPECT KIDNEY DISEASE TO PROGRESS

![Graph showing progression of kidney disease]

Source: Klay, 1981.

Dietary Protein Restriction (DPR) is a third approach for treating chronic renal failure. The focus is on first arresting kidney function decline. Since one of the main functions of the kidney is to remove nitrogenous waste derived from protein catabolism, minimizing protein intake reduces the workload of the kidneys. DPR is thought to be most useful if administered before the disease has reached end-stage. Though kidney deterioration seldom reverses itself, DPR may slow the decline of kidney function, sometimes arresting it altogether. DPR is also an inexpensive low-risk treatment as protein deficiency is considered a manageable risk.28

These three treatment approaches for chronic renal failure are representative of options for treating many types of chronic illnesses in that both less invasive and more invasive treatments exist. Each treatment approach represents a trajectory, and the mix of treatments actually employed reflects the larger institutional approach towards health care that any society embraces. In particular, the mix of treatments says much about how specific societies choose between invasive and non-invasive treatments, at what stage in a diseases progression do physicians of that society intervene, and whether the choice of treatments represents a true cure, or a halfway technology that merely treats the symptoms without addressing the underlying causes for the disease. Moreover, the mix of approaches pursued has significant implications regarding the cost of medicine as well as how a medical system is structured. We believe that
unraveling the forces that sustain (or impede) each of the three kidney treatment approaches will provide us with an understanding of the larger medical system in the U.S. We undertake this task by providing an historical account of the development of the three treatments. A summary of the main historical events is summarized in Table 1.

**TABLE 1: KEY HISTORICAL EVENTS IN THE DEVELOPMENT OF TECHNOLOGIES TO TREAT CHRONIC RENAL FAILURE**

<table>
<thead>
<tr>
<th>Year</th>
<th>Dialysis</th>
<th>Transplantation</th>
<th>DPR</th>
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<tbody>
<tr>
<td>1827</td>
<td>Richard Bright documents renal failure patients' symptoms including protein in the urine.</td>
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<td>1854</td>
<td>Thomas Graham demonstrates movement of various types of solutes through a membrane. He coin the term &quot;dialysis.&quot;</td>
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<td>1869</td>
<td>Lionel Beale's textbook on kidney appears</td>
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<tr>
<td>1905</td>
<td>Otto Folin experiments with a very low protein diet to reduce urea in patients.</td>
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<td>1906</td>
<td>First attempts at clinical renal transplantation on humans using animal donors.</td>
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<tr>
<td>1913</td>
<td>John Jacob Abel develops the first hemodialysis machine at Hopkins.</td>
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<tr>
<td>1920s</td>
<td>DFR extensively used by Thomas Addis in his Stanford Lab. Later reports maintaining patients for well over a decade on DFR.</td>
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<tr>
<td>1936</td>
<td>The first human to human kidney transplantation reported in the Soviet Union. The patient dies in a few hours.</td>
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<tr>
<td>1940s</td>
<td>Willem Kolff successfully treats acute renal failure patients with dialysis in occupied Holland.</td>
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<tr>
<td>1960</td>
<td>Dr. Belding Scribner develops a shunt that permits the repeat dialyzing of chronic renal failure patients.</td>
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<tr>
<td>1962</td>
<td>First drug therapy for immunosuppression is implemented.</td>
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<tr>
<td>1963</td>
<td>Drs. Giordano and Giovannetti show how patients' nutritional balance can be maintained on a very low protein diet in CRF.</td>
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<td>1965</td>
<td>Public Health Service funds 12 dialysis test centers around the US.</td>
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<tr>
<td>1969</td>
<td>Public Health Service backs seven transplant centers around the U.S.</td>
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<tr>
<td>Year</td>
<td>Event</td>
<td>Details</td>
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<tr>
<td>1972</td>
<td>The End-stage Renal Disease program is passed by the US Congress as an amendment to Social Security. The program funds nearly all dialysis and renal transplantation treatments. Program costs are estimated to be $35-75 million in 1973, they are in fact $240 million.</td>
<td>Dr. Bergstrom successfully employs a very low protein including amino acid supplementation in Sweden. Dr. Walser commences a series of successful patient trials of DPR in the US. He also introduces ketoacid supplementation.</td>
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<td>1974</td>
<td>Dr. Walser presents data at a major European Conference that a DPR/ketoacid regimen not only reduces symptom but actually slows the progression of CRF. The reaction at the conference is one of &quot;surprise.&quot;</td>
<td>Immunosuppression therapy with cyclosporine improves transplanted organ survival time.</td>
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<tr>
<td>Late 1970s to early 1980s</td>
<td>Due to rapidly escalating costs of the ESRD program, legislation is proposed to expand the use of cheaper home dialysis. As a result of effective lobbying by corporate interests, the bill is severely weakened. Home dialysis continues to recede in the US while for-profit in-clinic dialysis increases.</td>
<td>DPR funding is continued in Italy by the new, more centralized funding plan. No comparable funding for DPR treatments exists in the US. Ketoacids still considered experimental by FDA. Dr. William Mitch &amp; colleagues introduce a method to more accurately track kidney function decline.</td>
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<td>1981</td>
<td>A new federal law in the US is passed forbidding the buying and selling of organs. This hinders the development of an infrastructure for &quot;organ transactions.&quot;</td>
<td>Dr. Barry Brenner introduces the hyperfiltration hypothesis. This renews attention toward DPR.</td>
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<td>1983</td>
<td>Modification of Diet in Renal Disease (MDRD) study commences. An act of Congress was required to get the study going. This 10 year prospective randomized</td>
<td>Problems with cyclosporine leads to aggressive search for new immunosuppressants. FK506 is one such substitute, but also suffers from deficiencies.</td>
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<tr>
<td>1988</td>
<td>Problems with cyclosporine leads to aggressive search for new immunosuppressants. FK506 is one such substitute, but also suffers from deficiencies.</td>
<td>Xenograft experiments are renewed in earnest. One patient is given a baboon organ, yet dies in a few hours. FK506 is approved &amp; starts to replace cyclosporine.</td>
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<td>1994</td>
<td>The ESRD program reaches $7 billion dollars in annual costs, growing at twice the rate of inflation. Dialysis costs alone are $6 billion. DPR is not yet funded by the government to any significant degree.</td>
<td>Results of the MDRD suggest that DPR is useful for certain patient groups. More study is called for before DPR can be more fully recommended.</td>
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<td>1995</td>
<td>Dr. Walser introduces data that patients on DPR enter dialysis or transplant healthier. They show a mortality rate that is one-fourth of the control group for the first year. He presents further data showing that patients' nutritional status improves on DPR contrary to what had been thought.</td>
<td>The Halfway Technology: Dialysis</td>
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Dialysis is simply a technique for diffusing solute molecules from an area of high concentration to one of lower concentration across a semi-permeable membrane. The term dialysis first appeared in the medical literature in 1854. Thomas Graham, a Scottish chemist, demonstrated the movement of different solutes through a membrane he had fashioned with an ox bladder. The first device to incorporate the basic apparatus common to contemporary dialysis machines was developed shortly after the turn of the century at Johns Hopkins University and several experiments with animals were carried out. Although the basic mechanism was fairly simple, several technical problems remained pertaining to the development of biomaterials that would not cause blood clots.

