

## Renal care dynamics

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**Abstract:** Human kidneys remove metabolic waste products and regulate our body's water, electrolyte and acid/base balance. Our kidneys filter approximately 190 liters of blood per day. End-stage renal disease (ESRD) is the state of advanced chronic kidney failure, characterized by the irreversible loss of kidney function that requires routine kidney dialysis or transplantation. A system dynamics model capturing end-stage renal care dynamics shows behavior patterns that interest both the private sector and the US federal government. The model's computed scenarios result from the distribution frequency of the available treatments for ESRD. As far as the private sector is concerned, biotechnology firms, for example, while deciding where to invest their resources, they must know what form(s) of treatment is (are) most frequently used, the rate of donations and the results of various treatments on the affected population. The model building process helped biotechnology firms understand which treatment option represents a better business opportunity. As far as public policy is concerned, the modeling team's objective was to identify the cost/benefit of increasing organ donation. The simulation results show the relationship between the level of organ donation and the relative reduction in dialysis costs, attributed to expenses corresponding to non-surgical patient care.

## Kidneys and Nephrons

The kidney is a complex organ in human beings and all other vertebrates. Our two kidneys perform many vital functions, of which the most important is the production of urine. This fluid carries various waste materials out of the body. If the kidneys fail to function, poisons build up in the body, eventually causing death (Beck, 1998).

The kidneys look like purplish-brown kidney beans, about the size of an adult's fist. They lie below the middle of the back on each side of the spine (Fig. 1a). The right kidney, located under the liver, is a little lower than the left one. Some people are born with only one kidney. However, they are able to lead a normal life.

Human kidneys consist of three layers. These layers are, in order, the cortex on the outside of the organ, the medulla and the pelvis (Fig. 1b). Blood flows into the medulla through the renal artery. In the medulla and cortex, the renal artery branches into increasingly smaller arteries. Each artery ends in a blood filtration unit called a nephron (Fig. 2a). Two healthy kidneys contain a total of about 2 million nephrons, which filter about 50 gallons (190 liters), of blood daily.

A nephron consists of a network of tiny blood vessels, the glomerulus, surrounded by Bowman's capsule, a two-layer membrane that opens into a convoluted tubule. Pressure forces much of the blood plasma (fluid portion of the blood) through the glomerulus and into Bowman's capsule (Fig. 2b). The resulting tubular fluid, which contains water and dissolved chemicals, then passes into the convoluted tubule. The portion of the blood that remains in the glomerulus flows into small vessels called capillaries, which surround the convoluted tubule (Fig. 2b). As the

Figure 1. (a) The urinary systems with (b) cross-section of the left kidney.

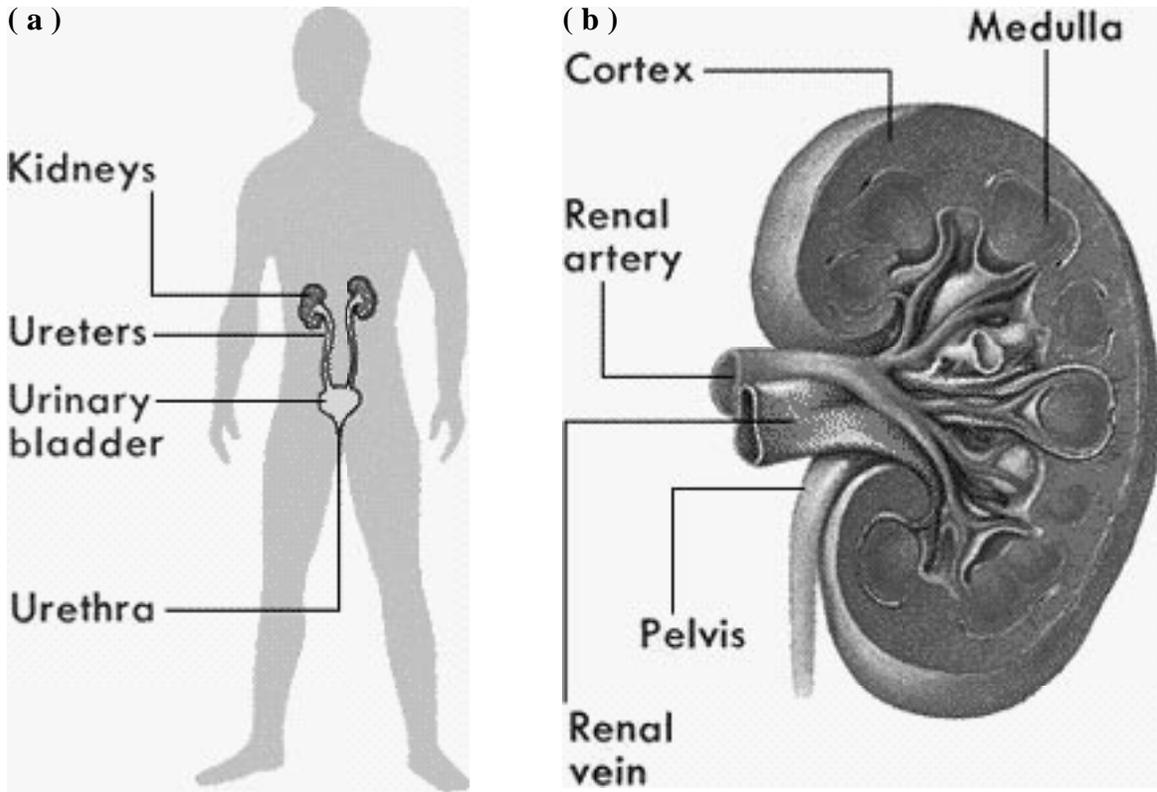
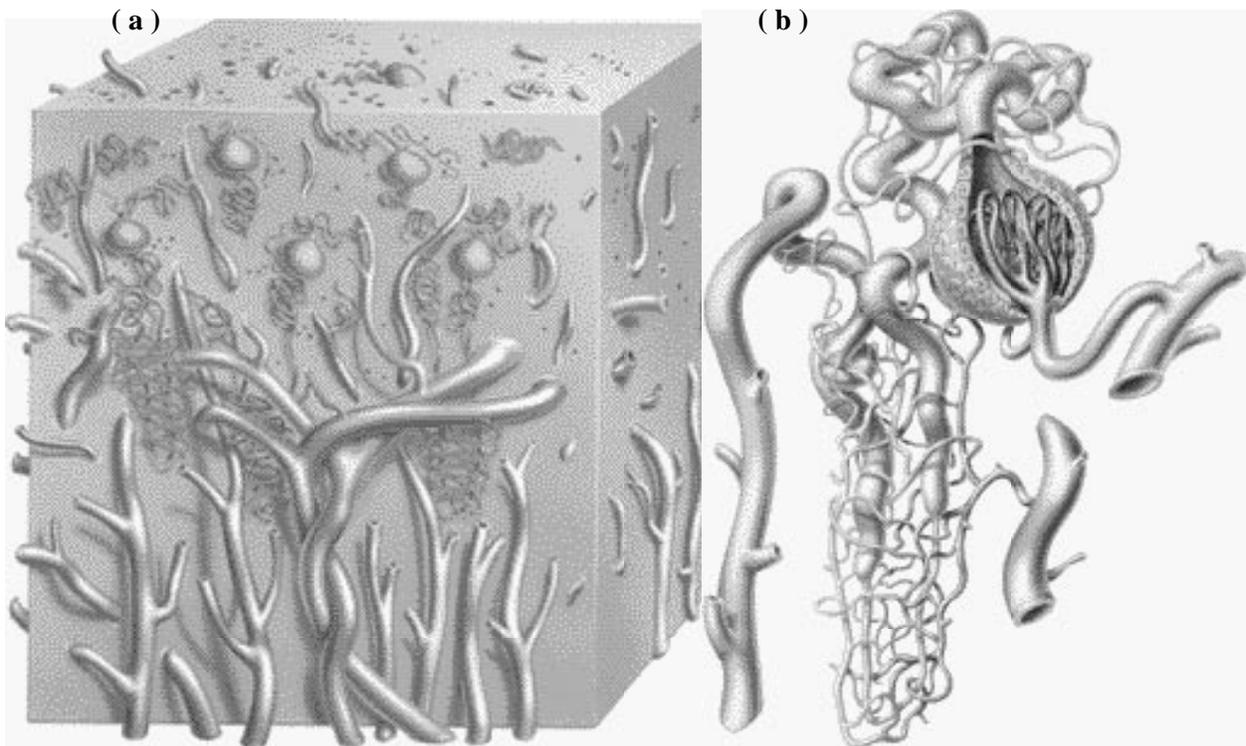


