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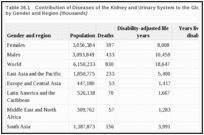
DEPARTMENT: PHARMACOLOGY

COURSE: PHS212

DISCUSS THE DISEASES OF THE RENAL SYSTEM

**Causes and Characteristics of the Burden of Diseases**

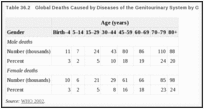
Estimates of the global burden of disease indicate that diseases of the kidney and urinary tract account for approximately 830,000 deaths and 18,467,000 disability-adjusted life years annually, ranking them 12th among causes of death (1.4 percent of all deaths) and 17th among causes of disability (1.0 percent of all disability-adjusted life years). This ranking is similar across World Bank regions ([table 36.1](https://www.ncbi.nlm.nih.gov/books/NBK11791/table/A5064/?report=objectonly)).

[](https://www.ncbi.nlm.nih.gov/books/NBK11791/table/A5064/?report=objectonly)

[**Table 36.1**](https://www.ncbi.nlm.nih.gov/books/NBK11791/table/A5064/?report=objectonly)

Contribution of Diseases of the Kidney and Urinary System to the Global Burden of Disease by Gender and Region *(thousands)*.

Recent research suggests that the data shown in [table 36.1](https://www.ncbi.nlm.nih.gov/books/NBK11791/table/A5064/?report=objectonly) underestimate the global prevalence of kidney disease. Chronic kidney disease (CKD) patients often suffer from cardiovascular or cerebrovascular disease, and their deaths may be attributed to either complication ([Hostetter 2004](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Altered kidney function is often found in patients with hypertensive and ischemic heart disease, both of which are associated with increased cardiovascular morbidity and mortality. Approximately 30 percent of patients with diabetes have diabetic nephropathy, with higher rates found in some ethnic groups ([King, Aubert, and Herman 1998](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). [Table 36.2](https://www.ncbi.nlm.nih.gov/books/NBK11791/table/A5065/?report=objectonly) shows that both genders are similarly affected by kidney disease ([Coresh and others 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

[](https://www.ncbi.nlm.nih.gov/books/NBK11791/table/A5065/?report=objectonly)

[**Table 36.2**](https://www.ncbi.nlm.nih.gov/books/NBK11791/table/A5065/?report=objectonly)

Global Deaths Caused by Diseases of the Genitourinary System by Gender and Age.

Generally, renal diseases progress to a final stage as end-stage renal disease (ESRD) and function is substituted by renal replacement therapy (RRT), hemodialysis, peritoneal dialysis, or transplantation. National and international registries of patients on RRT are useful for providing information on the prevalence of renal diseases in a given country. Data combined from different sources show that more than 1.5 million people worldwide are on RRT, 80 percent of whom live in Japan, Europe, and North America ([Weening 2004](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

The percentage of patients on regular dialysis varies across countries as a consequence of the capacity of health care systems to provide treatment. Europe is an example. Whereas in the 15 countries of the European Union (before 2004) the prevalence rate of RRT was approximately 650 patients per 1 million people, in Central and Eastern Europe it was only 160 patients per 1 million people, reflecting differences in gross national product.

Much less is known about the prevalence of earlier stages of CKD, when symptoms may be mild, ignored, or undiagnosed. A lack of standardization of the stages of CKD has hampered assessments of the burden of CKD. In an attempt to carry out such an assessment, the National Center for Health Statistics of the Centers for Disease Control and Prevention in the United States conducted a survey from 1988 to 1994. The center analyzed a sample of 15,625 noninstitutionalized individuals age 20 and older and defined five stages of renal dysfunction according to estimates of renal function and urine albumin level. [Coresh and others (2003)](https://www.ncbi.nlm.nih.gov/books/NBK11791/) found that the estimated prevalence of CKD in the United States is 11 percent of the adult population, or 19.8 million people. Nationally representative data on U.S. adults older than 20 show that 6.3 percent, or 11 million people, have stage 1 CKD, or kidney damage (proteinuria) with normal kidney function (Glomerular Function Rate (GFR) at least 90 milliliters per minute in 1.73 per meter squared) or stage 2 CKD, that is, mildly reduced kidney function (60 to 89 ml/min/1.73 m2). Furthermore, 4.3 percent, or 7.6 million people, exhibit stage 3 CKD, or moderately reduced kidney function (30 to 59 ml/min/1.73 m2), and 0.2 percent, or 400,000, have stage 4 CKD, or severely reduced kidney function (15 to 29 ml/min/1.73 m2) ([Coresh and others 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/); [Coresh, Astor, and Sarnak 2004](https://www.ncbi.nlm.nih.gov/books/NBK11791/); [National Kidney Foundation 2002](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). A sizable proportion (360,000) of these patients eventually progress toward ESRD (stage 5, or less than 15 ml/min/1.73 m2) and require RRT. Early detection of CKD is, therefore, important to retard or arrest the loss of renal function. Late detection of CKD is a lost opportunity for making lifestyle changes and initiating therapeutic measures.

