Chapter 13

Kidney Disease

Shuchi Anand, Bernadette Thomas, Giuseppe Remuzzi, Miguel Riella, Meguid El Nahas, Saraladevi Naicker, and John Dirks

INTRODUCTION

Deterioration in kidney function, whether acute or chronic, can lead to substantial morbidity and mortality. Acute kidney injury (AKI) is a powerful indicator for in-hospital mortality; those who survive face increased length and cost of hospitalization. Some individuals with chronic kidney disease (CKD) develop progressive renal dysfunction and require costly therapy with dialysis, transplant, or both. Even more often, individuals with CKD face high risks for cardiovascular events, anemia, and fractures.

This chapter reviews current data on the epidemiology and trends in the etiology of AKI, CKD, and end-stage renal disease (ESRD), with a focus on low- and middle-income countries (LMICs). We also review management of these conditions, highlighting several interventions—treatment for AKI, screening for CKD, and modality choice for ESRD—with available data on cost or cost-effectiveness.

ACUTE KIDNEY INJURY

The Condition

Incidence

AKI occurs commonly, although quantifying its exact burden has been challenging. Before 2004, no standardized definition existed. Symptoms do not occur unless severe disease develops. The causes vary widely according to setting—whether AKI is acquired in hospitals or in communities—and establishing practice patterns for screening is difficult. Community-based studies of prevalence illustrate the wide variation in estimates of AKI that are subject to definition and population; studies report annual incidence rates ranging from 22 to 175 per million population (Himmelfarb and Ikizler 2007).

In the mid-2000s, however, the nephrology community began to establish standardized criteria for a case definition of AKI, and evidence indicates that an increasing number of epidemiology reports rely on this definition (Mehta and others 2015). First released in 2004 (Bellomo and others 2004) and updated in 2007 (Mehta and others 2007) and 2012 (Palevsky and others 2013), these definitions emphasize recognizing early signs of kidney injury, with attention to relatively small changes from baseline serum creatinine or expected urine output—since even these small changes are linked with a substantially increased risk for in-hospital mortality (annex 13A) (Chertow and others 2005).

Standardizing 130 studies to the Kidney Disease: Improving Global Outcomes definition of AKI, an extensive global meta-analysis estimates that one in four adults and one in three children throughout the world suffer from AKI during hospitalized care; about 10 percent of these patients develop AKI severe enough to require dialysis (Hoste and Schurgers 2008; Mehta and others 2015; Susantitaphong and others 2013). The overall AKI incidence rate among adults and children was 23.2 percent (95 percent confidence interval [CI] 21.0 to 25.7 percent), with the highest incidence

Corresponding author: John Dirks, Gairdner Foundation, Toronto, Ontario, Canada; john.dirks@gairdner.org. Shuchi Anand and Bernadette Thomas contributed equally to the work.

rate of 31.7 percent occurring in the critical care setting (95 percent CI 28.6 to 35.0 percent). The severe AKI incidence rate was 2.3 percent. Data available on the incidence rate of community-acquired AKI—that is, patients presenting to the hospital after developing symptoms of kidney dysfunction, rather than presenting with a systemic illness that during its treatment course is associated with AKI (hospital-acquired AKI)—were scarce (only seven studies reported this data); however, the rate was relatively lower than that of hospital-acquired AKI at 8.3 percent (95 percent CI 1.6 to 33.0 percent) (Susantitaphong and others 2013).

This analysis also includes only two studies from LMICs. However, a recent update capturing more data from Africa, Asia, and Latin America reports incidence of AKI in these regions comparable to that in high-income countries (HICs) (Mehta and others 2015).

Mortality

Mortality from AKI in HICs has traditionally been reported to be higher than in LMICs, but a recent report indicates that, at least among patients with severe AKI requiring dialysis, mortality rates in LMICs are equivalent or higher (Bouchard and others 2015). A prospective study of AKI in patients hospitalized in intensive care units collected data from three middle-income countries (MICs), Brazil, China, and India; findings indicate that patients in MICs experienced twofold higher odds of mortality and nonrecovery of renal function, despite having lower severity of illness, compared with patients in HICs (Bouchard and others 2015). Single-center studies from LMICs have reported large variation in mortality from AKI requiring dialysis, likely reflecting not only the lack of equipment but also variable levels of expertise (table 13.1).

Etiology

Although rigorous registry data are lacking, experts suggest that the incidence of community-acquired AKI is higher in LMICs than in HICs. Severe systemic diseases, such as sepsis or major surgical procedures, cause the majority of cases of AKI in HICs and in urban areas of LMICs. Some community-acquired reasons for AKI are more common in LMICs: obstetric complications; toxins, including snake venom; diarrheal illness; advanced human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS); leptospirosis; and malaria.

In Africa, nephrologists report that major causes of AKI are related to the burden of HIV/AIDS, malaria,

Table 13.1 Selected Studies with Mortality Estimates for Acute Kidney Injury

Study	Study population	Overall mortality (percent of patients with AKI)	Mortality for AKI cases receiving dialysis (percent)
Low- and middle-income countries			
Susantitaphong and others 2013	Pooled global mortality rate	8.0–22.6[a]	—
Mishra and others 2012	Children receiving PD	—	36.8
Ademola and others 2012	Children receiving PD	—	30.0
Bagasha and others 2015	Patients with sepsis at a Ugandan teaching hospital	21	100
Ponce and others 2012	Patients receiving PD for AKI	—	57.3
Trang and others 1992	Patients receiving PD for AKI	—	26.0
Kilonzo and others 2012	PD for AKI in children (20 percent) and adults (80 percent)	—	20.0
Mehta and others 2016	Pooled global mortality rate from community- and hospital-acquired AKI, seven-day mortality	11.5[b]	17.0[b]
High-income countries			
Susantitaphong and others 2013	Pooled global mortality rate	20.9	49.4[c]
Waikar and others 2006	In-hospital mortality, 1998–2002	20.3	28.1
Talabani and others 2014	Community-acquired AKI, three-month mortality	16.5	—

Note: AKI = acute kidney injury; — = not available; PD = peritoneal dialysis.

a. Represents one study from low-income countries and one from low- and middle-income countries.

b. From 1,153 AKI patients from low- and lower-middle-income countries.

c. Of the 31 studies pooled for this estimate, 2 were from low- and middle-income countries.

leptospirosis, and diarrheal diseases (Lameire and others 2013; Naicker, Aboud, and Gharbi 2008; Prakash and others 2015). More than 50 percent of adults with advanced HIV/AIDS or severe malaria develop AKI (Lameire and others 2013). Noninfectious causes specific to LMICs include obstetric and surgical complications, such as severe hemorrhage or late diagnosis of eclampsia, as well as widespread use of traditional herbal remedies or nonsteroidal anti-inflammatory agents (Luyckx and Naicker 2008; Naicker, Aboud, and Gharbi 2008). Such community-acquired AKI more likely afflicts a younger age group and, especially in cases of malaria or diarrheal illness, exhibits seasonal peaks during rainy seasons (Cerda and others 2008; Lameire and others 2013).

Effectiveness of Interventions

AKI management largely depends on etiology and severity. Treatment algorithms in HICs recommend optimizing volume using crystalloid solutions until clinical dehydration is corrected followed by vasopressor support to maintain perfusion pressure (Kellum, Lameire, and KDIGO AKI Guideline Work Group 2013). In conjunction with this approach, treatment of the underlying cause of AKI, such as antibiotics for infection and avoidance of nephrotoxic medications or procedures, often leads to resolution of mild-to-moderate AKI. In HICs, availability of intensive care units, adequate nursing staffing, and rapid-turnaround laboratory facilities allow for frequent and close monitoring of urine output and serum creatinine. Relatively prompt interventions to ameliorate AKI are performed. If AKI progresses to severe renal failure despite these measures, temporary dialysis may be initiated, either to treat volume and electrolyte imbalances or to remove toxins. Continuous hemodiafiltration and intermittent hemodialysis (HD) are the modalities of choice in HICs, although a meta-analysis highlights equivalent survival in patients receiving peritoneal dialysis (PD) versus HD or continuous hemodiafiltration (Chionh and others 2013).