Figure 2. (a) Nephron with (b) Bowman's capsule and capillaries.



tubular fluid flows through the tubule, the cells of the tubule wall absorb substances needed by the body. These substances, which include amino acids, glucose and about 99 per cent of the water then rejoin the blood in the capillaries. The capillaries return the blood to the heart by way of the renal vein (arteries are red and veins are blue in Fig. 1 & 2).

Substances not absorbed in the tubule are wastes that the body cannot use. Other wastes are secreted into the tubular fluid by the tubular cells of the kidney. These various substances, which include ammonia, urea, uric acid and excess water, make up urine. The urine passes from the convoluted tubules into larger collecting tubules and then into the pelvis layer of the kidney. A tube called the ureter carries urine from each kidney into the urinary bladder. Urine collects in the bladder until it passes out of the body through another tube, the urethra. Healthy kidneys produce from 1 to 2 quarts (0.95 to 1.9 liters) of urine daily.

In addition to producing urine, the kidneys secrete a hormone called erythropoietin, which controls the production of red blood cells. The kidneys also convert vitamin D from an inactive to an active form. The active form is essential for normal bone development. Moreover, the kidneys help maintain the blood pressure of the body by releasing an enzyme called renin.

### **Kidney Diseases**

If one kidney is lost in an accident or by disease, the other may enlarge and do the work of both. But if both kidneys are damaged or lost, waste materials accumulate in the body, causing death. Kidney infection, called pyelonephritis, ranks as the most common kidney disease. Most cases result from infection that spreads upward from the bladder. Unless it is complicated by blockage of the urinary tract, pyelonephritis rarely leads to kidney failure. Antibodies produced to fight bacteria or viruses elsewhere in the body also can damage the kidneys. Such reactions lead to inflammation of the glomerulus. This type of inflammation is called glomerulonephritis, formerly known as Bright's disease (Beck, 1998).

Long-term or severe high blood pressure can seriously damage the kidneys, as can diabetes. Cysts, kidney stones and tumors may block the flow of urine. The blocked urine can damage the kidneys by exerting pressure upon them, or it may lead to pyelonephritis. Kidney disorders may also result from birth defects, injuries, poisoning, or as a side effect of certain medications. When both kidneys fail, the body holds fluid. The blood pressure rises. Harmful wastes build up in the body and prevent it from making enough red blood cells. When this happens, one needs treatment to replace the work of failed kidneys.

End-stage renal disease (ESRD) is the state of advanced chronic kidney failure that is characterized by the irreversible loss of kidney function and requires lifetime kidney treatment. ESRD occurs when chronic renal failure progresses to the point at which the kidneys are permanently functioning at less than 10 percent of their capacity. At this point, the kidney function is so low that without dialysis or kidney transplantation, complications are multiple and severe and death will occur from accumulation of fluids and waste products in the body.

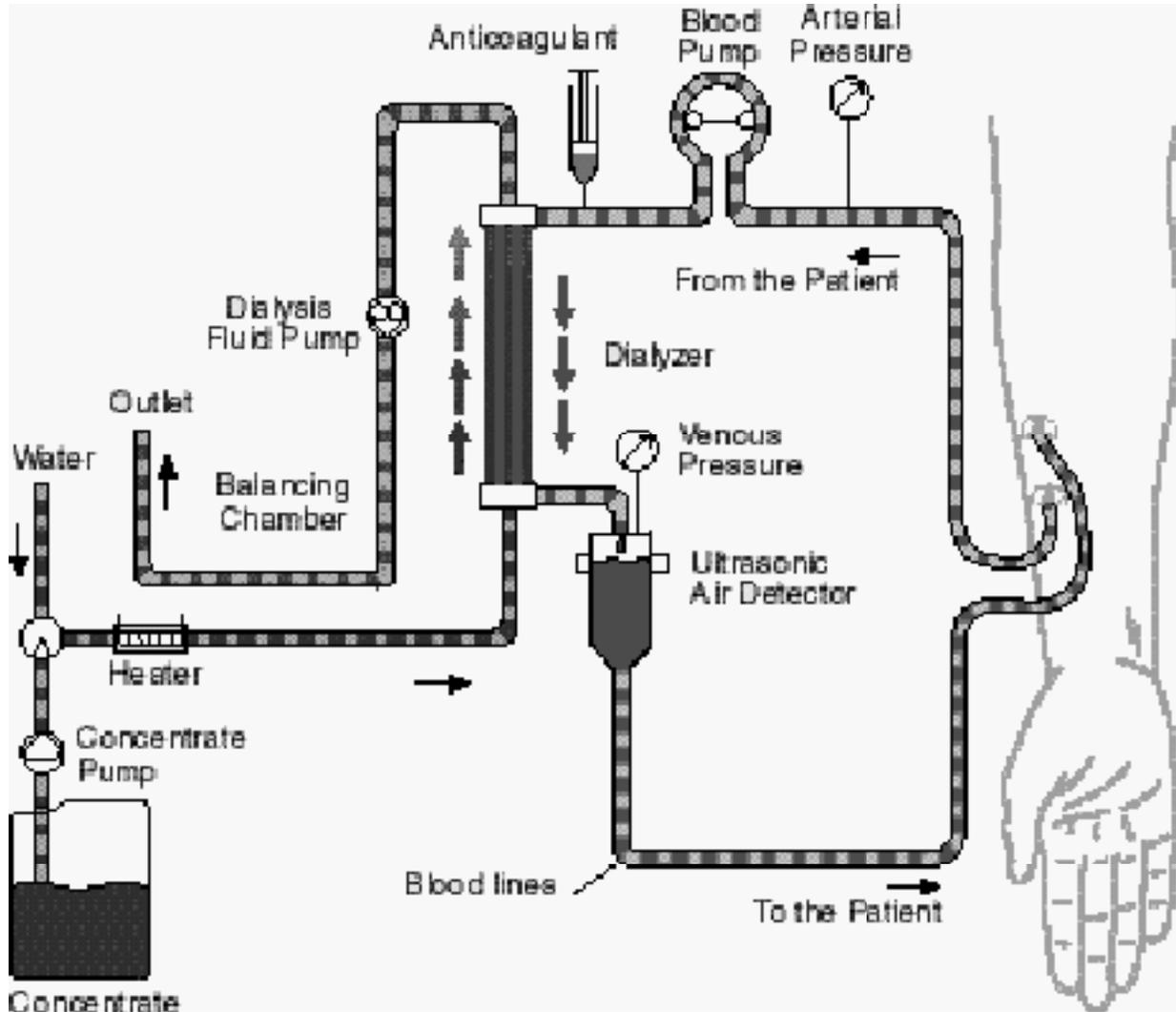
About 4 out of every 10,000 people have end-stage renal disease. In the U.S. almost 100,000 people are on chronic dialysis and more than 20,000 people have a functioning transplanted kidney. Almost half of the people with ESRD are those with diabetes mellitus. ESRD almost always follows chronic kidney failure, which may exist for 10 to 20 years or more before progression to ESRD. Associated diseases that cause or result from chronic renal failure must be controlled. Hypertension, congestive heart failure, urinary tract infections, kidney stones, obstructions of the urinary tract, glomerulonephritis and other disorders should be treated as appropriate. Blood transfusions and medications such as iron and erythropoietin may be needed to control anemia. Fluids may be restricted to an amount nearly equal to the volume of urine produced. Dietary restrictions may slow the build-up of wastes in the bloodstream and control

associated symptoms such as nausea and vomiting. Restrictions include low protein in diet, with high carbohydrate levels to make up calories. Salt, potassium, phosphorus and other electrolytes may be restricted (Brameld et al., 1999; Davies, & Roderick, 1998; Mesler et al., 1999).