[Go to:](https://www.ncbi.nlm.nih.gov/books/NBK11791/)

**Causes of Diseases of the Kidney and Urinary System**

Kidney disease leading to ESRD has many causes. The prevalence varies by country, region, ethnicity, gender, and age.

**Genetic Diseases**

Knowledge of inherited kidney disease has changed radically with advances in molecular biology and gene-sequencing technology. The characterization of inherited kidney diseases has improved, and novel mutations leading to selective renal defects have been described. Inherited kidney diseases are rare, with the exception of autosomal dominant polycystic kidney disease, the fourth most common cause of ESRD in developed countries. This disease has a prevalence of 1 in 1,000 people and affects approximately 10 million people worldwide ([Grantham 1997](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Autosomal recessive polycystic kidney disease is less frequent, with an incidence of 1 in 40,000, but is an important hereditary disease of childhood ([Guay-Woodford, Jafri, and Bernstein 2000](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Many other inherited diseases can lead to ESRD, but together they account for only a small percentage of all people with ESRD.

**Glomerulonephritis**

Glomerulonephritides are a group of kidney diseases that affect the glomeruli. They fall into two major categories: *glomerulonephritis* refers to an inflammation of the glomeruli and can be primary or secondary, and *glomerulosclerosis* refers to scarring of the glomeruli. Even though glomerulonephritis and glomerulosclerosis have different causes, both can lead to ESRD. Glomerulonephritis ranks second after diabetes as the foremost cause of ESRD in Europe. ([Stengel and others 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)) and is the second leading cause of ESRD in the United States, according to the United States Renal Data System (<http://www.ifrr.net/>). Approximately 20 to 35 percent of patients requiring RRT have a glomerular disease.

Glomerular diseases are more prevalent and severe in tropical regions and low-income countries ([Seedat 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). A common mode of presentation is the nephrotic syndrome, with the age of onset at five to eight years. Estimates indicate that 2 to 3 percent of medical admissions in tropical countries are caused by renal-related complaints, most resulting from glomerulonephritis.

A number of kidney diseases that result from infectious diseases, such as malaria, schistosomiasis, leprosy, filariasis, and hepatitis B virus, are exclusive to the tropics. HIV/AIDS can be complicated by several forms of kidney disease; however, patient data are sparse ([Seedat 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

Acute poststreptococcal nephritis following a throat or skin infection caused by Group A streptococcus has almost disappeared in high-income countries because of improved hygiene and treatment but remains an important glomerular disease in India and Africa, where epidemics have been reported ([Seedat 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

The eradication of endemic infections, along with improvements in socioeconomic status, education, sanitation, and access to treatment, is a crucial step toward decreasing the incidence of glomerular diseases in developing countries.

**Infections, Stones, and Obstructive Uropathy**

Infections of the urinary tract are a common health problem worldwide and can be categorized as either uncomplicated or complicated. Uncomplicated infections include bladder infections such as cystitis, seen almost exclusively in young women ([Hooton 2000](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Among sexually active women, the incidence of cystitis is 0.5 episodes per person annually, and recurrence develops in 27 to 44 percent of cases. Acute, uncomplicated pyelonephritis, involving the kidney, is less frequent in women than is cystitis. Males are less susceptible to acute, uncomplicated infections of the bladder or the kidney, with an incidence of five to eight episodes per 10,000 men annually. Even though uncomplicated urinary tract infections are considered benign, they have significant medical and financial implications estimated at approximately US$1.6 billion per year ([Foxman 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

As for complicated urinary tract infections, hospitalization results in almost 1 million such infections per year in the United States. Bladder catheterization is the most important cause.