This level of care is not available in most LMICs. The limitations of diagnosis and treatment for advanced AKI are particularly stark in rural areas, but they are also demonstrated in urban university-based hospitals (Bouchard and others 2015; Cerda and others 2008). Data on missed or delayed diagnosis of AKI in LMICs are nonexistent; by their nature, reports on epidemiology of AKI must apply screening criteria that may not be used in standard practice in LMICs. However, studies have confirmed not only a lack of provision of dialysis or transplant but also a lack of intensive care units as crucial gaps in care (Bagasha and others 2015); the infrastructure and budget required to develop renal replacement therapy (RRT) programs to support AKI are often lower priorities in LMICs still struggling with other pressing public health issues, such as infectious diseases, maternal and perinatal health, and nutrition management (Mushi, Marschall, and Flessa 2015). To address such gaps, the International Society of Nephrology has developed an initiative called "0by25." The objective of the initiative is to eliminate preventable deaths from AKI by 2025 by calling for global strategies that permit timely diagnosis and treatment (including dialysis) of potentially reversible AKI, with particular emphasis on LMICs (Mehta and others 2015; Remuzzi and Horton 2013) (see box 13.1 for an example of a dialysis provision program in AKI in LMICs).

Box 13.1

Case Study: Acute Kidney Injury (AKI) Treatment with Peritoneal Dialysis (PD) in Tanzania

An AKI treatment program started in 2007 at Kilimanjaro Christian Medical Centre in Tanzania is a leading example of renal replacement therapy provision for AKI in a low-income country (Burki 2015). The program uses PD.

The program was developed with support from the International Society of Nephrology and the Sustainable Kidney Foundation, which funded training in Brazil for physicians and nurses from Tanzania for PD catheter insertion technique and prescription (Callegari and others 2012; Callegari and others 2013; Kilonzo and others 2012). In a report on the program, directed by Dr. Karen Yeates of Queen's University, Canada, PD was successfully administered to 32 Tanzanian patients with AKI (Burki 2015). The AKI treatment costs were low: approximately US$150–US$400 for the duration of in-hospital treatment, ensuring sustainability once the center assumes total program management.

One of the major lessons has been that nephrologists are not essential for the successful development of such programs. Skilled internists and nurses willing to be trained in PD delivery can achieve satisfactory results (Burki 2015).

Cost and Cost-Effectiveness of Interventions

AKI-related health expenditures reflect costs associated with RRT as well as prolonged hospital stay and increased complexity of care once kidney function has been compromised during illness course, even if compromise of renal function is modest (Chertow and others 2005; Rewa and Bagshaw 2014):

- Prolonged hospitalization
- Intensive care unit services
- Dialysis
- Increased monitoring and intervention
- Increased risk of rehospitalization.

The cost-effectiveness of dialysis provision depends largely on the posthospitalization survival of patients. The SUPPORT study assessed the cost-effectiveness of initiating dialysis in seriously ill hospitalized patients in the United States. Only 27 percent of patients survived after six months; the cost per quality-adjusted life year (QALY) gained was calculated to be US$128,200 (Hamel and others 1997). A study in Finland to assess the cost utility of acute RRT from the societal perspective reported the intervention to be cost-effective only if survival exceeded a year—which occurred only in 43 percent of enrolled patients. Among the first year survivors, mortality was 20 percent over the remaining four years (Laukkanen and others 2013). The study involved a five-year follow-up of patients who received acute RRT in a largely intensive-care-unit-based setting.

Because the demographics of AKI in LMICs skew toward a younger population with lower illness severity, it is likely that the benefits of dialysis provision are greater in LMICs (Anand, Cruz, and Finkelstein 2015; Bouchard and others 2015). However, few cost data are available. One report from Tanzania finds that the cost of one life saved using acute PD was US$370 (Cullis and others 2014). George and others (2011) report that the equipment and solution costs of PD were 3,009 rupees (Rs; US$47), approximately 40 percent of continuous HD filtration costs (Rs 7,184 [US$112]), with equivalent survival.

Recommendations for Policy Makers in LMICs

Although the current understanding of AKI in LMICs is limited, the nephrology community generally agrees on the following (Mehta and others 2015):

- Known incidence is similar to that in HICs.
- Community-acquired causes are more common than in HICs.
- Affected patients are younger than in HICs.
- Lack of intensive care units and access to acute dialysis results in high mortality rates.

This consensus is largely drawn from expert opinions or single-center studies; additional studies are required to estimate the burden, etiology, and mortality of AKI in LMICs.

Based on current consensus, however, the prevention of community-acquired AKI (table 13.2) may play a more crucial role in LMICs. Management algorithms that take the most common region-specific causes into account are crucial in areas with limited staffing of trained physicians. When the need for dialysis arises,

Table 13.2 Prevention and Management of Acute Kidney Injury in LMICs

Recommended intervention	Potential benefit
Prevention or management at the community level	
Improve access to, and quality of, drinking water and sanitation	Prevent AKI related to diarrheal illness, kidney stones, and volume depletion in strenuous working conditions
Educate health care workers, pharmacists, and general populations about nephrotoxic medications and herbs	Reduce AKI related to heavy NSAID, illegal alcohol, or herbal toxin use
Involve local health care workers in the identification of patients at risk of AKI	Prevent or limit exposure to environmental risk factors for AKI, such as parasites, infection-carrying vectors, and obstetric complications
Educate and train nonphysicians, such as nurses or clinical officers, or non–health professionals to locally manage AKI, especially with telemedicine support	Limit the progression of AKI to more severe stages that require dialysis

table continues next page

Table 13.2 Prevention and Management of Acute Kidney Injury in LMICs (continued)

Recommended intervention	Potential benefit
Prevention or management at the hospital level	
Improve perinatal care at first-level hospitals	Reduce AKI related to peripartum hemorrhage or preeclampsia
Enhance region-specific understanding of common causes of AKI at first- and second-level hospitals	Provide rapid treatment of underlying causes of AKI
Implement protocols for intensive or intermediate care at first- and second-level hospitals	Resolve mild-to-moderate AKI via rapid fluid resuscitation, vasopressor support, and antibiotic administration
Provide training in PD provision for AKI at second-level hospitals	Treat severe AKI by training non-nephrology physicians in PD catheter insertion and prescription; enable wider availability of dialysis for severe AKI
Create referral centers for provision of intermittent or continuous HD for patients in whom PD is contraindicated	Select individuals with severe AKI who need specialized care, and efficiently allocate resources for dialysis

Note: AKI = acute kidney injury; HD = hemodialysis; LMICs = low- and middle-income countries; NSAIDs = nonsteroidal anti-inflammatory drugs; PD = peritoneal dialysis.

temporary PD—a less technologically demanding and less costly modality—can be used for both pediatric and adult acute cases. The International Society of Peritoneal Dialysis has published guidelines to standardize the provision of acute PD (Cullis and others 2014). Successful programmatic implementation of PD—training staff, acquiring dialysis equipment, and prescribing dialysis appropriately—has occurred in third-level centers in Benin, Cambodia, Ghana, Sudan, and Tanzania (Finkelstein and others 2014; Wilkie 2014). However, the challenges of scalability and managing patients who do not recover renal function and require long-term dialysis remain (Kilonzo and others 2012).

CHRONIC KIDNEY DISEASE AND END-STAGE RENAL DISEASE

The Condition

Epidemiology of CKD

CKD is diagnosed when an individual has evidence of persistent kidney dysfunction, as reflected by albuminuria, reduction in estimated glomerular filtration rate (eGFR), or both. Identifying individuals with CKD arguably facilitates treatment to reduce cardiovascular events and slow the progression to ESRD (Levey and Coresh 2012).

However, guidelines for streamlining CKD diagnosis have generated controversy because of their reliance on the glomerular filtration rate (GFR) (annex 13B) (Kidney Disease: Improving Global Outcomes Work Group 2012; Levey and others 2003). Older adults who have isolated modest eGFR reductions may have kidney function at the lower end of the normal-for-age range (Wetzels and others 2007), creating the potential for false positives and overutilization of medical resources (Moynihan, Glassock, and Doust 2013; Poggio and Rule 2009). Most cross-sectionally obtained prevalence estimates fail to fulfill the criteria of repeating assessment at three months to determine persistence (Plata and others 1998). Finally, interpretation of albuminuria requires caution in LMICs, where hygiene, malnutrition, and dietary habits may affect urinary excretion of albumin and creatinine.