### ESRD Treatment Modes

Dialysis and kidney transplantation are the only treatments for ESRD. The physical condition of the person and other factors determine which of these to use for treatment. Other treatments of chronic renal failure may continue but are ineffective without dialysis or transplantation.

Figure 3. Hemodialysis treatment.

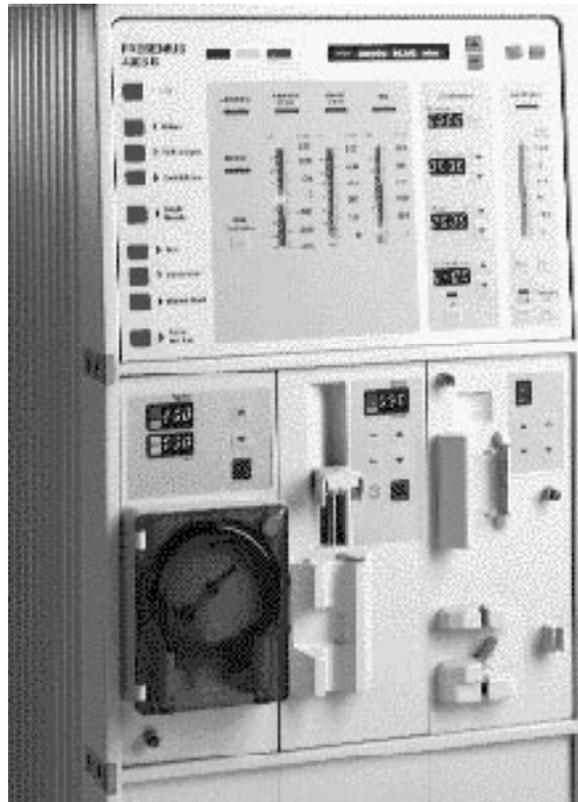


There are two primary methods of dialysis: hemodialysis and peritoneal dialysis. Many people who have lost their kidneys or have suffered kidney damage are kept alive by a dialysis machine. Hemodialysis is a procedure that cleans and filters the blood (Fig. 3). It rids the body of harmful wastes and extra salt and fluids. It also controls blood pressure and helps the body keep the proper balance of chemicals such as potassium, sodium and chloride. Hemodialysis uses a dialyzer, or special filter, to clean the blood. The dialyzer connects to a machine (Fig. 4). A tube connects this machine to an artery in the patient's arm. Another tube carries the blood back into a vein in the arm. During treatment, the blood travels through tubes into the dialyzer. The dialyzer

filters out wastes and extra fluids. Then the newly cleaned blood flows through the other set of tubes and back into the body. A typical patient receives treatments three times a week, lasting 3-6 hours each .

An adequate vascular access should permit blood flow to the dialyzer of 150-450 ml/min. An arteriovenous fistula (Fig. 4) enables ready access to the blood circulation for routine dialysis treatment. Optimal blood access and blood flow in the fistula influences dialysis efficiency. Blood reentering the patient by the venous needle may recirculate and thus effectively reduce the volume of nondialyzed blood entering the extracorporeal circuit. Some hemodialysis machines can detect the degree of recirculation and can thus contribute to improving hemodialysis therapy.

Figure 4. Arteriovenous fistula (left) and hemodialysis machine (right).



*Online*

... bloody literally!

The dialysis machine comprises different systems such as blood pump to deliver blood to the dialyzer, pressure monitors, blood leak detector, air detector, dialysate pump and proportioning system. Ultra-filtration devices control the transport of fluid across the dialyzer membrane. Dialyzers differ in semi-permeable membranes, permeability and method of sterilization. The dialyzer selected affects treatment biocompatibility. Membrane permeability and dialyzer designs determine performance. Low or high flux indicates membrane permeability. High-flux membranes allow the passage of large molecules and display higher water permeability than low-flux ones, thus necessitating the use of machines with volumetric fluid removal controls.

The quality of the therapy provided is determined by the biocompatibility and performance characteristics of the dialyzer and the treatment parameters selected, e.g. treatment time or blood/dialysate flow. Blood may clot when exposed to an artificial surface. Heparin is the most commonly used anticoagulant in hemodialysis. A bolus dose of heparin is generally administered at the beginning of dialysis and thereafter either continuously or intermittently up until the last hour of dialysis. The dialysate creates the solute concentration gradients to drive diffusion across

the dialysis membrane. Dialysate fluid composition corrects the acid/base balance in dialysis patients who display pre-dialysis acidosis. High-quality products are largely the result of proprietary production technology knowledge, while highly automated product manufacturing helps maintain high-quality standards and low manufacturing cost (Fig. 5).

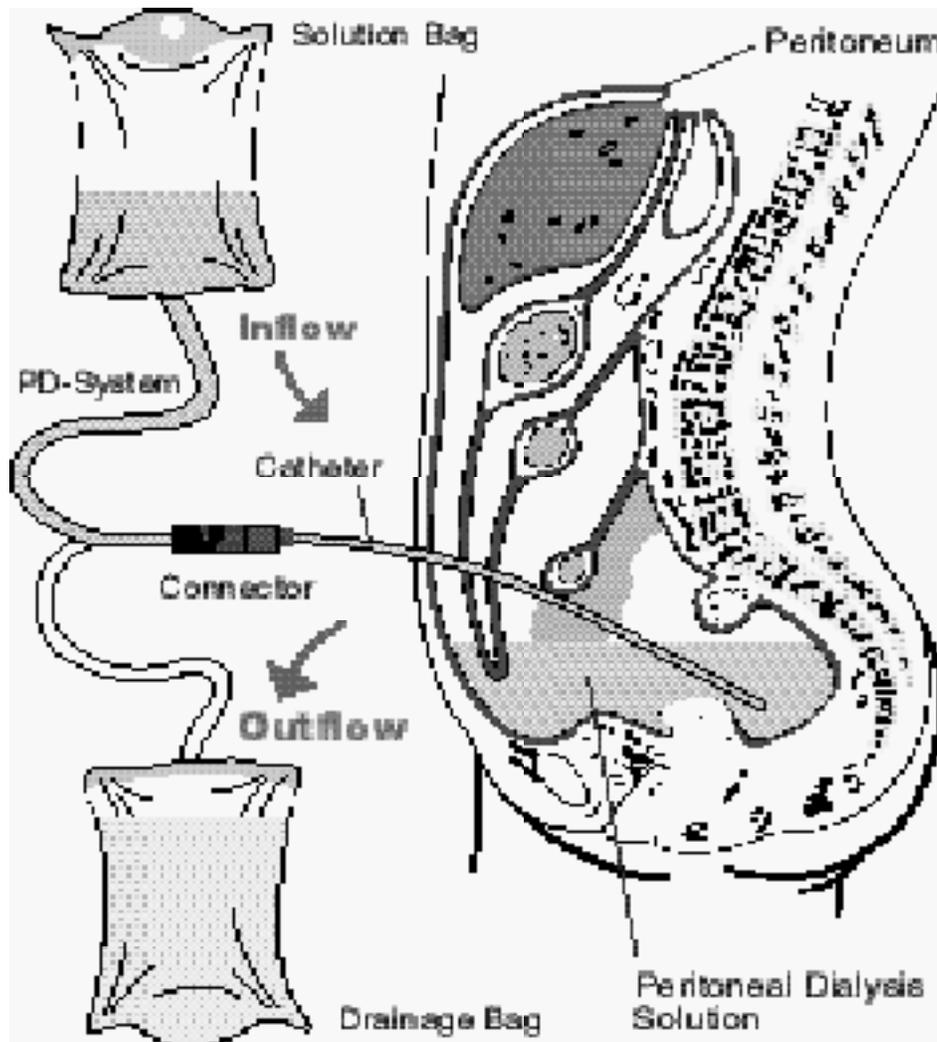
Figure 5. High-quality consumables in ESRD dialysis treatments.