Developing countries exhibit a different pattern of urinary tract infection. Obstructive or reflux nephropathy is often attributed to urinary schistosomiasis ([Barsoum 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Worldwide, 200 million people are affected and an estimated 300 million are at risk. The disease causes lesions in the bladder and predisposes those with the condition to secondary infections, bladder cancers, and chronic pyelonephritis.

Some 15 to 20 million people have tuberculosis (TB) worldwide, of whom 8 million to 10 million are infectious. Genitourinary TB is a common form of extrapulmonary TB and is always secondary to the primary lesion, which usually occurs in the lung ([Pasternak and Rubin 1997](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Lesions referred to as *ulcerocavernous* or *miliary* affect the kidneys. If left untreated, such lesions may progress to kidney destruction. Early recognition of and effective therapy for TB substantially decrease the consequences in relation to kidney function.

In the industrial countries, kidney stones are a common problem ([Morton, Iliescu, and Wilson 2002](https://www.ncbi.nlm.nih.gov/books/NBK11791/)), affecting 1 person in 1,000 annually, and the incidence is increasing in tropical developing countries ([Robertson 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Factors such as age, sex, and ethnic and geographic distribution determine prevalence. The peak age of onset is in the third decade, and prevalence increases with age until 70.

Although largely idiopathic, the following risk factors are associated with stone disease: low urine volume, hyperuricosuria, hyperoxaluria, hypomagnesuria, and hypocitraturia. Diarrhea, malabsorption, low protein, low calcium, increased consumption of oxalate-rich foods, and low fluid intake may play a role in the genesis of stone disease. In developing countries, 30 percent of all pediatric urolithiasis cases occur as bladder stones in children. The formation of bladder stones in children is caused by a poor diet high in cereal content and low in animal protein, calcium, and phosphates.

Kidney stones can have different clinical presentations, ranging from asymptomatic to large obstructing calculi in the upper urinary tract that can severely impair renal function and lead to ESRD. Although specific causes of kidney stones should be treated appropriately, general treatment includes increased fluid intake, limited daily salt intake, moderate animal protein intake, and medical treatment with alkali and thiazides.

The Afro-Asian stone-forming belt stretches from Sudan, the Arab Republic of Egypt, Saudi Arabia, the United Arab Emirates, the Islamic Republic of Iran, Pakistan, India, Myanmar, Thailand, and Indonesia to the Philippines. The disease affects all age groups from less than 1 year old to more than 70, with a male to female ratio of 2 to 1. The prevalence of calculi ranges from 4 to 20 percent ([Hussain and others 1996](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Urolithiasis accounts for some 50 percent of the urological workload and the bulk of urological emergencies. Patients may present with major complications leading to eventual ESRD and resulting in significant morbidity and mortality. In developed countries, only about 1 percent of patients are on dialysis because of obstructive uropathy, whereas in developing countries such as Indonesia and Thailand, obstructive uropathy is often the leading cause of ESRD, accounting for 20 percent or more of patients on dialysis. The availability of appropriately trained medical and surgical personnel and of equipment essential for treating stone disease promptly would reduce the incidence of obstructive uropathy and ESRD. Cost analyses indicate that the medical prevention of stones saves more than US$2,000 per person annually ([Parks and Coe 1996](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

**Benign Prostatic Hypertrophy**

Benign prostatic hypertrophy is a major cause of lower urinary tract symptoms and leads to obstructive renal failure and ESRD. By age 80, 80 percent of men have benign prostatic hypertrophy. The World Health Organization quotes a mortality rate of 0.5 to 1.5 per 100,000 ([La Vecchia, Levi, and Lucchini 1995](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). The actual incidence of benign prostatic hypertrophy is difficult to assess because of the lack of epidemiological data. In the developed world, the incidence varies between 0.24 and 10.90 per 1,000 annually from age 50 to 80, and the probability of prostate surgery for benign prostatic hypertrophy ranges from 1.4 to 6.0 percent ([Oishi and others 1998](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