The arrival of World War II in Europe yielded large numbers of patients with acute (sudden) kidney failure, often due to trauma or mercuric chloride poisoning. This produced a pressing need to refine the dialysis machine, which
only existed in crude form at that time. In response to the conditions in occupied Holland, Willem Kolff developed the rotating drum dialysis machine, and his innovation proved quite useful in treating short-term kidney failure. While subsequent improvements led to the diffusion of dozens of machines around the U.S. in the 1950's, many of them sat idle for lack of specially trained staff to operate them. The machines were used for the short-term management of acute renal failure as it was not possible to dialyze the same patient more than a few times. At that time, there were no alternative treatments to chronic end-stage renal failure as renal transplantation was still in its infancy.

By the close of the 1950's, the stage was clearly set for the widespread application of dialysis if solutions could be devised to the problems associated with repeat dialyzing, as well as the training of medical staff to apply the technique and monitor patients' conditions. A physician championing dialysis emerged in 1960, and he was able to supply solutions to the problems of repeat dialyzing and training for long-term care of patients suffering from chronic renal failure. Dr. Belding Scribner of the University of Washington Medical Center in Seattle and an engineering colleague invented an indwelling arterial venous shunt which permitted the repeat dialyzing of a patient. This simple but ingenious innovation touched off the application of dialysis to renal failure in the U.S. Although there was much early resistance within the organized nephrology community, Dr. Scribner became a tireless advocate of his innovation, traveling around the country with dialysis kits, teaching dozens of young nephrologists his technique while raising money to pay for the expensive treatments when patients were unable to.

In 1963 Scribner further increased the visibility of dialysis by convincing his old employer, the Veteran's Administration (VA), to implement dialysis at many of its facilities in 1963. Rettig asserts that the VA's endorsement was crucial. Not only was the VA the largest hospital chain in the country, but it was also an important stepping stone to getting visibility for a new treatment in medical schools, which often use VA hospitals for research and clinical training. Thus young nephrologists and medical students from all over the country were exposed to dialysis.

In 1965, dialysis received another key endorsement. Scribner and his colleagues convinced the Public Health Service to support twelve dialysis facilities, again with the physician-heads going to Seattle for training. As Freidson points out, the presence of institutions that train physicians and educate medical interns is crucial for gaining legitimacy for a new treatment. As with the acceptance of dialysis by the VA, the Public Health Service research centers increased the exposure of dialysis while giving many more (often young) nephrologists the opportunity to learn its techniques while introducing it to more medical schools around the country.

Despite Dr. Scribner's best efforts, after a few short years, dialysis had fallen well short of full acceptance within the nephrology specialty (although it was much more widely diffused in the U.S. than DFR and renal transplantation). As late as 1966, the first president of the American Society of Nephrology, Dr. Neal Bricker, and other important academic nephrologists opposed the extensive diffusion of dialysis, despite its apparent ability to keep patients with end-stage renal failure alive. A primary concern was the fear that widespread application of dialysis would drain resources from research into the root causes of renal failure while continuing to promote a halfway technology that neither cured nor provided a good quality of life for patients. They were also concerned that the teaching hospitals, where most dialysis was being performed, would be overwhelmed with new patients.

Yet later that year, Dr. Bricker and several other important opinion leaders such as Georgetown's Dr. George Schreiner, a prominent nephrologist in Washington D.C., withdrew their opposition. These important endorsements led to a newly unified specialty (of clinicians and academics) who could now lobby the federal government to pay for expensive dialysis treatments -- Scribner acting as the "outside man" and Schreiner as the "inside man" in Washington. Dialysis proponents were also able to convince transplant advocates that dialysis was complementary to transplantation and that the two groups should work together. There had been some competition and sniping between the two groups in the 1960s, but that seemed to lessen as the final goal of full federal government funding for their respective treatment approaches was in sight. The newly unified specialty's lobbying efforts culminated in the 1972 amendment to Social Security (Section 2991) -- the End-stage Renal Disease program -- which ensured that dialysis would be accessible to almost all patients, free of charge. During the debate on the amendment, a patient was wheeled into Congress and dialedyzed in front of the Congressmen. Although the dialysis session lasted only five minutes, the demonstration was convincing: the legislation passed both houses of Congress in less than an hour.

Nephrologists were thus granted unrestricted funds to provide dialysis or transplants for their patients. Chronic renal failure was now unique in that it became the only disease that the government would pay for irrespective of patient age or income. It was projected to cost the government $10,000 per patient around $100 million annually, with annual costs rising to one billion dollars in the coming years. The cost estimates were accepted with little debate.

The Proliferation of Diabetic Therapy. Proponents of the end-stage renal failure program had argued that the first year costs would range from $35 million to $75 million, rising slowly after that. In fact, first year costs were $240 million. Dialysis providers rapidly expanded the patient pool to include patients who only a few years earlier would have been considered ineligible due to poor health. By the end of the decade, costs had escalated to one billion dollars annually, much more rapidly than had been forecast, and the patient pool had increased more than eight fold. Much more aggressive use of dialysis to treat chronic renal failure coupled with the rise of for-profit dialysis clinics was attributed as leading to this increase.