Some kidney patients use ambulatory or peritoneal dialysis, which removes waste products from the blood by use of the peritoneum, the membrane covering the intestinal organs located in the abdominal cavity (Fig. 6). Using a surgically implanted catheter, a sterile dialysis solution called dialysate is introduced into the peritoneal cavity and the peritoneum operates as the dialyzing membrane. Fluid, wastes and chemicals pass from tiny blood vessels in the peritoneal membrane into the dialysate. After several hours, the dialysate gets drained from the abdomen, taking the wastes from the blood with it. Peritoneal dialysis usually requires the introduction and

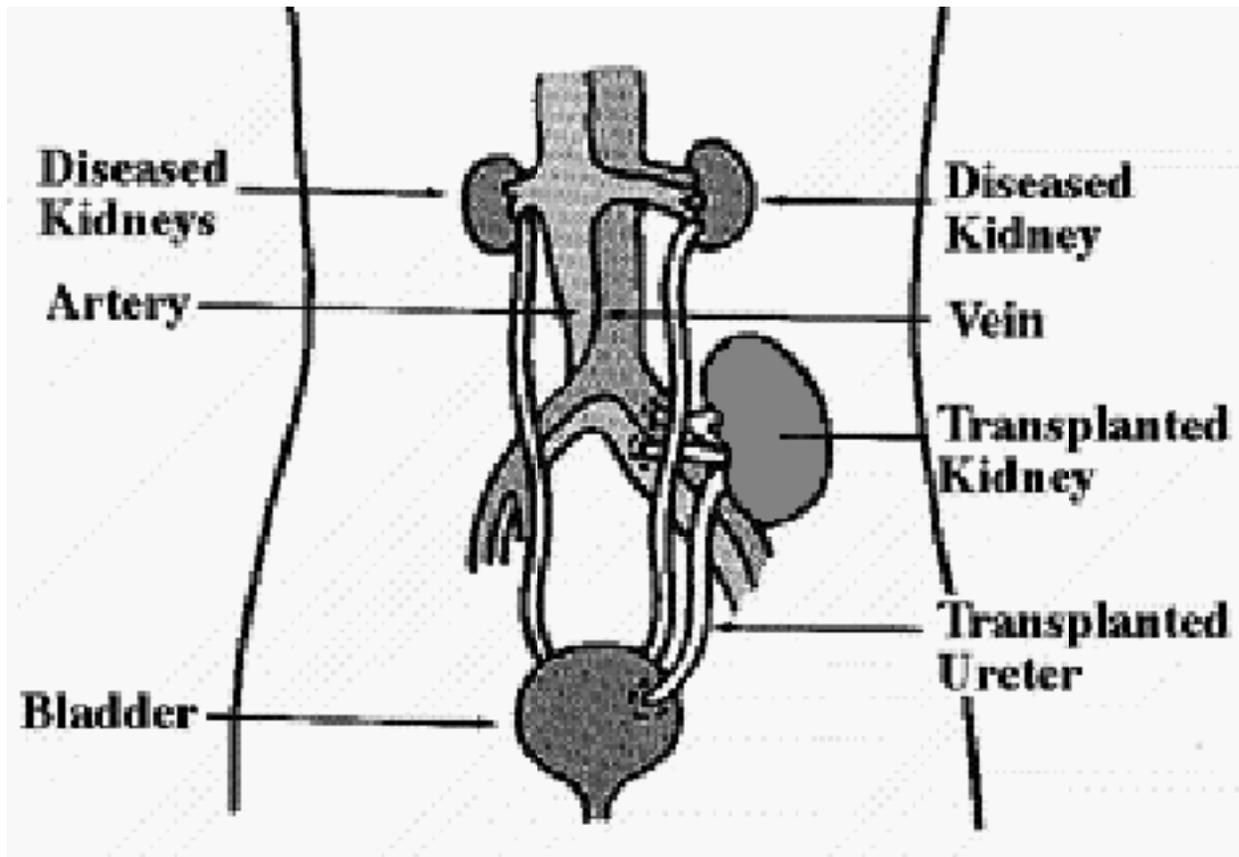
disposal of solutions four times a day (CAPD = Continuous Ambulatory Peritoneal Dialysis) or is supported by a machine cycling solution to and from the patient's peritoneum during sleep (APD = Automated Peritoneal Dialysis). Most peritoneal treatments are self-administered by patients in their homes and workplaces.

Figure 6. Peritoneal dialysis treatment.



Other kidney patients have their diseased kidneys replaced with healthy ones in a kidney transplant, a procedure that places a healthy kidney from another person into one's body. This one new kidney does all the work that the two failed kidneys cannot do. A surgeon places the new kidney inside the body between the upper thigh and abdomen. The surgeon connects the artery and vein of the new kidney to the patient's existing artery and vein (Fig. 7). The blood flows through the new kidney and makes urine. The new kidney may start working right away or may take up to a few weeks to make urine. The failed kidneys are left where they are, unless they are causing infection or high blood pressure. A replacement organ from a close relative is desirable because it closely matches the patient's tissues. But most replacement organs come from unrelated individuals who have died in accidents or from other causes. The patient's body always attempts to reject these foreign organs. However, modern medicines are usually able to control the rejection process and protect the transplanted kidney.

Figure 7. Kidney transplant.



Of the single kidney transplants performed in 1997, 3,579 were from living donors and 7,770 were from cadaveric donors. An additional 841 kidneys were donated in combination with pancreas transplants (National Kidney Foundation, 1998). The success rate of transplant surgery has improved dramatically over time due to advances in organ preservation, surgical technique and more effective drugs. But there is a growing shortage of organs and tissue available for transplantation.

More than 50,000 Americans die each year because of kidney disease. More than 300,000 Americans suffer from Chronic Kidney failure and need artificial kidney machine (dialysis) or a kidney transplantation to stay alive. Over 40,000 patients are waiting for Kidney transplants, but it is estimated that fewer than 11,400 will receive them because of a shortage of organ donations (National Kidney Foundation, 1998).