With these caveats in mind, we make the following interpretation from available population-based prevalence studies (annex 13C):

- CKD prevalence is understudied in LMICs.
- CKD prevalence in LMICs approaches that of HICs.
- Earlier stages of CKD—albuminuria alone—are common in LMICs, unlike HICs, where modest eGFR reductions with or without albuminuria (CKD stage 3) predominate.

At the same time, individuals with CKD in LMICs remain at high risk of adverse events. Notably, albuminuria has been associated with a linear and sizable increase in risk for all-cause mortality and cardiovascular events, starting at urine albumin-to-creatinine ratios above 10 milligrams/gram (Chronic Kidney Disease Prognosis Consortium and others 2010). Risk for ESRD is 4–11 times higher among individuals with albuminuria (Chronic Kidney Disease Prognosis Consortium and others 2010).

Epidemiology of ESRD

ESRD is rare. About 2 million people are undergoing RRT (either dialysis or kidney transplant) worldwide, with a prevalence of 300 per million adult population or 0.03 percent, compared with prevalence estimates in the range of 7 percent to 15 percent for earlier stages of CKD (Anand, Bitton, and Gaziano 2013; Grassman and others 2005; Thomas and others 2015). While the number of people on RRT has nearly doubled since 1990, 80 percent of the individuals receiving RRT live in HICs (Grassmann and others 2005). The latest Global Burden of Disease estimates from the World Health Organization note that 1.8 percent and 1.1 percent to 1.8 percent of deaths in HICs and LMICs, respectively, are attributable to kidney disease; the cause of death is presumably complications of ESRD.

Currently available data only capture information on patients who have access to RRT, not all those who develop ESRD. In HICs, these numbers are roughly equal because most patients who develop ESRD are diagnosed and offered therapy. In LMICs, however, RRT incidence is not a proxy for ESRD incidence, because individuals may die before or immediately after diagnosis, or they may withdraw from therapy because they cannot pay for it (Couser and others 2011).

Two analyses comparing RRT use with projected ESRD prevalence highlight a large disparity (Anand, Bitton, and Gaziano 2013; Liyanage and others 2015); fewer than 5 percent of patients projected to have ESRD actually access therapy in China, India, and Nigeria (Anand, Bitton, and Gaziano 2013). The provision of RRT closely tracks a country's gross national product rather than the prevalence of risk factors.

Trends in Prevalence and Etiology of CKD and ESRD

Despite concerns about accurate diagnosis, most experts agree that CKD is a growing concern worldwide because of the skyrocketing prevalence of its major correlates: diabetes and hypertension. As noted in chapter 2 in this volume (Ajay, Watkins, and Prabhakaran 2017), LMICs are projected to experience the largest percentage increases in the prevalence of diabetes and hypertension (Hossain, Kawar, and El Nahas 2007). Individuals in LMICs are more likely to develop end-organ damage, including progressive CKD, because of delayed diagnosis and poor management of diabetes and hypertension. In a study of individuals with diabetes in Cambodia, more than 50 percent had CKD (Thomas and others 2014), compared with about one-third in the United States (de Boer and others 2011). Not surprisingly, these diseases are an increasingly common cause of ESRD in LMICs. In 2011, 28 percent of cases of ESRD in Brazil were attributed to diabetes, compared with 8 percent in the mid-1990s; 35 percent were attributed to hypertension, compared with 15 percent in 2002 (Oliveira, Romao, and Zatz 2005; Sesso Rde and others 2012).

Although the prevalence of CKD and ESRD related to diabetes and hypertension will increase across the world, HIV nephropathy—a disease of untreated HIV/AIDS resulting in proteinuric kidney disease—will potentially decline. As more individuals with HIV/AIDS have received treatment with antiretroviral drugs, CKD related to side effects of antiretrovirals, comorbid diabetes, or hypertension has already become more common in HICs, a trend that LMICs may follow (Mallipattu, Salem, and Wyatt 2014).

However, kidney diseases related to other infectious diseases—malaria, hepatitis B or C, leptospirosis, and dengue—continue to disproportionately affect individuals in LMICs (Soderland and others 2010). Unusual causes of CKD, including stones and environmental toxins, are also concentrated in LMICs. Stone-related kidney disease is relatively more important in certain regions. In HICs, 3 percent of cases of ESRD are attributed to obstructive uropathy (Jungers and others 2004); in countries along the "stone belt" (a region encompassing North Africa and South and Southeast Asia), up to 6 percent to 11 percent of cases of ESRD are attributed to obstructive uropathy (Jha 2009). Hot climates that predispose individuals to volume depletion or low urine output, low potassium diets, and chewing of calcium hydroxide containing betel leaf all increase the risk for stone formation (Lopez and Hoppe 2010). Limited access to treatment increases the risk for CKD and ESRD.

Individuals in LMICs may experience higher risk for CKD related to environmental toxins, such as lead, arsenic, cadmium, and aristolochic acid. Public health experts from Sri Lanka and the west coast of Central America report that scores of agricultural workers are being diagnosed with CKD unaccompanied by diabetes or hypertension (box 13.2) As yet, there are many unknowns about this phenomenon, including whether the same disease entity is afflicting workers in both regions, and whether strenuous work in high heat may be a major contributing factor.

In summary, while the majority of cases of CKD in both HICs and LMICs is likely to be associated with diabetes or vascular disease, kidney disease from rarer etiologies—from HIV/AIDS to environmental toxins—is much more likely to occur in LMICs than in HICs. It is increasingly apparent that CKD in LMICs is a multifactorial condition caused by interacting factors such as poverty and social deprivation, poor sanitation and hygiene, exposure to water- and food-borne toxins, pollution, and infectious diseases. Accordingly, the epidemiology and treatment of CKD

Box 13.2

Case Study: Investigating Kidney Disease in Farm Workers

Since the early 2000s a form of chronic kidney disease unaccompanied by diabetes or significant hypertension has been reported primarily in rice paddy farmers in the dry zone of Sri Lanka (Chandrajith and others 2011) and sugarcane workers in the lowlands of Nicaragua and El Salvador (Weiner and others 2013). Estimates of mortality are high. In 2009, kidney disease was the second-largest cause of death among men in El Salvador (Wesseling and others 2013). Some distinguishing features of the disease have been described: it afflicts middle-age men more than women, lacks heavy proteinuria, and tends to progress to end-stage renal disease. On kidney biopsy, pathologists note tubulointerstitial nephritis (Nanayakkara and others 2012; Wijkstrom and others 2013).

A rural lowland community in Nicaragua is referred to as "La Isla de las Viudas" (the Island of Widows) because of the high rates of death among men in the village from renal failure. One of the nongovernmental organizations working to address this problem, La Isla Foundation, is based in this region. La Isla Foundation has extended its efforts beyond activism to generate media attention and to support collaborative research in the field. In addition, scientists from a variety of institutions, including Boston University, the National Autonomous University of Nicaragua at León, and the University of Colorado at Denver, are investigating potential triggers for kidney disease. The Consortium for the Epidemic of Nephropathy in Central America and Mexico has been formed to help researchers communicate and coordinate.

One prevailing hypothesis for the cause of this epidemic is recurrent dehydration resulting from strenuous work in high heat conditions (Roncal Jimenez and others 2013). However, there is widespread belief among local populations in Meso-America and in Sri Lanka that exposure to agrochemicals is at least partly responsible for the occupational nature of this form of CKD (Jayasumana and others 2015). An as-yet undefined infection also remains an important consideration (Murray and others 2015).

Most of those afflicted by the disease earn their livelihoods from agricultural work; a diagnosis of progressive CKD is disabling for them and their families. There is little to no provision of dialysis therapy in these regions, lending great urgency to identifying an etiology and preventing the disease.

should be studied in LMICs as an entity separate from the end-organ consequence of diabetes or vascular disease.