**Acute Renal Failure**

Acute renal failure refers to a sudden and usually temporary loss of kidney function that may be so severe that RRT is needed until kidney function recovers. Even though acute renal failure can be a reversible condition, it carries a high mortality rate. Acute renal failure is a prominent feature of major earthquakes, where many suffer from crush syndrome accompanied by severe dehydration and rapid release of muscle cell contents, including potassium. Kidney function shuts down unless body fluid and blood pressure are rapidly corrected and frequent hemodialysis is available. Recent earthquake rescues in the Islamic Republic of Iran and Turkey have demonstrated the benefits of rapid hydration and dialysis ([Sever and others 2001](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

**Diabetes**

Diabetes is one of the most common noncommunicable diseases (see [chapter 30](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A4308/)). With the serious complication of nephropathy, diabetes has become the single most important cause of ESRD in the United States and Europe, according to [Stengel and others (2003)](https://www.ncbi.nlm.nih.gov/books/NBK11791/) and the United States Renal Data System (<http://www.ifrr.net/>). Diabetes may account for one-third of all ESRD cases.

Family-based studies and segregation analyses suggest that inherited factors play a major role in people's susceptibility to diabetic renal complications ([Seaquist and others 1989](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). In the United States, the burden of ESRD is threefold to fivefold greater among African Americans, Mexican Americans, and Native Americans than other Americans, and [Imperatore and others (2000)](https://www.ncbi.nlm.nih.gov/books/NBK11791/) find a 200 percent greater possibility of the occurrence of inherited diabetic nephropathy. A family history of [hypertension](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10637/) has also been associated with an increased risk of diabetic nephropathy. When specific markers of risk are found, high-risk individuals can be identified early and monitored for the development of proteinuria and kidney dysfunction.

The earliest sign of diabetic nephropathy is the appearance of small amounts of protein in the urine (*proteinuria*). As proteinuria increases and blood pressure rises, kidney function declines. The complete loss of kidney function occurs at different rates among type 2 diabetes patients, but it eventually occurs in 30 percent of proteinuria cases. The latter have a 10-fold increased risk of dying from associated coronary artery disease, which may obviate the progression of diabetic nephropathy to ESRD. As therapies and interventions for coronary artery disease improve, patients with type 2 diabetes may survive long enough to develop kidney failure.

**Hypertension**

[Hypertension](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10637/) and kidney disease are closely related. Most primary renal diseases eventually produce hypertension. Arterial hypertension accelerates many forms of renal disease and hastens the progression to ESRD ([Luke 1999](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Recent studies have firmly established the importance of continuous blood pressure reduction to slow the progression of many forms of renal injury, particularly glomerular disease ([Agodoa and others 2001](https://www.ncbi.nlm.nih.gov/books/NBK11791/); [Peterson and others 1995](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Over the long term, damage to the heart and cardiovascular system resulting from hypertension represents the major cause of morbidity and mortality among ESRD patients ([Martinez-Maldonado 1998](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

Before the development of effective antihypertensive agents, 40 percent of hypertensive patients developed kidney damage and 18 percent developed renal insufficiency over time ([Johnson and Feehally 2000](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Elevated serum creatinine develops in 10 to 20 percent of hypertensive patients, with African Americans and Africans at particularly high risk. In 2 to 5 percent of hypertensive patients, progression toward ESRD will occur in 10 to 15 years. Despite the relatively low rate of progression, [hypertension](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10637/) remains the most common cause of ESRD after diabetes in the United States, is the foremost cause of death in all developed countries, and is a likely primary cause in developing countries given its high global prevalence rate. Native Americans and Hispanic Americans are disproportionately affected relative to Caucasian Americans.

**Global Perspectives in Relation to RRT**

Despite the lack of uniform data worldwide, the medical community is aware that the total number of patients requiring RRT is growing in all high- and middle-income countries. In the United States, for example, 360,000 people with ESRD were on RRT in 2003, compared with 150,000 in 1994, and according to a recent forecast, by 2014 the figure will have increased to 650,000 ([Xue and others 2001](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). This increase represents a linear growth in new cases combined with longer survival by existing patients.

Levels in middle-income countries are lower, but rising. In Eastern Europe between 1990 and 1996, following economic changes, the number of hemodialysis and peritoneal dialysis centers increased by 56 and 296 percent, respectively ([Rutkowski 2002](https://www.ncbi.nlm.nih.gov/books/NBK11791/)), and the number of patients rose by 78 and 306 percent, respectively.