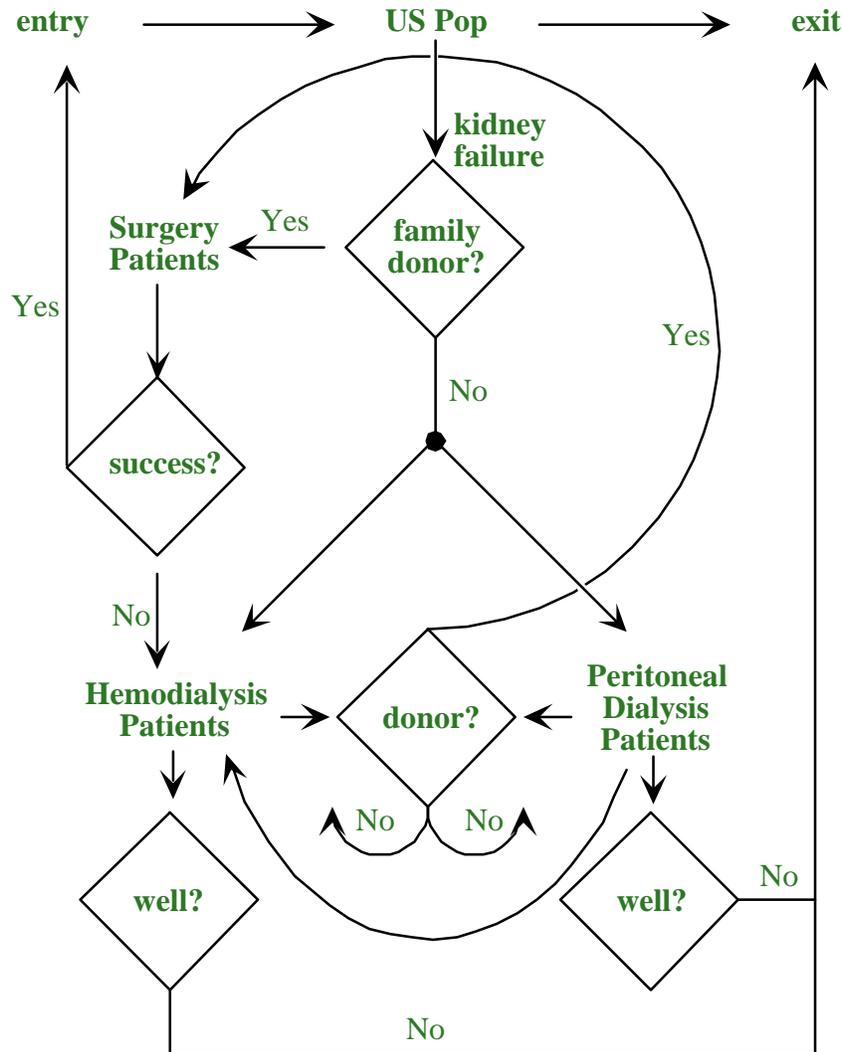
According to the USRDS 1999 Annual Data Report, during the last twenty-five years, the ESRD patient population has increased more than a twenty-five fold, from approximately 10,000 persons in 1973 to nearly 304,000 in 1997. This number represents an approximate increase of 7 percent when comparing with the total number of patients in 1996—283,932 persons (Nissenson & Rettig, 1999). The system dynamics model below captures these end-stage renal care dynamics, showing behavior patterns that interest both the private sector and the US federal government.

### Model Description

Figure 8 shows the project team's rough-cut process map of end-stage renal care. The first thing they do once diagnosed with ESRD, members of the US population (Pop) look for a family

donor. If a family donor comes forth, then the ESRD patients undergo surgery. Otherwise, they must decide between hemodialysis and peritoneal dialysis.

Figure 8. Rough-cut process map.



Because patients are not required to make frequent visits to a hemodialysis clinic, those on peritoneal dialysis may experience much less disruption to life than patients on hemodialysis. The risk of infections leading to episodes of peritonitis, however, a bacterial infection of the peritoneum can limit peritoneal dialysis. Additionally, patients using peritoneal dialysis must have some residual renal function. Both factors limit peritoneal dialysis as a long-term therapy for some patients. Therefore, in general, patients with end-stage renal disease require hemodialysis treatment at some point during their life [Brameld et al., 1999]. Most surgery patients successfully return to the US population. Those with kidney transplant failure, invariably join the hemodialysis patient population because of the high risk of bacterial infections listed above (Davies, 1998).

Hemodialysis is in effect the more frequently used treatment. Approximately 85 percent of the worldwide ESRD patients are treated with hemodialysis while 15 percent are on peritoneal dialysis. Depending on different factors, however, such as status of the medical infrastructure

and reimbursement differences for treatment, there are significant differences in the utilization of hemodialysis and peritoneal dialysis in various states and countries (Nissenson, 1999).

Figure 9. The US population (Pop) sector.

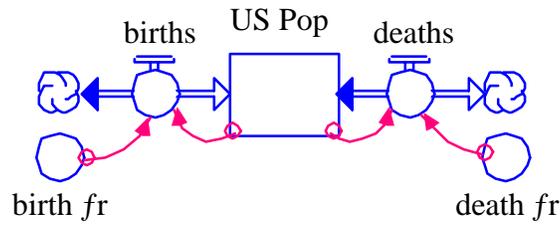
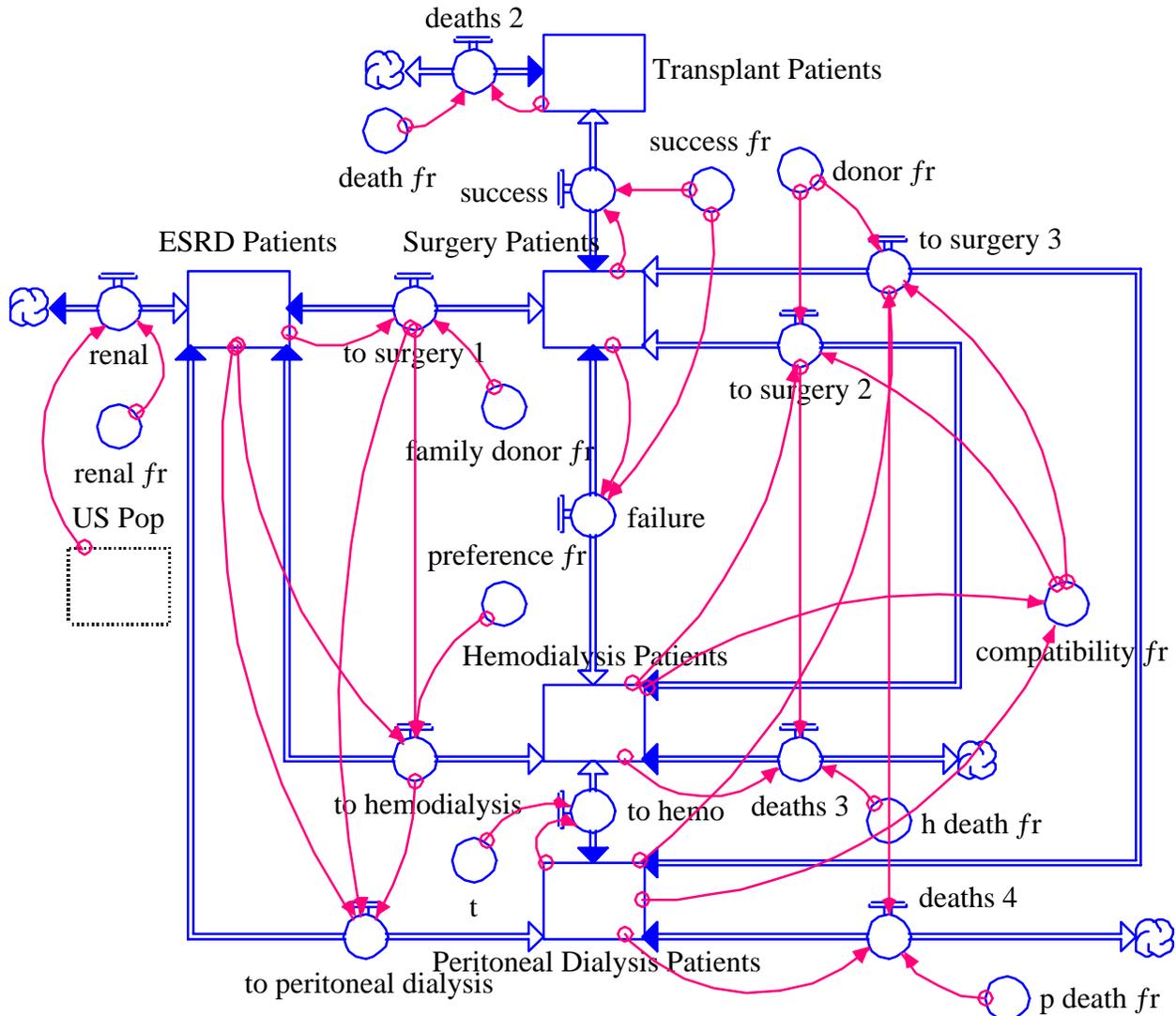


Figure 10. End-stage renal disease (ESRD) treatment sector.