Effectiveness of Interventions

Screening for CKD

Major primary care and nephrology guidelines in HICs do not advocate universal screening for CKD. The National Kidney Foundation Kidney Disease Outcomes Quality Initiative recommends first evaluating individuals for risk factors for CKD during routine clinical encounters; if risk is determined, individuals should be further evaluated for serum creatinine and urine abnormalities. The risk factors include age; diabetes; hypertension; autoimmune disease, such as lupus; urinary tract abnormalities, such as infections, stones, and neoplasia; low birth weight; and exposure to toxins, such as drugs, environmental agents, or infections. In practice, physicians target screening to individuals with diabetes or hypertension. Because serum creatinine and automated reporting of eGFR are often part of routine studies in primary care, even individuals without specific risk factors for CKD are recognized at an early stage (Wyatt and others 2007).

The adoption of a targeted screening strategy in LMICs needs to be reassessed, given the lack of self-awareness of underlying risk factors for CKD. For example, in a community-based sample from urban India, individuals with and without knowledge of diabetes had similar prevalence of CKD (Anand and others 2015). Accordingly, selecting high-risk individuals for CKD screening may not be feasible.

Prevention of ESRD

Pharmacotherapy for CKD associated with diabetes or hypertension. Nephrologists use angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor

blockers (ARBs) as the primary medical therapies for delaying the progression to ESRD. Data from several randomized clinical trials have shown that these medications can slow the progression of CKD among individuals with proteinuric (diabetic and nondiabetic) kidney disease, with risk reduction approaching 40 percent for a composite endpoint of doubling of serum creatinine or ESRD (Kshirsagar and others 2000). A trial in China replicated these findings for individuals with proteinuria and advanced renal disease (Hou and others 2006). Some evidence indicates that even among individuals with CKD and hypertension without significant proteinuria, the use of ACE inhibitors may delay the progression of CKD beyond the effects achieved by other standard antihypertensive agents (Wright and others 2002). Whether the effect of ACE inhibitors is totally independent of improved blood pressure control has been debated. These medications, which are relatively inexpensive in their generic form, are well tolerated but require laboratory monitoring for hyperkalemia or significant change in serum creatinine among older patients and those with advanced CKD because of associated risk for AKI.

Pharmacotherapy for glomerular diseases. CKD associated with diabetes or renovascular disease is often diagnosed only with screening. Individuals with glomerulonephritis, in contrast, often have classic symptoms, such as edema, hematuria, or arthralgias, and are referred to nephrologists for immunotherapy. Steroids are the initial choice of therapy for many glomerular processes: minimal change disease, membranous nephropathy, focal segmental glomerulonephritis, and IgA nephropathy. Newer steroid-sparing therapies, such as calcineurin inhibitors, are used in individuals at serious risk for adverse events related to steroids or for maintenance therapy. Cyclophosphamide had been the mainstay of therapy for severe glomerulonephritis resulting from lupus or vasculitis. Mycophenolate mofetil (Ginzler and others 2005) and rituximab (Stone and others 2010) have been shown to be equally efficacious in treating severe glomerulonephritis resulting from lupus or vasculitis, respectively.

Race or ethnicity may affect the efficacy of immunotherapy. African-American and Hispanic individuals with lupus reportedly respond better to mycophenolate mofetil than to cyclophosphamide (Isenberg and others 2010). Initial clinical trials from China report the efficacy of mycophenolate mofetil in individuals with IgA nephropathy, but these results have not been replicated in clinical trials in Belgium and the United States (Floege and Eitner 2011).

Data on availability and appropriate use of these pharmacotherapies in LMICs are limited. One study from Mexico reports that one-third of primary care physicians working in the public sector scored in the "very low knowledge" category in a competence evaluation of diabetic kidney disease (Martinez-Ramirez and others 2006). Only 50 percent of patients with diabetes underwent simple screening for kidney disease; fewer than 20 percent of patients with proteinuria had been placed on ACE inhibitors in a third-level center in Nigeria (Agaba and others 2009).

CKD-specific programs in LMICs. We conducted a PUBMED and EMBASE systematic search to capture any programs designed specifically to improve care of patients with CKD or ESRD in LMICs. Of the 292 articles captured by the search, we culled 18 with available full text in English for further review; articles were excluded if they were not applicable to LMICs, if they were presented in abstract only at conferences, or if they did not describe a specific intervention. After excluding reports that were too general or did not capture any outcomes, we found 11 studies that described CKD care programs in LMICs (table 13.3). Although the data on evaluation of these programs were of poor to fair quality, an emerging theme in these reports is the importance of education of primary care physicians in identifying and treating patients at risk for CKD progression.

Treatment of ESRD

Survival on dialysis. Survival on dialysis—equivalent for HD and PD—is generally poor in HICs, with annual mortality rates nearing 20 percent to 25 percent (van Dijk and others 2001). Many LMICs report equivalent, if not better, survival on dialysis (Anand, Bitton, and Gaziano 2013). At the same time, several studies have noted poorer provision of long-term care in LMICs: late referral to nephrologists, greater reliance on twice-weekly HD (Bieber and others 2013), less frequent laboratory draws and use of ancillary medications (Bieber and others 2013), and lack of enforcement of standards for water treatment for HD (Braimoh and others 2012). Patient selection factors may explain this incongruity between better survival despite reported poorer quality of care. In South Africa, where government-sponsored dialysis is offered to patients who fulfill the criteria for eventual transplantation, patients older than age 60 years and patients with diabetes are significantly less likely to receive dialysis (Moosa and Kidd 2006). Thus, a rationing process—whether at a societal or familial level—may create artificially better outcomes in LMICs, because a younger, healthier population is most likely to be able to access expensive dialysis therapy; see chapter 21 in this volume (Sakuma and others 2017) for a more detailed discussion.

Survival on transplantation. Compared with dialysis, first-year post–kidney transplant mortality is less than 10 percent in most HICs (van Dijk and others 2001). Better survival after a kidney transplant reflects a combination of selection factors—a healthier group of patients receiving transplants, and greater efficacy of therapy (Wolfe and others 1999). Most individuals in HICs receive cadaveric transplants.

In LMICs, reported outcomes for living donor transplantation are similar to those in HICs (Anand, Bitton, and Gaziano 2013). Cadaveric donation is much less common in LMICs because of the lack of deceased-donor registries; in one center's report, cadaveric donation was associated with poorer outcomes than in HICs (Medina-Pestana 2006). Reasons behind the poorer transplant outcomes in LMICs should be

Table 13.3 Summary of Programs Targeted to Caring for Patients with CKD in LMICs

Authors	Country	Intervention	Level	Outcomes
Mastroianni-Kirsztajn, Bastos, and Burdmann 2011	Brazil	Previna-se: A campaign by the Brazilian Society of Nephrology to increase awareness of CKD among health professionals and the public	National	• In 2009, 700 local programs registered for educational campaigns • Generated pamphlets and videos for PCPs and public • Attempted to standardize reporting of GFR • Undertook several screening campaigns in São Paulo
Zhang and others 2008	China	Established a renal management clinic study at Peking University that incorporated nephrologists, dieticians, and nurses	Third-level hospital	• Challenges in follow-up, with 10 percent of patients with advanced CKD not returning for follow-up • Despite creation of multidisciplinary clinic, lack of involvement of nurses or dieticians
Jiang and Yu 2011	China	Created 12 satellite PD clinics to an academic hospital Used standardized protocols for training staff	Third-level and first-level care partners	• Increased capacity • Decline in peritonitis rate (from 1 episode/39.4 to 1 episode/46.2 patient months) • Fewer patient drop outs, from 28 percent to 18 percent per year
Wong, Chow, and Chan 2010	China	Randomized PD patients to renal and general nephrology nurse follow-up versus usual care (physicians only)	Third-level hospital	• With involvement of nurses, improved diet adherence, symptom control, and quality of life
Mani 2010	India	Developed a protocol for titration of ACEi/ARB among patients with CKD who lived remotely from the specialists; instructions were faxed after patients relayed results of protocol labs	Community	• Among patients who were able to follow the protocol, rate of decline in kidney function was significantly slower • Able to perform titration despite only 6 or 12 months of follow-up from patients
Cortes-Sanabria and others 2008	Mexico	Randomized PCPs to usual care versus six months of CKD education in patients with type 2 diabetes	Primary care	• Improved PCP clinical competence • Better controlled BP and albuminuria, with higher doses of ACEi/ARB used among patients of educated PCPs
Cueto-Manzano, Martinez-Ramirez, and Cortes-Sanabria 2013	Mexico	Prospective study of patients with type 2 diabetes and early CKD assigned to participate in multidisciplinary (educated PCP, dietician, physical therapist, and social worker) versus usual care	Primary care	• Improved medication compliance • Improved BP, hemoglobin A1c, and waist circumference in patients with multidisciplinary care
Garcia-Garcia and others 2013; Murray and others 2015	Mexico	Created a multidisciplinary clinic (nurse, physician, dietician, and social worker) to care for patients without insurance, referred from community or via screening	Third-level hospital	• Compared with baseline intake, patients seen in the clinic improved in several parameters, including in meeting targets for blood pressure and ACEi/ARB use (90 percent)

table continues next page

Table 13.3 Summary of Programs Targeted to Caring for Patients with CKD in LMICs (continued)