Corporate involvement has proved to be important in the proliferation and rising costs of dialysis. National Medical Care (NMC) was founded by former Harvard nephrologist Dr. Constantine Hampers in 1970 with the intent of operating stand-alone for-profit dialysis clinics and providing ancillary services including the manufacture of dialysis supplies. In 1972, NMC had 15 centers
and provided 77,000 dialysis treatments annually. At the time most patients were
dialyzed in hospitals, nonprofit clinics, or at home. By 1975, NMC had 48
centers and provided 388,000 annual treatments.\textsuperscript{51} Such rapid growth caught the
attention of the financial community which reported favorably on NMC's
prospects, noting that NMC was basically recession proof as its earnings were
driven only by the number of patients that it could attract. Payments for dialysis
was not a concern as the 1972 ESRD legislation committed, the federal
government to funding dialysis treatments for nearly all patients and without
limit.\textsuperscript{52}

Dr. Hampers, the longtime head of NMC, maintained that NMC's rapid
growth was based on the support they received from the local medical community
in the areas they were expanding into.\textsuperscript{53} Sometimes, for example, NMC invited
the local medical school to recommend who should be appointed director of the
new clinic. Working closely with the local medical community not only ensured
referrals and secured legitimacy, but also made it difficult to oppose NMC's
efforts to push its stand-alone clinics. More often than not and thanks to NMC's
co-opting tactics, new clinics were specifically backed or run by highly influential
local nephrologists.

Due to the rapidly expanding costs of the ESRD program, in 1976, a bill
was drafted to increase the prevalence of less expensive home dialysis -- $4,000
to $6,000 per patient annually versus $14,000 to $20,000 at a clinic at that
time.\textsuperscript{54} The growing importance and financial stake of these firms in the renal
care business suggests that they would lobby to protect their interests and seek
passage of favorable laws to enforce the use of their treatments.\textsuperscript{55} Advocates
of the for-profit clinics successfully lobbied to considerably weaken the bill and
remove any mandates.\textsuperscript{56} Although home dialysis has become a major modality in
Canada and in parts of Europe, it has continued to decline in importance in the
U.S. particularly vis-a-vis for-profit dialysis.\textsuperscript{57} Political scientist and long time
historian of the field, Richard Reitting described the final language of the bill as
"National Medical Care's revenge."\textsuperscript{58}

According to some observers, physicians may have an interest in
expanding patient rolls on their dialysis facilities. Bovbjerg and colleagues point
out that "Most nephrologists' financial security is more tied to a specific
therapeutic modality than is that of other doctors," that is many nephrologists
have a financial interest in one or more dialysis units.\textsuperscript{59} In a 1983 study, 83
percent of dialysis unit medical directors indicated that they wanted to attract
more patients.\textsuperscript{60} Concerning the issue of physician interest and dialysis
proliferation, Greenspan concludes:

ESRD legislation guaranteed facilities a constant source of federally subsidized patients for an indefinite period, irrespective of
the quality or cost-containment of services rendered. This has been a true windfall to . . . some [nephrologists] who became
responsible for an increasing segment of the dialysis population by developing proprietary 'chains' of facilities after convincing
regional agencies of the need for [their] dialysis services.\textsuperscript{61}

Nearly 60 percent of dialysis patients are currently treated in for-profit clinics
around the country. Financial motivations could be one force in maintaining
dialysis' dominance as kidney treatment modality.\textsuperscript{62}

\textbf{Efficacy and Cost of Dialysis.} Dialysis has been part of the medical
landscape for so many years that it is easy to think of it as a routine treatment.
Yet a host of comorbidities are associated with dialysis and quality of life
continues to be difficult for many patients. Expected life span is only about three
years;\textsuperscript{63} one-third of dialysis patients survive more than five years and less than
10\% survive ten years (See Figure 2).

The morbidity figures of dialysis also attest to continuing problems; the
functional rehabilitation of dialysis patients has been termed "dismal."\textsuperscript{64} A recent
study by the Healthcare Financing Administration (HCFA) reported that over 80\%
of dialysis patients felt limited in doing anything, over two-thirds felt they had no
energy, and nearly a third had trouble using their eyes for reading.\textsuperscript{65} Older
patients have reported that they spend most of their time indoors due to fatigue.
Only 32 percent participated in activities outside their home other than going for
dialysis treatments. Dialysis is also expensive, costing over $30,000 annually per
patient.\textsuperscript{66}

Since the 1960s, large and increasing amounts of resources have been
directed toward dialysis treatments and research. From initial projections of less
than $100 million, annual spending for dialysis treatments has risen to $6 billion
and shows little sign of leveling off.\textsuperscript{67} The nephrology specialty has grown greatly
in importance, having moved from a small "back bench" research oriented
specialty in 1960 to one that has a high level of political influence, financial
strength, and corporate ties.\textsuperscript{68} Dialysis is used more intensively in the U.S. than
anywhere in the world, and remains far and away the dominant treatment for
chronic renal failure.

\textbf{KIDNEY TRANSPLANTATION: THE FINAL SOLUTION}

The history of transplantation has both similarities and difference with dialysis.
The first attempts at clinical renal transplantation were made in Europe in the
early 20th century using pig, sheep, goat and primate donors. The immune
systems of the human recipients promptly rejected these grafts, and none survived
for more than a few days.\textsuperscript{69} The first human to human kidney transplant was
reported in 1936 in the Soviet Union. That patient survived only 48 hours.\textsuperscript{70} The
procedure was tried sporadically over the next two decades and made little impact
on the treatment of renal failure. In 1954, a transplant between identical twins
was successfully performed in Boston at the Brigham by Drs. Francis Moore,
George Thorn, John Merrill and 1990 Noble Laureate, Dr. Joseph Murray. Still
early transplant patients were plagued with very high morbidity and mortality
rates; rejection of the new graft was the norm and patients seldom lived longer
than one year.\textsuperscript{71}
Renal transplantation received a boost in the 1960's when immunosuppressive drugs were first utilized by Dr. Starzl's University of Colorado group in 1962. Yet problems persisted. Organ rejection and serious morbidity problems raised serious questions about transplantation's viability as a feasible technology.