Both hemodialysis and peritoneal dialysis patients keep looking for kidney donors. Relative or not, once a donor is found, ESRD patients go to surgery, hoping to successfully return to the active US population. Until a donor is found, however, both hemodialysis and peritoneal dialysis patients continue their respective renal care treatment (White, 1998).

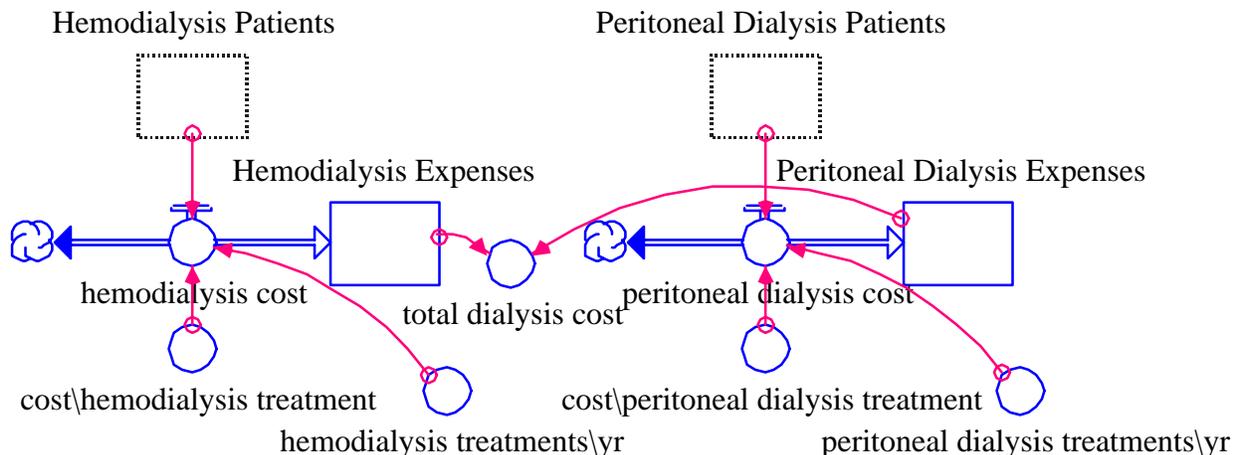
The actual model consists of three sectors. The inflow of total births minus the outflow of total deaths determine the size of the US population (Fig. 9), which feeds ESRD patients to the end-stage renal disease treatment sector (Fig. 10). Together, the type of treatment administered, and the patients that undergo each type of treatment, determine the total treatment cost in the ESRD dialysis cost sector (Fig. 11). The model building process helped biotechnology firms understand which treatment represents a better business opportunity. As far as public policy is concerned, the modeling team's objective was to identify the cost/benefit of increasing organ donation. The simulation results show the relationship between the level of organ donation and the relative reduction in dialysis costs, attributed to non-surgical patient care expenses.

Figure 10 shows that once diagnosed as such, ESRD Patients look for family donors. If a family donor comes forth, according to the family donor fraction ( $fr$ ), then ESRD Patients become Surgery Patients. Otherwise, if no family donors come forth, ESRD Patients must decide between hemodialysis and peritoneal dialysis. As is real life, hemodialysis is the more frequently used treatment in Fig. 10 too. Eighty-five percent of ESRD patients who cannot find a family donor become Hemodialysis Patients, while 15 percent become Peritoneal Dialysis Patients. Again, depending on the factors mentioned above, there might be significant differences in the utilization of hemodialysis and peritoneal dialysis in various states and countries.

Most Surgery Patients successfully return to the US population as Transplant Patients (top of Fig. 10). Those with kidney transplant failure invariably become Hemodialysis Patients because of the high risk of bacterial infections. Even Peritoneal Dialysis Patients require hemodialysis treatment at some point in their life, so is a matter of time ( $t$ ) until they become Hemodialysis Patients. Unless they die per the peritoneal dialysis death fraction ( $p$  death  $fr$ , bottom of Fig. 10).

Depending on the donor fraction ( $fr$ ) parameter (top of Fig. 10), once a donor is found, ESRD patients become Surgery Patients according to their compatibility fraction ( $fr$ ) on the right of Fig. 10. Until a donor is found, however, both hemodialysis and peritoneal dialysis patients continue their respective ESRD treatment. Improved technology and patient care has enabled older patients, and those who previously could not tolerate hemodialysis due to other illnesses, to benefit from this life-prolonging treatment.

Figure 11. ESRD dialysis cost sector.



ESRD treatment type, combined with the number of patients that undergo each treatment type, determine the total treatment cost in the ESRD dialysis cost sector (Fig. 11). Namely, changes in the ghost stock Hemodialysis Patients determine the hemodialysis cost inflow to the Hemodialysis Expenses stock, depending on the unit cost per hemodialysis treatment and the number of hemodialysis treatments per year. Similarly, changes in the ghost stock Peritoneal

Dialysis Patients determine the peritoneal dialysis cost inflow to the Peritoneal Dialysis Expenses stock, depending on the unit cost per peritoneal dialysis treatment and the number of peritoneal dialysis treatments per year. Lastly, total dialysis cost is the sum of Hemodialysis Expenses and Peritoneal Dialysis Expenses.

### Simulation results

Figures 12 and 13 show the base-run simulation results from years 2000 through 2025; the model's specified simulation length. The rest of the simulation specifications entail the computation time interval  $DT=0.0625$ , integration method=Runge-Kutta 4, run mode=normal, interaction mode=normal and simulation speed=0 (zero). Hopefully, ESRD patient growth will remain low compared to the US population, and will resemble the behavior and magnitude that Fig. 12 shows.

Figure 12. US population (Pop) and ESRD patients.