Overall, the incidence of ESRD is increasing worldwide at an annual growth rate of 8.0 percent, far in excess of the annual population growth rate of 1.3 percent. Nearly 1.6 million people, or only 15 percent of those affected, are receiving RRT, 80 percent of them in developed countries. The remaining 20 percent are treated in more than 100 developing countries, whose populations account for more than 50 percent of the world's population. A large proportion of people living in the poorest countries die of uremia because of a complete lack of RRT.

**Risk Factors for Kidney Disease**

The identification of risk factors can prevent or limit disease through lifestyle modifications or specific therapeutic interventions ([Appel 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/); [McClellan and Flanders 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). For example, familial predisposition for a disease, which is not amenable to modification, can be used to identify high-risk populations for future monitoring.

Low socioeconomic status and limited access to health care are strong risk factors for kidney failure but account for only part of the excess of ESRD among African Americans ([Perneger, Whelton, and Klag 1995](https://www.ncbi.nlm.nih.gov/books/NBK11791/)), whereas racial and social factors account for most ESRD incidence ([Pugh and others 1988](https://www.ncbi.nlm.nih.gov/books/NBK11791/); [Rostand 1992](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Factors associated with the progression of CKD include the following:

* unmodifiable variables
  + old age
  + gender
  + genetics
  + ethnicity
* risk factors susceptible to social and educational interventions
  + low birthweight
  + smoking
  + alcohol abuse
  + illicit drug abuse
  + analgesic abuse and exposure to toxic substance such as lead
  + sedentary lifestyle
* risk factors susceptible to pharmacological interventions
  + [hypertension](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10637/)
  + [dyslipidemia](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10632/)
  + poor glycemic control in diabetic patients
  + proteinuria
* biological markers
  + hemoglobin
  + insulin-resistant syndrome
  + proteinuria
  + serum creatinine.

Growing evidence suggests that fetal exposure to an abnormal intrauterine environment leads to an increased risk of chronic disease later in life. For example, children of diabetic mothers are prone to obesity and diabetes at a young age, and intrauterine growth retardation can lead to ischemic heart disease, diabetes, [hypertension](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10637/), and kidney disease. Disadvantaged racial minorities in developed countries and the impoverished in developing countries are at risk of intrauterine growth retardation caused by malnutrition ([Nelson 2001](https://www.ncbi.nlm.nih.gov/books/NBK11791/); [Nelson, Morgenstern, and Bennett 1998](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). Attention to maternal nutrition and other factors that would reduce low birthweight and impaired nephron development may have long-term implications for the development of CKD.

In low-income countries, poverty is associated with increased exposure to infectious diseases that increase susceptibility to CKD, including glomerulonephritis and parasitic diseases. Obesity caused by a diet rich in saturated fats and high in salt are risk factors for diabetic nephropathy and hypertensive kidney disease. Change in dietary habits and physical activity can reduce the overall incidence of diabetes (see [chapter 44](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A6349/)). Smoking and excessive alcohol consumption increase the risk of ESRD ([McClellan and Flanders 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)), and analgesic abuse and exposure to toxic substances such as lead may affect progressive renal insufficiency ([Lin and others 2001](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

**Interventions to Delay CKD**

During the past 20 years, human and animal research has developed our understanding of CKD and led to preventive measures. The notion of renoprotection has resulted in a dual approach to renal diseases based on effective and sustained pharmacological control of blood pressure and reduction of proteinuria. Lowering blood lipids, stopping smoking, and maintaining tight glucose control for diabetes form part of the multimodal protocol for managing renal patients monitored by specific biological markers ([Ruggenenti, Schieppati, and Remuzzi 2001](https://www.ncbi.nlm.nih.gov/books/NBK11791/)).

Abnormal urinary excretion of protein is strongly associated with the progression of CKD in both diabetic and nondiabetic renal diseases. Clinical studies have established that a reduction in proteinuria is associated with a decreased rate of kidney function loss. A specific category of drugs that lower blood pressure, the angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers, appear to be more effective than other antihypertensive drugs in slowing the progression of both diabetic and nondiabetic CKDs ([Brenner and Zagrobelny 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). The administration of an ACE inhibitor (or of an angiotensin receptor blocker) is an important treatment for controlling blood pressure and slowing the rate of progression of chronic kidney failure. Other drugs to lower blood pressure are added as necessary to achieve current targets of 120/80 to 130/80 millimeters of mercury. Concurrent diuretic therapy is often necessary in patients with renal insufficiency, because fluid overload is an important determinant of [hypertension](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10637/) in such cases.