Authors	Country	Intervention	Level	Outcomes
Edefonti and others 2010	Nicaragua	Partnership between Milanese and Nicaraguan hospitals to create a pediatric nephrology program	National	• Trained three pediatric nephrologists and two pathologists • Created a network of PCPs in six other regions; these PCPs have access to basic diagnostics and could streamline referral to main hospital • Covers 61 percent of pediatric population
Schwedt and others 2010	Uruguay	A national renal health care program that focused on education of both PCPs and nephrologists, with referral to nephrologists recommended at advanced CKD	National	• Post implementation, patients getting care from PCPs and from nephrologists demonstrated improved BP and lipid control
Sharma and others 2014	Nepal	An intervention program in resource-poor setting of eastern Nepal with cheap antihypertensive, antidiabetic, or renoprotective (ACE) drugs	Rural communities of eastern Nepal	• 76 percent on active monitoring after three-year follow-up • Improved BP and glycemic control • 63 percent of participants with dipstick proteinuria >1+ at baseline decreased to normal values • 48 percent of participants with eGFR <60 ml/min/1.73 m^2 at baseline improved renal function

Note: ACE = angiotensin-converting enzyme; ACEi/ARB = angiotensin-converting enzyme inhibitors/angiotensin II receptor blocker; BP = blood pressure; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; GFR = glomerular filtration rate; LMICs = low- and middle-income countries; PCP = primary care physician; PD = peritoneal dialysis.

further studied, especially considering that recipients tend to have fewer comorbidities and are younger. In most LMICs with flourishing transplant centers—such as Brazil, India, the Islamic Republic of Iran, Pakistan, South Africa, and Tunisia—the technical training of surgeons and nephrologists is comparable to that in HICs. However, two factors specific to LMICs may be at play:

- Funding of immunosuppression medication varies; some governments, such as Brazil, pay the full costs; others expect a majority of patients to self-pay. Because immunosuppression medications are expensive, patients might minimize or discontinue use if asked to self-pay.
- Risks for serious posttransplant infection are likely to be higher in LMICs. An estimated 10 percent to 15 percent of individuals with kidney transplants develop tuberculosis in endemic regions (Malhotra 2007; Rizvi and others 2003). Among those who have a co-infection, the mortality rate has been reported to be 75 percent (Chen and others 2008).

Use of modality. Kidney transplant offers the best survival rates and quality of life for individuals with ESRD when transplantation is performed using optimal practice standards. In HICs, kidney transplants meet the needs of 30 percent to 40 percent of prevalent ESRD patients (Grassmann and others 2005). Advances in patient selection, organ suitability, and organ availability have increased transplantation rates. National and regional organ donation chains can maximize adequate donor-recipient pairing over a large geographical area to ensure maximal chance of transplantation rate and allograft survival (Gentry, Montgomery, and Segev 2011). Recent changes to the deceased-donor system in the United States are anticipated to allocate organs more efficiently.

As in HICs, HD is the most commonly used therapy in LMICs. Transplants are relatively more commonly used in the Middle East and North Africa and in South Asia, compared with other LMIC regions (figure 13.1). In the Islamic Republic of Iran, compensation for organ donation may drive this trend (Ghods and Savaj 2006). PD is relatively more commonly used in Latin America and the Caribbean.

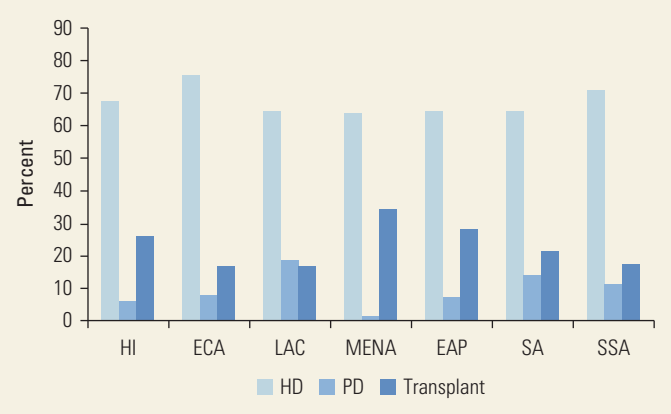
In addition to limits to organ availability, many LMICs struggle with inadequate infrastructure for safe transplantation and postsurgical care (Rizvi and others 2011). Deceased-donor registries do not exist in most countries. Practices such as black market trade and

financial compensation are more prevalent and often disproportionally target poorer members of the population as donors (Mendoza 2010).

The preponderance of efficacy data demonstrate equivalent survival for patients on HD compared with PD, but HD predominates as the primary mode of therapy. Approximately 20 percent of patients who receive RRT in HICs receive PD (Anand, Bitton, and Gaziano 2013). Some reasons for this low uptake include skewed provider incentives toward in-center care, lack of patient education about alternate modalities, and patient fear of self-care.

PD, a relatively low-technology technique that requires neither a high ratio of trained nurses and nephrologists nor specialized facilities with water treatment capabilities, can have greater uptake in LMICs. Mexico and Thailand are exceptions to the generally low use of PD. Historically, Mexican clinicians have been trained in PD and disseminated the technique (Riella and Locatelli 2007); internists have been able to prescribe PD (Pecoits-Filho and others 2007). Following the model of Hong Kong SAR, China, the Ministry of Health in Thailand has tied use of PD first (before other interventions) to reimbursement and has supported expansion of PD; see chapter 21 in this volume (Sakuma and others 2017) for a detailed discussion.

Figure 13.1 Use of Renal Replacement Therapy by Modality



Source: Anand, Bitton, and Gaziano 2013.
Note: EAP = East Asia and Pacific; ECA = Europe and Central Asia; HD = hemodialysis; HI = high income; LAC = Latin America and the Caribbean; MENA = Middle East and North Africa; PD = peritoneal dialysis; SA = South Asia; SSA = Sub-Saharan Africa.

Cost and Cost-Effectiveness of Interventions

Screening for CKD

The cost-effectiveness of screening for CKD has been extensively studied in HICs. The accuracy of creatinine-based eGFR alone in predicting outcomes and progression has remained questionable; not surprisingly, its use in the general population resulted in incremental cost-effectiveness ratios (ICERs) exceeding US$100,000 per QALY gained (Komenda and others 2014). Narrowing to the diabetic population, however, the ICER for screening was US$23,680 per QALY gained.

Assessment of proteinuria via urine albumin-to-creatinine ratio is generally considered to be a more reliable test, although Jafar and others (2007) have shown high specificity but moderate sensitivity (46 percent to 60 percent) in an Indo-Asian population. The cost of testing for urine albumin-to-creatinine ratio is significantly higher than that of serum creatinine, but more acceptable ICERs were noted for its application to those ages 50 years and older: US$73,000 per QALY gained if performed annually, to US$22,000 per QALY gained if performed every 10 years, compared with no screening (Hoerger and others 2010). ICERs for individuals with diabetes or hypertension were US$15,000 per QALY gained if urine albumin-to-creatinine testing is performed every 10 years.