Transplant surgeons have kept the training of new transplant teams under close supervision, and the number of teams and sites certified to do renal transplantation was kept quite low. Indeed in 1989, only 184 hospitals in the U.S. were certified to perform kidney transplants as compared with 2,000 dialysists. In 1969, the PHS established seven transplantation centers around the country -- five fewer and four years later than with dialysis. The large numbers of physicians trained on dialysis in the U.S. and DPR in Italy lie in contrast to the small numbers of surgeons trained to conduct transplants, thereby dampening the acceptance of the technique.

Today, kidney transplantation is an important technology for treating chronic renal failure. The technology's proponents have convinced their colleagues in the medical profession, government policy makers, and the media that the procedure is "established" and is "90 percent successful." Yet the technology has not been as widely adopted and utilized as dialysis.

Though transplantation was also funded by the 1972 amendment, its diffusion has been hindered by technical difficulties. As noted earlier, the training of transplant teams is a meticulous and difficult process, and the securing of suitable organs for transplant is even more difficult. Dialysis is easier to execute than transplantation. Patients can be trained to dialyze themselves at home, while renal transplantation is a complex surgery which requires months of specialty training.

Moreover, organ rejection is a continuing problem. Although cyclosporine often proves to be nephrotoxic, ironically destroying the kidney that it is supposed to protect. This means many patients face re-hospitalization, and second (and sometimes third) transplants, and often have to go on dialysis while awaiting these transplants.

In addition to technical problems, proponents of transplantation have not succeeded in co-opting resources, crafting legislation and developing institutional links to the extent that dialysis proponents have. Rettig noted that:

...transplant surgeons barely participated in the policy events of the 1970's...They left much of the work of defining end-stage renal failure policy to the nephrologists...

Transplantation faces a technological hurdle that dialysis does not have: it requires a steady supply of suitable transplantable kidneys. As renal transplants increased in number through the 1970s, surgeons clamored for mechanisms to guarantee a reliable supply. One physician proposed a kidney spot market, even providing for imports from developing countries. However, in 1983, transplant proponents received a major setback. A federal law was passed forbidding the buying and selling of organs in the United States.
As a response to the organ shortage problem, transplant protagonists became aggressive users of the media. For example, Ted Koppel's Nightline show was devoted to organ transplantation ten separate times from 1983 through 1988. Several times in the 1980’s, the media depicted human interest stories describing the plight of a patient waiting for an organ donor. Often the patient was a little child who was desperately ill. Former President Reagan even participated in the publicizing of transplantation. In July 1983, on his regular radio broadcast, he appealed to the country on behalf of a little girl named Ashley Bailey. Reagan even indicated that Air Force One would be standing by in case commercial transportation was unavailable. The developer of FK-506, Dr. Paul Terasaki, an important player in immunosuppressant research, has also encouraged transplant recipients to speak to groups to encourage more active participation in organ donation programs.

Despite this favorable media coverage, kidney transplantation has not succeeded in co-opting support to the extent that dialysis has. Although transplant proponents also had a champion to “sell” the technology, and train scores of young doctors, they seemed to be less effective in institutionalizing rules, monopolizing patients, and in getting favorable laws passed. These issues, coupled with the more difficult technical problems of finding suitable kidneys and minimizing graft rejection have placed additional infrastructural constraints on transplantation. It is not surprising that kidney transplantation lags behind dialysis in terms of both number of patients and economic importance.

Efficacy and Cost of Transplantation. Renal transplantation is theoretically superior to dialysis in that it is supposed to cure chronic renal failure by replacing the damaged kidneys with a new one. In practice, however, transplantation is plagued by the problems associated with a major surgical procedure and the body’s tendency to reject foreign tissue. Transplantation also is not as effective as is commonly thought and reported. It is frequently reported that kidney transplants are 90 percent successful. "Success" in these cases is defined as a patient who receives a kidney transplant and is alive 366 days later. This definition of success does not indicate if the graft itself (the transplanted kidney) is still functioning, nor if any mention made of patient morbidity – which can be very poor on immunosuppressive drugs such as cyclosporine. A more accurate proxy for "success" should probably be the function of the graft itself. For one year, graft survival is about 70 percent, and five year survival is less than fifty percent and the ten year survival rate is about 20 percent (See Figure 2). The average life expectancy of a renal transplant patient is roughly five years, but survival time may involve multiple kidney transplants.

With respect to morbidity, transplant patients face some difficult problems associated with the immunosuppressive drugs they must take. Despite the feverish work on the cyclosporines and the newest one, FK506, high morbidity and mortality rates continue to plague renal transplantation. The primary immunosuppressant, cyclosporine, creates difficult complications including hot flashes, sweating, neurological problems such as numbness and tingling, uncontrollable shaking of hands and feet, and hypertension. Cyclosporine has been also implicated in causing cancer and is regularly nephrotoxic - destroying the kidney that it is supposed to protect. Researchers concede that the new immunosuppressant, FK506, has a number of possible side effects including vomiting, weight loss, and blood sugar elevation. The release form that patients had to sign before taking the drug read: "[c]hief side effects, including death, are possible in humans, but cannot be anticipated."

Renal transplantation can easily cost from $100,000 - $200,000 over the life of the treatment. Treatment costs can rise significantly if repeat surgery and re-hospitalization are considered. Given the expensive medication that patients must take can also cost roughly $10,000 per year.

Transplantation has received a large amount of attention in its several decade history. The public is captivated by the human interest stories that surround transplant surgery. The problem of immunosuppression has attracted some of the finest minds in biomedicine and industry. Kutner observes:

Viewed within the broad spectrum of modern medicine, it is probably fair to say that organ transplantation has received an undue amount of attention. Individuals whose survival depends on the timely receipt of a suitable organ quickly become the focus of human-interest media accounts. Physicians remain intrigued by the challenge of trying to outsmart the human body's natural response of rejecting a foreign organ, and successful transplantation represents a "quick fix" (the most satisfying aspect of medical practice to many medical students and physicians).

Kutner goes on to comment also about the prestige, financial rewards, and the ability to expand related research. Although transplantation lags well behind dialysis in treatment terms, transplantation has generated five times the academic research in the past 25 years as has dialysis and roughly 200 times as much as DPR.