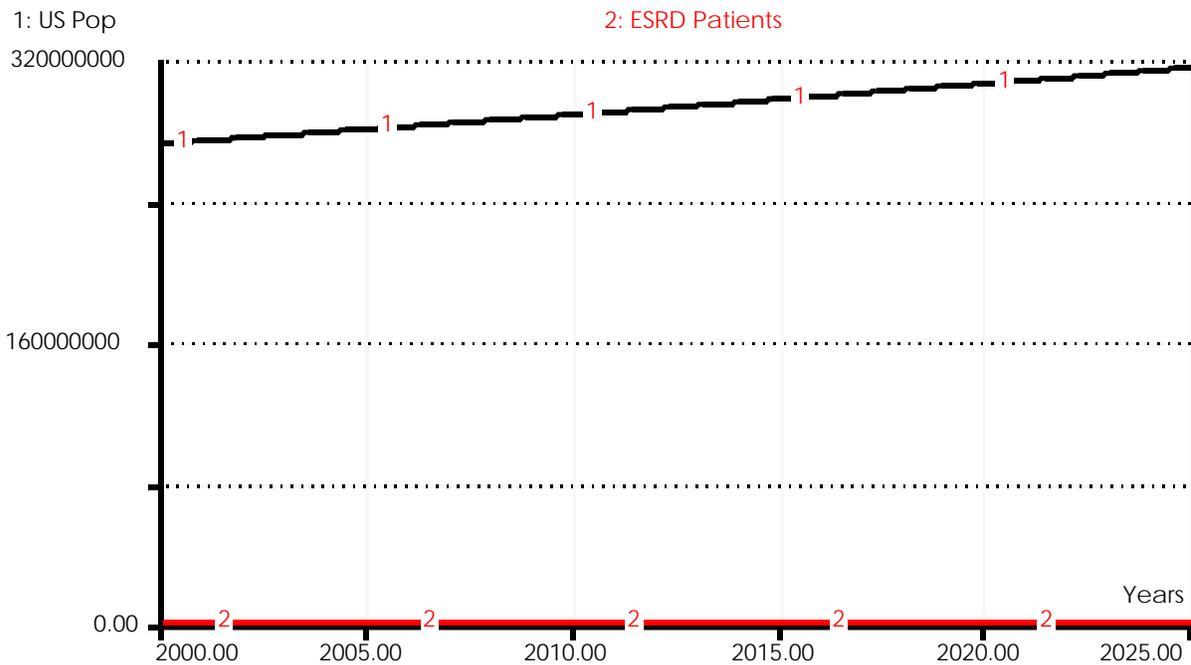
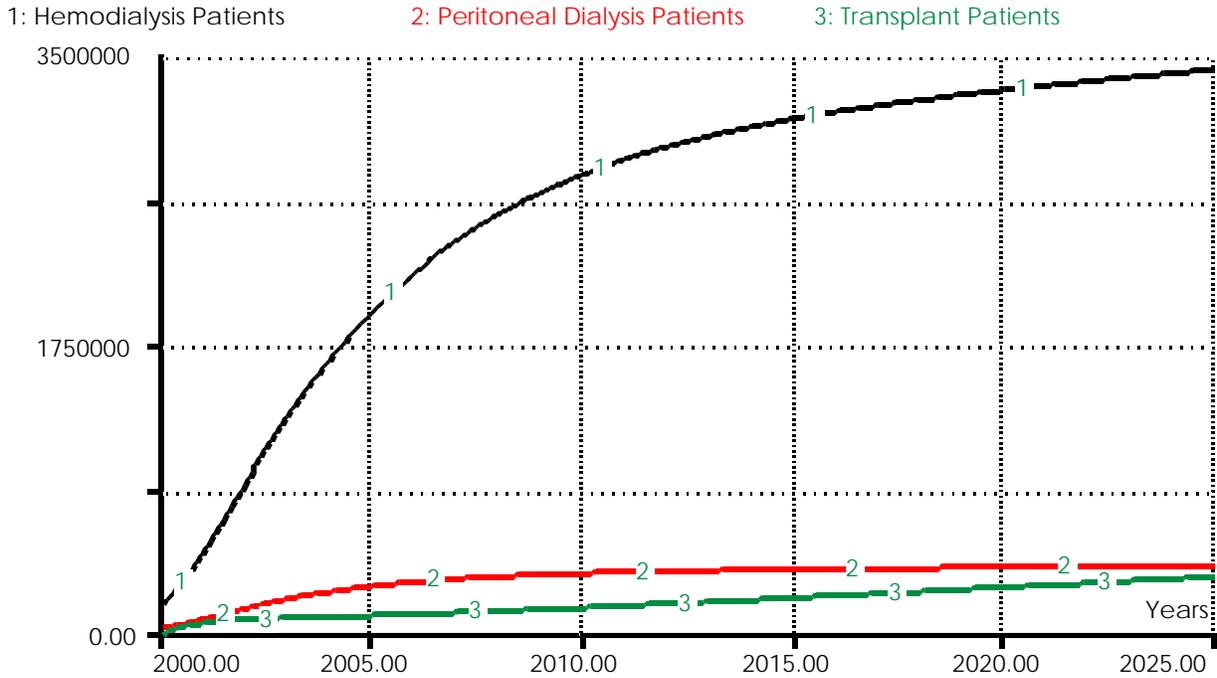


Figure 13 shows the hemodialysis, peritoneal dialysis and transplant patients for the model's base-run simulation. The large accumulation of hemodialysis patients is not surprising since all patients with end-stage renal disease require some hemodialysis treatment. Approximately 85 percent of the worldwide ESRD patients are treated with hemodialysis while only 15 percent are on peritoneal dialysis. Neither is surprising that transplant patients show the least accumulation through year 2025. The initial family donor fraction ( $fr$ ) in the model's ESRD treatment sector (Fig. 10) is about one percent, while the subsequent donor fraction ( $fr$ ) is less than half-a-percent. The growing shortage of organs and tissue available for transplantation explains these low parameter values as well as the minute accumulation of transplant patients.

Figure 13. Hemodialysis, peritoneal dialysis and surgery patients.



Five computed scenarios explore the possibility of a government campaign to reduce the shortage of organs and tissue available for transplantation. Figures 14 and 15 show the effect of increasing the donor fraction ( $fr$ ) parameter of Fig. 10, from less than half-a-percent to one percent, on the hemodialysis and peritoneal dialysis expenses. The simulation results show a dramatic decrease in both the hemodialysis and the peritoneal dialysis expenses (Fig. 14 & 15).

Figure 14. Hemodialysis expenses scenarios.

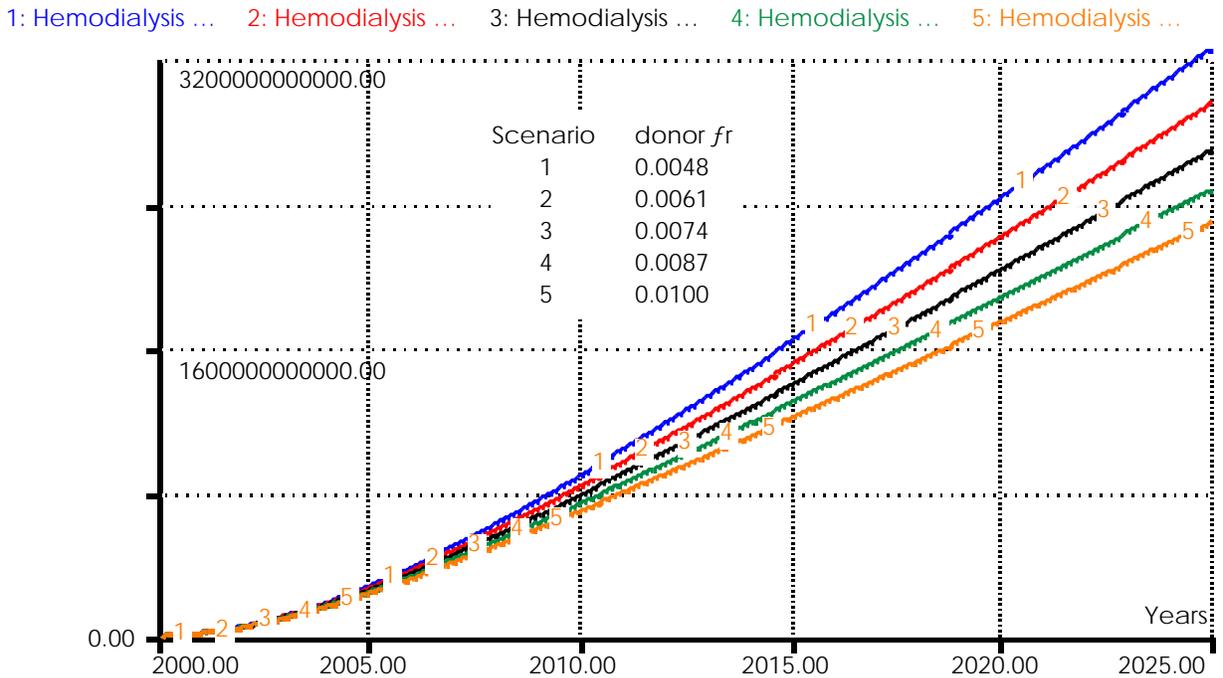
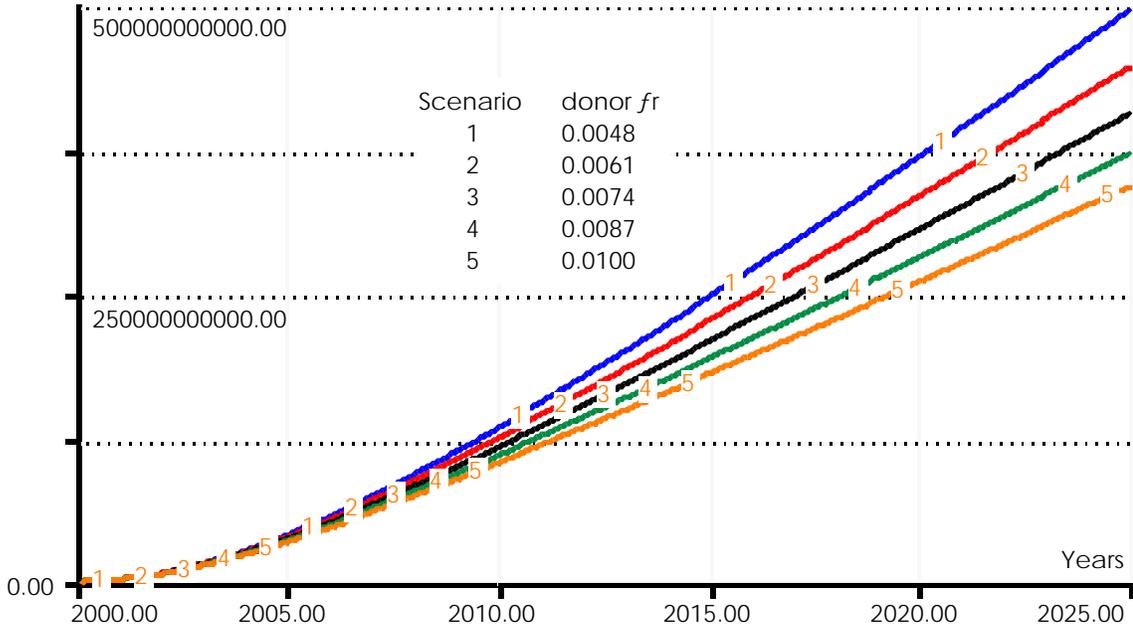