Targeted screening may be the most cost-effective strategy for HICs, but identifying high-risk individuals in LMICs is difficult, and the cost of and utility loss from the development of ESRD is higher, given the restrictions on RRT. Two-stage screening may be a strategy worth investigating (box 13.3). When Howard and others (2010) modeled the use of annual dipstick screening for proteinuria in all Australians ages 50–69 years, followed by confirmatory urine protein-to-creatinine ratio and initiation of treatment, the resulting ICERs were US$5,298 per QALY gained. Similarly, a study of elderly patients at Veterans Administration hospitals in the United States finds that the number needed to treat to prevent a case of ESRD over a three-year period was substantially lower among individuals with dipstick proteinuria, compared with those without proteinuria and modest reductions in eGFR (O'Hare and others 2014).

Renal Replacement Therapy Program and Modality Choice

No recent studies from HICs have evaluated the cost-effectiveness of supporting an individual's decision to pursue RRT rather than palliative care. Most HICs include RRT as part of universal health care packages or government-sponsored insurance programs. In 2011, the U.S. Medicare agency paid US$87,945 per patient for HD, US$71,630 for PD, US$99,826 for first year of transplant, and US$12,019 for ongoing post-transplant care (U.S. Renal Data System 2013). Other HICs report similar ranking of costs across modalities.

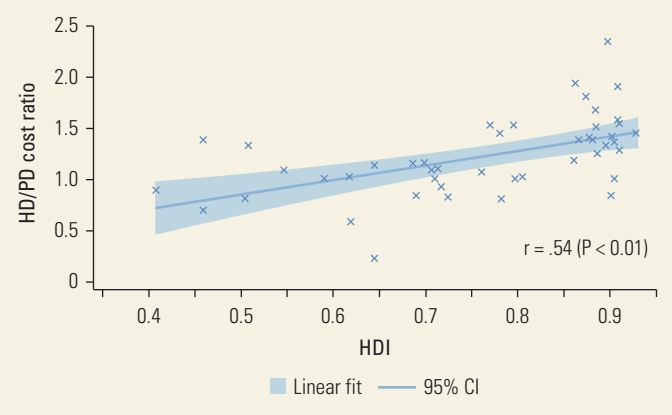
Box 13.3

Case Study: Integrated Screening Program in Tamil Nadu

A low-cost integrated screening program can be radically effective (Mani 2003, 2005). Working with the Kidney Help Trust of Chennai, M. K. Mani has implemented a program in rural Tamil Nadu in which lay health workers perform a urine test for protein and glucose, and record blood pressure in individuals over age five years (N = 25,000). Any abnormalities are further investigated with more specific laboratory tests after physician evaluation; treatment with low-cost drugs is initiated.

The program cost was US$0.27 cents per capita. After two years, compared to an area with similar demographics, the proportion of individuals with eGFR < 80 ml/min/1.73m^2 was significantly lower in the treatment area.

Figure 13.2 Association of HD/PD Cost Ratio to the Human Developmental Index



Sources: Karopadi and others 2013.
Note: Countries with higher Human Developmental Indexes had cost ratios favoring use of PD. CI = confidence interval; HD = hemodialysis; HDI = Human Development Index; PD = peritoneal dialysis.

Despite the high upfront procedural costs, transplantation is the most cost-effective form of therapy in the long term because of its efficacy and low maintenance costs (Winkelmayer and others 2002). Data from LMICs are limited, but these results are likely to be confirmed even in resource-limited settings. However, transplantation has several unmodifiable limitations: it can rarely be preemptive; it is contraindicated in patients with serious comorbidity, such as cardiovascular disease, cancer, or infection; and most important, it faces a limited supply of organs.

PD offers similar survival and quality of life compared with HD; based on its cost rankings in HICs, PD could be hypothesized to be more cost-effective than HD (Karopadi and others 2013). Uptake remains low. Efforts to rein in costs related to ESRD led to the 2011 implementation of bundling rules in the United States, which require that several ancillary services be packaged into a fixed payment to dialysis facilities. Although the impact of bundling on patient outcomes has yet to be studied in detail, these measures provide incentives for home-based PD or HD. After only two years of implementation, the number of prevalent individuals on PD had risen by 30 percent for two of the largest dialysis providers in the United States (Golper 2013).

Despite its lower requirements for specialized treatment facilities and nephrology-trained staff, costs associated with PD in LMICs are estimated to be equivalent to or higher than those of HD (figure 13.2) (Karopadi and others 2013). Although further study is required to determine the reason for these cost differences, economies of scale and costs of importing PD solutions and equipment likely play a substantial role. Local manufacturing of PD solutions and equipment in India and Mexico, for example, has resulted in PD costs being lower than those for HD.

Recommendations for Policy Makers in LMICs

Although the data on caring for patients with CKD and ESRD in LMICs are limited, some cornerstones of management—such as educating primary care physicians to recognize diabetic CKD or prioritizing kidney transplants in RRT programs—will translate directly, even in low-resource settings (table 13.4). However, others—in particular, CKD screening and innovative ways of maximizing dialysis provision—require research specific to LMICs.

Table 13.4 Recommendations for CKD and ESRD care in LMICs

Intervention	Platform	Potential benefit	Evidence
CKD			
Consider two-step screening in chronic disease surveillance programs	Government	Identify high-risk individuals for further testing or referral	Limited: Economic modeling based on two observational studies in HICs
Educate physicians about diabetic CKD, the most common form of progressive CKD	Primary care	Prevent ESRD and CV events among patients with diabetes	Strong: RCT evidence from HICs and LMICs
Ensure availability of ACEi or ARBs	Primary care	Delay progression of ESRD for a majority of patients with CKD (particularly proteinuric CKD)	Strong: RCT evidence from HICs and LMICs
ESRD			
Develop deceased-donor registries	Government	Increase organ availability for kidney transplant, the most efficacious and cost-effective therapy	Strong: Large observational studies and economic modeling from HICs
Create high-throughput transplantation centers	Third-level hospital	Take advantage of volumes to develop surgical expertise and standardized immunosuppression protocols	Limited: Observational studies from one LMIC
If not able to provide transplantation, create relationships with middle-income countries with high-throughput transplantation centers	Government	Increase worldwide accessibility for kidney transplant	Expert opinion
Provide incentives for the use of PD	Government	Use economies of scale to decrease costs associated with dialysis provision; create wider access to dialysis using a less-specialized work force	Modest: One meta-analysis and a real-life implementation in Thailand
Create palliative care programs for patients unable to sustainably afford dialysis	Government or community level		Expert opinion

Note: ACEi = angiotensin-converting enzyme inhibitors; ARBs = angiotensin II receptor blockers; CKD = chronic kidney disease; CV = cardiovascular; ESRD = end-stage renal disease; HICs = high-income countries; LMICs = low- and middle-income countries; PD = peritoneal dialysis; RCT = randomized controlled trial.

CONCLUSIONS

Overall, care provision for patients with either AKI or CKD is limited in LMICs, especially since the severe forms of each require the use of expensive RRT. However, several current gaps can be addressed with careful policy consideration.

For AKI, gathering more data on its true incidence and risk factors is crucial. Because the community-based form of AKI may be more prevalent in LMICs, if we can identify the most common etiologies, we can work to prevent them. In addition to identifying regional centers that can accommodate patients who acutely require RRT, protocols that optimize intensive care at first- or second-level hospitals are an initial first step in its management. Use of PD for AKI may be achievable even at second-level hospitals but requires further study.

LMICs are likely to face a growing burden of individuals with CKD and ESRD. Current data indicate that screening a high-risk, older population for CKD is cost-effective, but identifying such a population in countries without first-level health care systems is a key challenge. Low-cost strategies, such as the use of a urine dipstick, can be readily integrated into programs for chronic disease surveillance but also require further study. Most patients with proteinuric and, to a modest extent, hypertensive CKD benefit from initiation of ACE inhibitor and ARB therapy, which are available as low-cost generics.

Finally, although ESRD is rare, large gaps remain between LMICs and HICs in the provision of therapy. Efforts to increase access to RRT need to first focus on increasing the provision of transplantation—the most effective and cost-effective form of RRT. Because transplantation is not appropriate for all individuals with

ESRD, dialysis is required for any RRT program. PD—while not clearly more cost-effective in LMICs—holds the most promise in its ability to reach a larger swath of individuals without intensive technical and equipment requirements.