Summary. The mortality and morbidity figures of dialysis and transplantation along with the high price tags they carry raise several questions as to their appropriateness except as treatments of last resort. They do save lives – though for some, it has been argued, these treatments merely "postpone death" due to the poor quality of life that patients often experience. Concerning the aggressive use of dialysis, Dr. Sergio Giovannietti, a leading Italian nephrologist comments:

This policy of starting dialytic therapy without prior DT [dietary therapy] is difficult to understand; it is like treating all newly diagnosed diabetics with insulin, without considering that many of them may be successfully treated with diet only.
THE FORGOTTEN PATH: DIETARY PROTEIN RESTRICTION

As far back as the 1700s, physicians suspected that kidney problems were related to a rich diet high in meats and fowl. The literature of the day had numerous references to problems associated with renal failure. Benjamin Franklin was troubled by kidney problems, which he attributed to a rich diet. It is also thought that Mozart suffered from renal failure and likely died of kidney failure. In the J.S., kidney problems had become increasingly common among the upper classes after the revolution, suggesting that protein consumption was a cause. By the early 19th century, physicians had accumulated some knowledge of how the kidney functioned. A rich diet high in "meats" was thought to be a main cause of kidney problems.90

One of the first medical texts on the kidney appeared in the U.S. shortly after the Civil War.91 In it, Beale argued that a low protein diet could reduce injury to the kidneys and help people with kidney disorders. At that time, there were several "pure-food" movements around the country urging people to consume a simple diet of natural, unprocessed grains while limiting meat consumption. Kidney patients were sometimes treated with a low protein diet, and those exhibiting severe uremic patients were also treated with very hot baths - to remove nitrogenous waste products through sweat. Still there was little that could be done for patients suffering from end-stage renal failure whose disease would soon lead to kidney shutdown and death.

More formal dietary studies emerged in the early 20th century. Otto Folin showed that a protein-free diet consisting of starch and cream greatly reduced nitrogen and urea excretion thus alleviating uremic symptoms.92 Other formal investigations found that high protein diets given to animals with renal failure increased nitrogen retention and uremic symptoms thereby shortening their survival.93 Based upon these largely retrospective and anecdotal results, low protein diets were proposed for conservative treatment of both acute and chronic renal failure.94

Concurrent with early experiments on renal transplantation and dialysis in the early 20th century, work on DPR was codified into texts on treatment of renal failure. Of these, Thomas Addis' work is perhaps the best known.95 His seminal text on renal failure included a discussion of DPR and its benefits. Yet Addis, although generally well-respected, was also seen as somewhat as a west coast concloid, and that coupled with his rather untimely death at the time of the text's publication may have impeded the spread of DPR to other parts of the country. Hence American nephrologists' interest in the low protein diet remained sporadic.

When Willem Kolff brought his new dialysis machine to the U.S. after World War II, many hospitals purchased the new machines to treat acute failures, but few knew how to properly operate them and they were used sparingly.96 Scribner's invention of the shunt in early 1960's coupled with the large numbers of these machines already in place made possible the widespread application of dialysis to treat chronic renal failure patients. Many U.S. nephrologists rapidly focused their attention on the treatments at the technological frontier such as dialysis and renal transplantation while DPR, lying within the technological interior started to languish.

Outside of the United States, however, a small group of Italian nephrologists renewed the work on DPR left off by Addis and his predecessors. In 1963, Dr. Giordano released results from a study concerning protein and urea.97 Giordano's work was extended by Drs. Giovannetti and Maggiori98 and DPR was on its way to becoming a fairly widespread treatment approach in Italy.99 In subsequent years the Giordano-Giovannetti diet as it was called became so well known that patients suffering from renal failure traveled to Italy from all over Europe and sometimes from the U.S. for treatment. Renal nutritionists today still refer to a version of the DPR diet as the "Giovannetti diet" in tribute to the extensive and continuing work of Dr. Giovannetti over the past four decades.100 Dr. Giovannetti is nearly as well known to Italians because of his work in treating patients suffering from renal failure despite of a paucity of resources as is Dr. Jonas Salk to Americans.

In Italy, training for young nephrologists emphasized dietary approaches while few doctors and medical students received training on dialysis. The few dialysis centers that did exist in Italy were able to operate only on a very limited basis due to lack of funds.101 Dr. Giovannetti's tireless advocacy of DPR led to government funding, both for research and treatment.102 To date, roughly one-third of all the bioscientific articles in English on DPR have originated in Italy.103

By the late 1960's, while DPR was becoming common medical practice in Italy, the work of the European researchers and clinicians caught the attention of a prominent nephrologist, Dr. MacKenzie Walser of Johns Hopkins University. Dr. Walser initiated a series of studies on DPR that have run uninterrupted since 1972, and have shown promising results.104 His work demonstrates that DPR can not only alleviate troublesome uremic symptoms faced by chronic renal patients, but could also slow the progression of the disease itself. Dr. Walser also improved upon the treatment with a drug he jointly patented with Johns Hopkins - an analog of amino acids called ketoacids. Ketoacids taken orally may make DPR easier to apply as they aid patients in minimizing protein intake while avoiding protein deficiencies. His innovation helped to eliminate a key problem associated with DPR: protein deficiency and may produce other positive effects.

The extensive work of Dr. Giovannetti and colleagues in Italy and Dr. Walser in the United States proved inadequate for American nephrologists to seriously consider DPR, particularly if there was money to pay for expensive dialysis treatments or kidney transplants. As Walser was just commencing his work on DPR at that time, there was no champion to lobby Congress on DPR's behalf. Hence the End-stage Renal Disease legislation did not provide funding for DPR treatments as it did for dialysis and transplantation.

Efficiency and Cost of DPR. Results for DPR continue to be promising. Morbidity is very low and problems with protein malnutrition are rare. Compliance with the strict demands of the diet has not proven to be a problem.105 The recently completed Modification of Diet in Renal Disease study confirm DPR's benefits for certain patient groups. Additional work demonstrates that not only does DPR slow progression of the disease, but that DPR patients enter
dialysis healthier than those that did not go on a DPR regimen. This slowed entry into end-stage hence postponing the need for dialysis or transplantation could produce extensive cost savings.

Figure 3 illustrates how DPR can work. The flatter sloped line indicates the slowed progression of patients into end-stage renal failure, by nearly thirty months in the hypothetical example. This means that DPR can postpone the need for dialysis or transplantation and in some cases, save a great deal of money.

**FIGURE 3**

**HYPOTHESIZED CHANGES IN GFR OVER TIME**

Delta t = 29 Mos.