Figure 15. Peritoneal dialysis expenses scenarios.

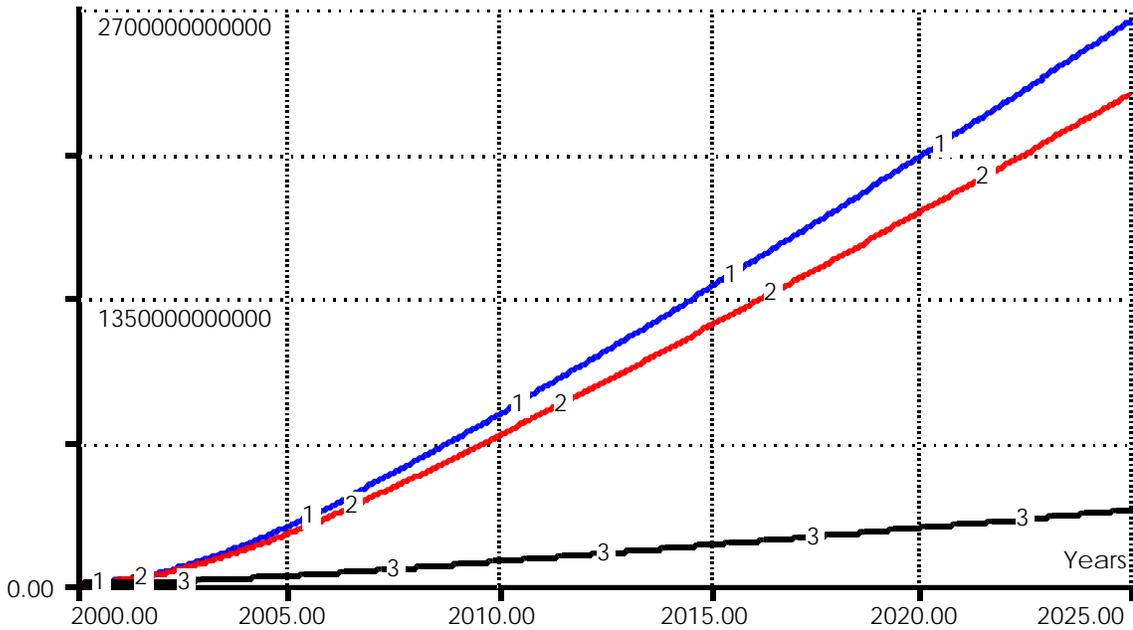
1: Peritoneal Dial... 2: Peritoneal Dial... 3: Peritoneal Dial... 4: Peritoneal Dial... 5: Peritoneal Dial...



Naturally, hemodialysis expenses continue to represent 85 percent of the total dialysis cost, while its balance (15 percent) consists of peritoneal dialysis expenses (Fig. 16).

Figure 16. Total dialysis cost = hemodialysis expenses + peritoneal dialysis expenses

1: total dialysis cost 2: Hemodialysis Expenses 3: Peritoneal Dialysis Expenses



**Conclusion**

The continued growth of the ESRD patient population should ring alarm bells in the minds of all

concerned with chronic care and its treatment. Primary kidney disease contributes modestly to end-stage kidney failure. The two largest feeder streams to ESRD by far are diabetes (an endocrine disorder) and hypertension (a cardiovascular disease). It is projected that by 2002 two-thirds of all U.S. ESRD patients will have a diagnosis of hypertension or diabetes mellitus as the principal cause of their renal failure (Nissenson, 1999).

This model's computed scenarios result from the distribution frequency of the available treatments for kidney disease. Biotechnology firms now know what form(s) of treatment is (are) most frequently used, the rate of donations and the outcome of the various treatments on the affected population. As far as public policy is concerned, model's results identify the cost/benefit of increasing organ donation. The results show the relationship between organ donation and the relative reduction in dialysis treatment costs.

As a consequence of ESRD cost-control efforts, dialysis facilities have been squeezed tremendously. Highly trained staff, such as registered nurses (RNs), are being replaced by less well trained persons at lower cost; reuse of dialysis filters is another economizing strategy adopted in response to capped payment; and old, outdated equipment is replaced only gradually (Kauf et al., 1999). Yet, the number of ESRD facilities in the United States continues to grow. Between 1996 and 1997 the number of treatment units grew by 341 to a total of 3,423 ESRD providers, including freestanding and hospital-based dialysis units, transplant centers providing dialysis services and centers providing transplant care only. As of June 1998 there were 3,470 ESRD providers. HCFA has interpreted this growth as evidence that payment rates are adequate. A different interpretation is that rates are adequate only for those dialysis units that are affiliated with large for-profit chains (Nissenson & Rettig, 1999).

The continued profitability of large for-profit dialysis chains financed mainly from the public sector, which provides an attractive and stable return for investors, creates an understandable resistance among policymakers to increasing reimbursement rates. Clearly, however, the financial pressures on smaller chains and individually owned units make their continued profitability questionable. The escape hatch for smaller units remains to sell to the chains, at \$25,000 to \$40,000 per patient. U.S. payment policy thus may be driving dialysis providers into larger corporate entities. Although industry consolidation may allow for greater efficiencies in service delivery and collection and analysis of outcomes data, the resulting trade-off may be reduced physician and patient choice and autonomy.

The early identification of at-risk patients and their improved medical management offers an opportunity to decrease the incidence of ESRD and to improve other aspects of health associated with great morbidity and cost. Many patients, however, will progress to ESRD despite early identification and appropriate medical care. More careful selection of patients likely to benefit from dialysis will raise yet again the specter of rationing access to this life-saving treatment.

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