ANNEXES

The annexes to this chapter are as follows. They are available at http://www.dcp-3.org/CVRD.

- Annex 13A. Kidney Disease Improving Global Outcomes: Criteria for AKI Severity
- Annex 13B. Kidney Disease Improving Global Outcomes: Stages of Chronic Kidney Disease
- Annex 13C. Selected Population-Based Studies Reporting Prevalence of Chronic Kidney Disease

NOTE

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  (a) lower-middle-income = US$1,046 to US$4,125
  (b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

REFERENCES

Ademola, A. D., A. O. Asinobi, O. O. Ogunkunle, B. N. Yusuf, and O. E. Ojo. 2012. "Peritoneal Dialysis in Childhood Acute Kidney Injury: Experience in Southwest Nigeria." *Peritoneal Dialysis International* 32 (3): 267–72. doi:10.3747/pdi.2011.00275.

Agaba, E. I., F. H. Puepet, S. O. Ugoya, P. A. Agaba, R. Adabe, and others. 2009. "Chronic Kidney Disease Screening and Renoprotection in Type 2 Diabetes." *Annals of African Medicine* 8 (1): 52–54.

Ajay, V. S., D. A. Watkins, and D. Prabhakaran. 2017. "Relationships among Major Risk Factors and the Burden of Cardiovascular Diseases, Diabetes, and Chronic Lung Disease." In *Disease Control Priorities* (third edition): Volume 5, *Cardiovascular, Respiratory, and Related Diseases*, edited by D. Prabhakaran, S. Anand, T. A. Gaziano, J.-C. Mbanya, Y. Wu, and R. Nugent. Washington, DC: World Bank.

Anand, S., A. Bitton, and T. A. Gaziano. 2013. "The Gap between Estimated Incidence of End-Stage Renal Disease and Use of Therapy." *PLoS One* 8 (8): e72860. doi:10.1371/journal.pone.0072860.

Anand, S., D. N. Cruz, and F. O. Finkelstein. 2015. "Understanding Acute Kidney Injury in Low Resource Settings: A Step Forward." *BMC Nephrology* 16: 5. doi:10.1186/1471-2369-16-5.

Anand, S., R. Shivashankar, M. K. Ali, D. Kondal, B. Binukumar, and others. 2015. "Prevalence of Chronic Kidney Disease in Two Major Indian Cities and Projections for Associated Cardiovascular Disease." *Kidney International* 88 (1): 178–85. doi:10.1038/ki.2015.58.

Bagasha, P., F. Nakwagala, A. Kwizera, E. Ssekasanvu, and R. Kalyesubula. 2015. "Acute Kidney Injury among Adult Patients with Sepsis in a Low-Income Country: Clinical Patterns and Short-Term Outcomes." *BMC Nephrology* 16: 4. doi:10.1186/1471-2369-16-4.

Bellomo, R., C. Ronco, J. A. Kellum, R. L. Mehta, P. Palevsky, and the Workgroup Acute Dialysis Quality Initiative. 2004. "Acute Renal Failure: Definition, Outcome Measures, Animal Models, Fluid Therapy and Information Technology Needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group." *Critical Care* 8 (4): R204–12. doi:10.1186/cc2872.

Bieber, B., J. Qian, S. Anand, Y. Yan, N. Chen, and others. 2013. "Two-Times Weekly Hemodialysis in China: Frequency, Associated Patient and Treatment Characteristics and Quality of Life in the China Dialysis Outcomes and Practice Patterns Study." *Nephrology Dialysis Transplantation* 29 (9): 1770–77. doi:10.1093/ndt/gft472.

Bouchard, J., A. Acharya, J. Cerda, E. R. Maccariello, R. C. Madarasu, and others. 2015. "A Prospective International Multicenter Study of AKI in the Intensive Care Unit." *Clinical Journal of the American Society of Nephrology* 10 (8): 1324–31. doi:10.2215/CJN.04360514.

Braimoh, R. W., M. O. Mabayoje, C. O. Amira, and H. Coker. 2012. "Quality of Hemodialysis Water in a Resource-Poor Country: The Nigerian Example." *Hemodialysis International* 16 (4): 532–38. doi:10.1111/j.1542-4758.2012.00682.x.

Burki, T. 2015. "Tanzania's Model Peritoneal Dialysis Programme." *The Lancet* 385 (9981): 1935–36. doi:10.1016/S0140-6736(15)60946-1.

Callegari, J. G., S. Antwi, G. Wystrychowski, E. Zukowska-Szczechowska, N. W. Levin, and M. Carter. 2013. "Peritoneal Dialysis as a Mode of Treatment for Acute Kidney Injury in Sub-Saharan Africa." *Blood Purification* 36 (3–4): 226–30. doi:10.1159/000356627.

Callegari, J. G., K. G. Kilonzo, K. E. Yeates, G. J. Handelman, F. O. Finkelstein, and others. 2012. "Peritoneal Dialysis for Acute Kidney Injury in Sub-Saharan Africa: Challenges Faced and Lessons Learned at Kilimanjaro Christian Medical Centre." *Kidney International* 81 (4): 331–33. doi:10.1038/ki.2011.408.

Cerda, J., N. Lameire, P. Eggers, N. Pannu, S. Uchino, and others. 2008. "Epidemiology of Acute Kidney Injury." *Clinical Journal of the American Society of Nephrology* 3 (3): 881–86. doi:10.2215/CJN.04961107.

Chandrajith, R., S. Nanayakkara, K. Itai, T. N. Aturaliya, C. B. Dissanayake, and others. 2011. "Chronic Kidney Diseases of Uncertain Etiology (CKDUE) in Sri Lanka: Geographic Distribution and Environmental Implications."

Environmental Geochemistry and Health 33 (3): 267–78. doi:10.1007/s10653-010-9339-1.

Chen, S. Y., C. X. Wang, L. Z. Chen, J. G. Fei, S. X. Deng, and others. 2008. "Tuberculosis in Southern Chinese Renal-Transplant Recipients." *Clinical Transplantation* 22 (6): 780–84. doi:10.1111/j.1399-0012.2008.00878.x.

Chertow, G. M., E. Burdick, M. Honour, J. V. Bonventre, and D. W. Bates. 2005. "Acute Kidney Injury, Mortality, Length of Stay, and Costs in Hospitalized Patients." *Journal of the American Society of Nephrology* 16 (11): 3365–70. doi:10.1681/ASN.2004090740.

Chionh, C. Y., S. S. Soni, F. O. Finkelstein, C. Ronco, and D. N. Cruz. 2013. "Use of Peritoneal Dialysis in AKI: A Systematic Review." *Clinical Journal of the American Society of Nephrology* 8 (10): 1649–60. doi:10.2215/CJN.01540213.

Chronic Kidney Disease Prognosis Consortium, K. Matsushita, M. van der Velde, B. C. Astor, M. Woodward, and others. 2010. "Association of Estimated Glomerular Filtration Rate and Albuminuria with All-Cause and Cardiovascular Mortality in General Population Cohorts: A Collaborative Meta-Analysis." *The Lancet* 375 (9731): 2073–81. doi:10.1016/S0140-6736(10)60674-5.

Cortes-Sanabria, L., C. E. Cabrera-Pivaral, A. M. Cueto-Manzano, E. Rojas-Campos, G. Barragan, and others. 2008. "Improving Care of Patients with Diabetes and CKD: A Pilot Study for a Cluster-Randomized Trial." *American Journal of Kidney Disease* 51 (5): 777–88. doi:10.1053/j.ajkd.2007.12.039.

Couser, W. G., G. Remuzzi, S. Mendis, and M. Tonelli. 2011. "The Contribution of Chronic Kidney Disease to the Global Burden of Major Noncommunicable Diseases." *Kidney International* 80 (12): 1258–70. doi:10.1038/ki.2011.368.

Cueto-Manzano, A. M., H. R. Martinez-Ramirez, and L. Cortes-Sanabria. 2013. "Comparison of Primary Health-Care Models in the Management of Chronic Kidney Disease." *Kidney International Supplements* (2011) 3 (2): 210–14. doi:10.1038/kisup.2013.16.