[Dyslipidemia](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10632/) accelerates atherosclerosis and may promote the progression of renal disease. Careful control of the blood glucose level in diabetic patients can be beneficial and may limit other complications. Obesity has not been directly linked to the progression of CKD but is an important risk factor for diabetes and cardiovascular morbidity and mortality. Many patients and health care professionals do not appreciate the benefits of smoking cessation, an important measure in protecting the kidneys from progressive disease resulting from cardiovascular disease (CVD). Additional elements of secondary prevention measures include the treatment of anemia and of abnormal calcium and phosphorus metabolism.

The International Society of Nephrology is developing a program that can be implemented according to the specific needs of a given developing country. The program has two objectives: (a) to identify the prevalence of renal disease among seemingly healthy subjects using a communitywide screening program, especially among populations at risk, and (b) to initiate interventions to prevent the progression of renal disease and affect both renal and CVD outcomes in subjects with or at risk of developing renal disease based on the screening program ([Weening 2004](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). The Kidney Help Trust of Chennai, India, has undertaken a screening program for a population of 25,000. All those who tested positive for high blood pressure, diabetes, or both (about 15 percent) were further studied and then treated with inexpensive antihypertensive and antidiabetic drugs. The cost of the one-year program was Rs 300,000 (US$7,500) or a per capita cost of US$0.27, well within the limits of the Indian government's per capita annual health expenditure of US$7.67 ([Mani 2003](https://www.ncbi.nlm.nih.gov/books/NBK11791/)). A similar program in Bolivia examined a population of 14,000 and also found that 15 percent were hypertensive, diabetic, or both.

An extremely successful program of detection and treatment of renal and cardiovascular diseases among Australian Aborigines was conducted from 1995 to 2000. The ESRD rate among Aborigines is 3 to 10 times that in developed countries. Treatment consisted of long-acting ACE inhibitors to lower blood pressure. After an average of 3.4 years of follow-up, the incidence of ESRD was reduced by 63 percent and nonrenal deaths were reduced by 50 percent. [Hoy and others (2003)](https://www.ncbi.nlm.nih.gov/books/NBK11791/) estimate that this two-year program may have saved US$500,000 to US$2.7 million in avoided or delayed dialysis costs.

Trained staff members can carry out screening programs inexpensively. Economic analysis, however, suggests that large-scale programs should be restricted to screening and treating only specific high-risk populations. Screening programs can be implemented using simple, cheap, and reliable tests consisting of measurements of bodyweight, blood pressure, blood glucose, and creatinine. Screening includes testing urine for hemoglobin, glucose, leukocytes, and protein (repeat tests may be necessary on a spot urine sample); calculating albumin to creatinine ratios; testing positive results for increased serum creatinine and fasting glucose (or glycosylated hemoglobin A1c test); and reassessing the urine protein excretion rate, a cornerstone of kidney assessment. Resulting albumin to creatinine ratio categories would indicate a scale of severity of glomerular disease, with a cardiovascular risk score based on body mass index, [hypertension](https://www.ncbi.nlm.nih.gov/books/n/dcp2/A10619/def-item/A10637/), fasting glucose level, microalbuminuria or gross albuminuria, and serum creatinine. Patients with positive markers for kidney disease would receive the best treatment available at the screening center. Incorporating screening for kidney disease within screening programs developed for CVD and diabetes is important because proteinuria and renal dysfunction are early sensitive markers of vascular dysfunction and CVD patients are at significantly higher risk of kidney disease than the general population.

Resultant medical treatment would focus on the use of ACE inhibitors or angiotensin receptor blockers with a target blood pressure of 120/80 to 130/80 millimeters of mercury. The greater the level of proteinuria, the more treatment is required; thus, the ACE inhibitor dose would be titrated up as proteinuria levels increased. Diuretics and other antihypertensives would be added to meet blood pressure targets. Efforts should be made to obtain low-cost (off-patent) ACE inhibitors or other low-cost antihypertensives. Such treatment should delay or stop the progression of kidney disease and reduce the risk of CVD. Other preventive measures include serum glucose and lipid control and low-dose aspirin if a risk of CVD exists