17.5 - 46.7 End-Stage GFR-10

b = -0.8

Moreover, the cost of a DPR regimen, which includes special low-protein foods and supplements, as well as regular testing of patient kidney function is quite low, costing roughly one or two thousand dollars per year. Many low protein foods are available in grocery stores and pharmacies in Europe, but in the U.S. are available in many cases only by mail.

To more fully determine DPR's value as part of a more complete care regimen, research on DPR in conjunction with dialysis or transplantation is needed. However, the MDRD did not compare patients treated only with dialysis with patients who first are treated with a DPR regimen, followed by dialysis. That is, it did not produce mortality or morbidity data exist controlling for the stage of treatment intervention. We explore some of the plausible reasons for this situation in the next section.

**TECHNOLOGICAL TRAJECTORIES AND THEIR INTER-RELATIONSHIPS**

This paper has outlined how, given a disease for which there was no cure, technological progress has made end-stage intervention possible through artificial or transplanted kidneys. Dialysis and transplantation have both benefited from the presence of technology champions who took it upon themselves to demonstrate the efficacy of the treatments and to ensure a stream of resources required to sustain each of these trajectories. They have also benefited from links to key scientific and educational institutions. The End-stage Renal Disease Program greatly aided the spread of dialysis and transplantation by guaranteeing payment for virtually all treatments. Dialysis has benefited from corporate links as well.

Our description also highlights that a cost-effective treatment such as DPR, an early intervention approach, has been largely ignored by the nephrology community in the U.S. despite its widespread use in Italy and other countries. DPR remains outside of the federal payment system, many nephrologists are unfamiliar with its use, and the special low protein foods that make the diet easier to stay on are not as widely available in the U.S. as they are in Europe. These factors all work to constrain the broader acceptance of DPR.

**Inter-relationships between trajectories.** These forces and their resultant outcomes are consistent with our understanding of how trajectories are formed and sustained. Renal failure treatment modalities, however, provide additional insights about technological trajectories. In particular, they illustrate the relationships between trajectories -- how they complement each other and how they might compete with one another. For instance, dialysis can be used till such time a kidney donor has been found. If the new kidney fails (more than half of the new grafts fail within three years) then they can move back onto dialysis. Both these treatment approaches employ similar end-stage intervention ideologies and downplay the need for earlier intervention.

The complementary relationship between these two end-stage treatments has led to changes in the way each approach has developed over time. Transplant physicians have become a little less aggressive in using drugs to forestall rejection because of the easy availability of dialysis in the case of graft failure. Reflecting on this relationship, Dr. Starzl concluded dialysis and transplantation had become interlocking treatments, especially after the passage of the 1972 end-stage renal failure program, at which time these two approaches no longer had to compete for scarce common resources.

However, the lack of complementarity and the presence of competition is nowhere more evident than between the end-stage intervention approaches and DPR. In Italy, DPR is regularly prescribed for those from chronic renal failure to alleviate their symptoms while slowing disease progression. However, this apparent complementarity between DPR and the end-stage intervention approaches has created a resistance towards the adoption of DPR as it can postpone or sometimes eliminate the need for dialysis or transplantation. As DPR is not reimbursed under the ESRD program it is more difficult for physicians to prescribe it. If a physician were employed by a for-profit dialysis facility, this would pose an additional disincentive to first prescribing a DPR regimen.
Those who have pursued end-stage intervention approaches have not just been indifferent about DPR; some have actively campaigned against DPR. One of the prime arguments against considering DPR for federal funding has been the lack of prospective randomized controlled trials to establish the treatment's validity.\textsuperscript{114} What is interesting to note is that lack of randomized controlled trials confirming the appropriateness of dialysis and transplantation has not stopped their widespread use in the U.S.\textsuperscript{115} Small numbers of successes have proved to be a strong basis for confirming the validity of dialysis and transplantation.\textsuperscript{116} While proponents of these approaches have acknowledged problems associated with chronic morbidity, mortality, and costs, they have not considered these to be concerns that should be taken into account when evaluating treatment validity.

The more stringent scientific standards of proof set for DPR has hindered its acceptance in the U.S. One patient saved by DPR from dialysis or transplantation, for example, is not considered to be an appropriate basis for treatment validation, though it was for dialysis. Although a significant number of single cases of success exist, the profession considers this inadequate evidence or DPR's validity.\textsuperscript{117}

**ECONOMICAL INTERIORS**

The current emphasis on end-stage treatments along with the rapidly rising costs, increasing patient rolls and associated quality of life problems all strongly suggest that the nephrology specialty may have lost sight of what broader society sees as a goal— to cure or prevent renal failure. Steps that might have been taken to prevent end-stage renal failure from even arising have been overlooked and they also tend to remain largely neglected despite the fact that noted and acknowledged search findings suggest that such possibilities may be achievable.\textsuperscript{118} While commitment to end-stage technologies have steadily escalated, there has been little attempt to reassess and reevaluate these ever increasing resource expenditures. The current situation is characterized by a mix of treatments that overlooks those treatment approaches that may reduce or delay the need for end-stage acute care. Instead, current practice actually promotes such treatments for renal failure. These preferred end-stage treatments are not only expensive; they also have many serious and unresolved quality of life issues associated with them.

DPR is an illustration of a larger phenomenon—one that has to do with exploring technological interiors. Implicit in the progression of trajectories is an image of discoveries occurring at the forefront of science and technology. But what of paths that were not taken? What of those that were taken and led to dead ends at that point in time because either markets were not ripe or complementary technologies not ready. And what of technologies that now appear to be passé just because they do not lie at the forefront of the growing trajectory? How might older or alternative trajectories be reexamined? We think that there is much to be done to explore these questions.

**ROLE OF ADVANCED TECHNOLOGIES IN MODERN MEDICINE**

Over the past several decades, medicine has increasingly been able to address end-stage conditions and treat patients who are terminally ill. As increasing amounts of (often public) resources are committed to medical care, questions arise that must be answered. These include how we determine what treatments should be pursued, where should resources be directed and how treatments should be evaluated. The large emphasis in the U.S. given to frontier technologies in medicine has meant that acute care end-stage intervention techniques, as opposed to preventative techniques, have received (and are continuing to receive) the bulk of medicine's attention and resources. Reflecting on the implications of such a situation, McGinnis points out that more than 95 percent of dollars spent for medical care goes to treat rather than prevent.\textsuperscript{119}

One result of the emphasis given to high-technology frontier medicine is that these technologies often do not address the underlying causes of illness and disability.\textsuperscript{120} Lewis Thomas has given the name halfway technologies to treatments that provide relief from symptoms but do not actually cure the disease in question.\textsuperscript{121} While these halfway technologies save lives, they often produce a poor quality of life in the process. Thomas also points out that these technologies seldom extend life for significant periods.\textsuperscript{122} In the case of renal failure for example, the expected life span on dialysis is about three years, and is just a little longer for transplant patients.\textsuperscript{123}

Thomas' argument against the heavy emphasis on these approaches stems partly from his observations of the development of cures for major infectious diseases. He argues that behind sulfa drugs and penicillin, there existed six decades of basic research in bacteriology and immunology. Research by Pasteur and others first identified microbial causes of infectious diseases long before cures were found. Observes Thomas:

...antibiotics did not simply drop into medicine's lap. If it had not been for those sixty odd years of research, penicillin could have come along in purified, stable form, and nobody would have known what to do with it.\textsuperscript{124}

What Thomas and other critics of halfway technologies contend is that such treatments divert resources from the basic research that must be undertaken if diseases are to be cured as opposed to simply treated. Similar concerns have been raised since dialysis was first used. The concern was that dialysis treatments would eventually command a lionshare of the resources for kidney treatment, while starving the field of resources to carry out basic research on the etiology and cure for chronic renal failure.\textsuperscript{125}

Ethical dilemmas also arise as a consequence of the emphasis placed on frontier technologies. As Daniel Callahan points out, there will always be people at the "ragged edge" of health—people with difficult new health problems that replace the problems that have just been treated.\textsuperscript{126} That is to say, given more technology, people can be kept alive, but then, more problems will inevitably
CONCLUSION

As we push forward at the frontiers of science and technology, we discover and implement new medical technologies that can enhance the quality and longevity of our lives. These advances offer many important benefits and must continue. But at the same time, these technological advances also raise many dilemmas concerning what treatments should be pursued and to what extent, and who should pay for them. Indeed, these issues will only intensify in the future as we continue to advance medicine’s boundaries.

Frontier medicine is appealing to physicians and patients, who like the idea of a quick fix, and to the public, who cannot resist the human interest story of people being plucked from certain death by heroic transplant surgeons. Moreover U.S. institutional and legal arrangements demand that physicians implement the most sophisticated technologies to address any disease. Because we have a hammer it must be used. Yet at the limit, simple remedies are forgotten and even downplayed as being but grandmothers’ cures without any basis for support and not worthy of our efforts.

Why don’t we pay attention to such preventive or alleviate therapies? It might appear that this is also due to our proclivity for something new and exciting; our focus and attention at the frontiers of science and medicine leads to an act of omission of what lies hidden in the interiors. However, as our description of approaches to treat chronic renal failure illustrates, there are in addition to social forces, many technological, economic and institutional forces that keep medicine at the frontiers and away from the interiors. The identification of these forces, therefore, becomes critical if we want to explore technological interiors. Methodological and epistemological binds in particular may play important roles in determining which technologies are pursued and which are shelved.

The case of chronic renal failure is representative of several other ailments such as chronic back problems, dehydration and heart disease. Technological advances in these areas offer exciting opportunities for humans to improve the quality of their lives. However, if we continue exploring the frontiers while abandoning the interiors, we might increasingly substitute simple and cost effective treatments with increasingly more sophisticated and expensive halfway treatments. The chronic renal failure case illustrates that there might be simple solutions that lie hidden in the interiors of medical technology. The rewards of exploring these interiors could be significant both in terms of improvement in the quality of our lives and the price we pay to maintain them.

Acknowledgments. We thank Dr. MacKenzie Walser and Roger L. M. Dunbar for their valuable comments and suggestions.

NOTES AND REFERENCES

1. For example, coronary bypass had become well-established before being properly assessed. Several recent studies have suggested that bypass may
design is less efficient than competing keyboard arrangements, too much is invested in the QWERTY for manufacturers or users to easily switch to newer designs. Moreover, positive feedback, where the more a technology is adopted the more it is improved, serve to reinforce a given technological path (See Paul David “Clio and the Economics of QWERTY”, *Economic History*, V.75, 1985, pp. 227-332; Arthur, Brian, "Self-reinforcing mechanisms in economics". In P. Anderson et al. (eds.), *The Economy as an Evolving Complex System*, Reading, MA, Addison-Wesley, 1988).


14. This position is consistent with the position taken by Van de Ven and Garud, who suggest that to understand the evolution of new industries, we must examine multiple arenas of action that include the institutional, resource procurement, and the institutional. See Van de Ven and Garud, "A framework for understanding the emergence of new industries", in: Rosenbloom, R.S. and Burgelman, R.A. Research on technological innovation, management and policy, Vol. 4, pp. 195-225, 1989.


Scientific Change Relevant? Dordrecht, Reidel, 1984, pp. 115-142) and technological regime (Nelson, R. and S. Winter "In Search of a Useful Theory of Innovation" Research Policy 6, 1977, pp.36-76). Rather than define each of the terms, we direct the reader to The Social Construction of Technological Systems by Bijker, Hughes and Pinch (1987) as an efficient way to understand these concepts in technology studies.


20. Chronic renal failure affects well over 100 thousand Americans and perhaps millions worldwide. Annual treatment costs have reached nearly seven billion dollars in the US alone (see U.S. Renal Data System 1991 and 1993 Annual Reports Bethesda, MD: The National Institutes of Health, National Institute of Diabetes and Digestive and Renal Diseases). The cost of the end-stage renal failure program (the federal program that pays for dialysis and transplantation) has risen at an annualized rate of roughly 20 percent per year since the program's inception in 1972 (Fox and Swazeys, 1978: 349; ibid note 3).


23. Professional discussions and biomedical research served as a good starting point to determine the issues and controversies involved with treating chronic renal failure. Further research on government policy gleaned from the medical policy literature concerning these treatments offered a fairly extensive picture of the crucial political and institutional support of dialysis and transplantation. Medical economic and sociological literature was also surveyed. Finally, open-ended, semistructured interviews were conducted with several important actors involved with these treatments from a variety of viewpoints including: clinical and academic nephrologists, patient groups (National Kidney Foundation), the federal government (National Institutes of Health), the biotechnology research field (National Academy of Sciences' Institute of Medicine), the dialysis industry, the nutrition field (participant in the development of the National Renal Diet) and U.S. and European doctors working with DPR. Over thirty interviews in all were conducted, and at least three people from each group listed above were interviewed. Articles written by the interviewees were also read as a check against retrospective rationality.

25. Fox and Swazeys, ibid note 3; and see Thomas, Lewis. The Lives of a Cell New York, Viking Press, 1974 especially pp. 31-36.
34. Fox and Swazeys, ibid note 3.
35. Dialysis patients require a great deal of monitoring to maintain sensitive electrolyte balance and blood chemistry.
36. Fox and Swazeys, ibid note 3.
41. Fox and Swazeys, ibid note 3; Thomas, ibid note 25; Bricker, Neal, M.D. Personal Communication December, 1991.
44. Fox and Swazeys, ibid note 3.
45. Retting, ibid note 37
46. Fox and Swazeys, ibid note 3; pp. 348-349; Retting, ibid note 43.
47. Fox and Swazeys, ibid note 3; p. 349.
51. Fox and Swazeys, ibid note 3; p. 363.
52. Kolata, ibid note 48; Retting, ibid note 36.


56. Starr, Ibd note 54 The outcome data on home dialysis was and has continued to be comparable to those of in-clinic dialysis (USRDS, 1994, ibid note 20).


59. Bovbjerg et al., Ibd note 55.


62. Barnett et al., ibid note 57; Ben Burton, long time head of the of the NIH contract program concerned with chronic renal failure also suggested the importance of economics in guiding the specialty’s technological emphasis.


67. Altman, ibid note 64.

68. Fox and Swazey, ibid note 3.


70. Starzi, ibid note 69.

71. Starzi, ibid note 69.

72. Starzi, ibid note 69. The new immunosuppressant, FK506 (prograf) was approved by FDA in 1994 and has shown some promise in reducing the morbidity and rejection rates that have plagued transplantation.


76. Rettig, Ibd note 73., p. 195.

77. Such a market has existed in India for several years. Poor people are known to sell a kidney for hundreds of thousands of rupees -- enough to purchase a new house.


79. Rettig, Ibd note 73.

80. Starzi, ibd note 74.

81. Rettig, Ibd note 73.


83. That figure can be found in respected publications such The New York Times (see Kolata, Gina. 1990. "American Transplant Pioneers Win Nobel Prize in Medicine" The New York Times. October 9, C3) as well as scientific publications. For instance the 90 percent transplantation success figure was commonly quoted in the recent book-length study by the National Academy of Science’s Institute of Medicine on renal failure (see Rettig, Richard and Levinsky, Norm. 1991. The Federal Government and End-stage Renal Disease. Washington, Institute of Medicine).

84. Kutner, Ibd note 78; Daniels, Ibd note 67.


88. MEDLINE (Database Online). 1989-. Bethesda, MD: National Library of Medicine. Research activity is determined using article counts from MEDLINE. There are roughly four times as many dialysis patients as transplant patients.


2. Addis, ibid note 94.
5. Giovannetti and Maggiore, ibid note 28.
7. Harum, Peggy Nutritional Consultant to the Department of Nephlogy, University of Miami School of Medicine, Personal Communication, May 1992.
14. A three year delay onto dialysis could save roughly $100,000, for example, given the low-end estimate of $31,000. Savings would be further positively affected by reduced morbidity, although savings would be based largely on the total amount of time spent on dialysis, which could go up or down.
15. Recent evidence from the MDRD study suggests that DPR can slow entry into stage renal failure for some groups. Cost savings can accrue if patients spend less time on dialysis, for example.
16. Monthly monitoring is conducted by measuring creatinine and GFR levels.
17. As DPR is an early stage intervention treatment, it is best applied to chronic kidney patients early in their disease much the way carbohydrate restricted diet is provided for new diabetes patients. Complete care would likely include a DPR regimen administered directly by a nephrologist and a renal dietitian, and would include regular blood tests for creatinine and glomerular filtration rate to determine kidney function over time. Renal dietitians would train patients in locating and preparing low protein and low phosphorous meals. Careful monitoring of the patient continues after entry onto dialysis.
18. A lively discussion is continuing regarding the interpretation of the MDRD and the recommendations that can be made based on the findings (Mitch, William. Personal communication, 1996).
19. Walser has produced data that show patients who have been on a DPR regimen enter dialysis healthier than a control group (eg. Walser, MacKenzie. 1993. "Does prolonged protein restriction preceding dialysis lead to protein malnutrition at the onset of dialysis" *Kidney International* V44/5, November: 1139-1144).
20. Fox and Swazey, ibid note 3.
21. Starzl, Thomas; R. Weil, and C.W. Putnam "Modern Trends in Kidney Transplantation" *Transplantation Proceedings* V9, March 1977, pp. 1-8; A similar pattern is emerging in the artificial heart area which is now seen as more of a stepping stone to transplantation as opposed to a permanent replacement.
23. That "shortcoming" of DPR was addressed by the recently completed *Modification of Diet in Renal Disease (MDRD)* a ten year prospectively conducted study, see Klahr et al., ibid note 105.
26. In the early 1980s, a prospective randomized controlled test on DPR and renal failure -- the Modification of Diet in Renal Disease -- was commenced. Despite the voiced concerns about the lack of controlled trials, a great deal of resistance against the study ensued. An act of Congress was finally required to get the study underway.
29. Thomas, ibid note 25.
30. Thomas, ibid note 25.
31. Thomas, ibid note 25.
32. Thomas, ibid note 25.
33. Eggers, ibid note 62.
35. Rottig, ibid note 37; Bricker, ibid note 39.
37. Callahan, ibid note 125, p 65.
40. Risjord, ibid note 127.
41. Sullivan, Mark D. "Placebo Controls and Epistemic Control in Orthodox Medicine" *The Journal of Medicine and Philosophy* 18/2 April, 1993, pp. 213-231.
42. Sullivan, ibid note 130.
43. Callahan, ibid note 125.
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