Cullis, B., M. Abdelraheem, G. Abrahams, A. Balbi, D. N. Cruz, and others. 2014. "Peritoneal Dialysis for Acute Kidney Injury." *Peritoneal Dialysis International* 34 (5): 494–517. doi:10.3747/pdi.2013.00222.

de Boer, I. H., T. C. Rue, Y. N. Hall, P. J. Heagerty, N. S. Weiss, and others. 2011. "Temporal Trends in the Prevalence of Diabetic Kidney Disease in the United States." *Journal of the American Medical Association* 305 (24): 2532–39. doi:10.1001/jama.2011.861.

Edefonti, A., G. Marra, M. C. Perez, M. S. Diaz, F. Sereni, and others. 2010. "A Comprehensive Cooperative Project for Children with Renal Diseases in Nicaragua." *Clinical Nephrology* 74: S119–25.

Finkelstein, F. O., W. E. Smoyer, M. Carter, A. Brusselmans, and J. Feehally. 2014. "Peritoneal Dialysis, Acute Kidney Injury, and the Saving Young Lives Program." *Peritoneal Dialysis International* 34 (5): 478–80. doi:10.3747/pdi.2014.00041.

Floege, J., and F. Eitner. 2011. "Current Therapy for IgA Nephropathy." *Journal of the American Society of Nephrology* 22 (10): 1785–94. doi:10.1681/ASN.2011030221.

Garcia-Garcia, G., Y. Martinez-Castellanos, K. Renoirte-Lopez, A. Barajas-Murguia, L. de la Torre-Campos, and others. 2013. "Multidisciplinary Care for Poor Patients with Chronic Kidney Disease in Mexico." *Kidney International Supplements* (2011) 3 (2): 178–83. doi:10.1038/kisup.2013.9.

Gentry, S. E., R. A. Montgomery, and D. L. Segev. 2011. "Kidney Paired Donation: Fundamentals, Limitations, and Expansions." *American Journal of Kidney Disease* 57 (1): 144–51. doi:10.1053/j.ajkd.2010.10.005.

George, J., S. Varma, S. Kumar, J. Thomas, S. Gopi, and R. Pisharody. 2011. "Comparing Continuous Venovenous Hemofiltration and Peritoneal Dialysis in Critically Ill Patients with Acute Kidney Injury: A Pilot Study." *Peritoneal Dialysis* 31 (4): 422–29.

Ghods, A. J., and S. Savaj. 2006. "Iranian Model of Paid and Regulated Living-Unrelated Kidney Donation." *Clinical Journal of the American Society of Nephrology* 1 (6): 1136–45. doi:10.2215/CJN.00700206.

Ginzler, E. M., M. A. Dooley, C. Aranow, M. Y. Kim, J. Buyon, and others. 2005. "Mycophenolate Mofetil or Intravenous Cyclophosphamide for Lupus Nephritis." *New England Journal of Medicine* 353 (21): 2219–28. doi:10.1056/NEJMoa043731.

Golper, T. A. 2013. "The Possible Impact of the US Prospective Payment System ('Bundle') on the Growth of Peritoneal Dialysis." *Peritoneal Dialysis International* 33 (6): 596–99. doi:10.3747/pdi.2013.00212.

Grassmann, A., S. Gioberge, S. Moeller, and G. Brown. 2005. "ESRD Patients in 2004: Global Overview of Patient Numbers, Treatment Modalities and Associated Trends." *Nephrology Dialysis Transplantation* 20 (12): 2587–93. doi:10.1093/ndt/gfi159.

Hamel, M. B., R. S. Phillips, R. B. Davis, N. Desbiens, A. F. Connors, Jr., and others. 1997. "Outcomes and Cost-Effectiveness of Initiating Dialysis and Continuing Aggressive Care in Seriously Ill Hospitalized Adults. SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments." *Annals of Internal Medicine* 127 (3): 195–202.

Himmelfarb, J., and T. A. Ikizler. 2007. "Acute Kidney Injury: Changing Lexicography, Definitions, and Epidemiology." *Kidney International* 71 (10): 971–76. doi:10.1038/sj.ki.5002224.

Hoerger, T. J., J. S. Wittenborn, J. E. Segel, N. R. Burrows, K. Imai, and others. 2010. "A Health Policy Model of CKD: 2. The Cost-Effectiveness of Microalbuminuria Screening." *American Journal of Kidney Disease* 55 (3): 463–73. doi:10.1053/j.ajkd.2009.11.017.

Hossain, P., B. Kawar, and M. El Nahas. 2007. "Obesity and Diabetes in the Developing World: A Growing Challenge." *New England Journal of Medicine* 356 (3): 213–15. doi:10.1056/NEJMp068177.

Hoste, E. A., and M. Schurgers. 2008. "Epidemiology of Acute Kidney Injury: How Big Is the Problem?" *Critical Care Medicine* 36 (Suppl 4): S146–51. doi:10.1097/CCM.0b013e318168c590.

Hou, F. F., X. Zhang, G. H. Zhang, D. Xie, P. Y. Chen, and others. 2006. "Efficacy and Safety of Benazepril for Advanced

Chronic Renal Insufficiency." *New England Journal of Medicine* 354 (2): 131–40. doi:10.1056/NEJMoa053107.

Howard, K., S. White, G. Salkeld, S. McDonald, J. C. Craig, and others. 2010. "Cost-Effectiveness of Screening and Optimal Management for Diabetes, Hypertension, and Chronic Kidney Disease: A Modeled Analysis." *Value in Health* 13 (2): 196–208.

Isenberg, D., G. B. Appel, G. Contreras, M. A. Dooley, E. M. Ginzler, and others. 2010. "Influence of Race/Ethnicity on Response to Lupus Nephritis Treatment: The ALMS Study." *Rheumatology (Oxford)* 49 (1): 128–40. doi:10.1093/rheumatology/kep346.

Jafar, T. H., N. Chaturvedi, J. Hatcher, and A. S. Levey. 2007. "Use of Albumin Creatinine Ratio and Urine Albumin Concentration as a Screening Test for Albuminuria in an Indo-Asian Population." *Nephrology Dialysis Transplantation* 22 (8): 2194–200.

Jayasumana, C., P. Paranagama, S. Agampodi, C. Wijewardane, S. Gunatilake, and others. 2015. "Drinking Well Water and Occupational Exposure to Herbicides Is Associated with Chronic Kidney Disease, in Padavi-Sripura, Sri Lanka." *Environmental Health* 14 (1):6. doi:10.1186/1476-069X-14-6.

Jha, V. 2009. "Current Status of Chronic Kidney Disease Care in Southeast Asia." *Seminars in Nephrology* 29 (5): 487–96. doi:10.1016/j.semnephrol.2009.06.005.

Jiang, Z., and X. Yu. 2011. "Advancing the Use and Quality of Peritoneal Dialysis by Developing a Peritoneal Dialysis Satellite Center Program." *Peritoneal Dialysis International* 31 (2): 121–26. doi:10.3747/pdi.2010.00041.

Jungers, P., D. Joly, F. Barbey, G. Choukroun, and M. Daudon. 2004. "ESRD Caused by Nephrolithiasis: Prevalence, Mechanisms, and Prevention." *American Journal of Kidney Disease* 44 (5): 799–805.

Karopadi, A. N., G. Mason, E. Rettore, and C. Ronco. 2013. "Cost of Peritoneal Dialysis and Haemodialysis across the World." *Nephrology Dialysis Transplantation* 28 (10): 2553–69. doi:10.1093/ndt/gft214.

Kellum, J. A., N. Lameire, and KDIGO AKI Guideline Work Group. 2013. "Diagnosis, Evaluation, and Management of Acute Kidney Injury: A KDIGO Summary (Part 1)." *Critical Care* 17 (1): 204. doi:10.1186/cc11454.

Kidney Disease: Improving Global Outcomes Work Group. 2012. "KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease." *Kidney International Supplements* 2013 (3): 1–150.

Kilonzo, K. G., S. Ghosh, S. A. Temu, V. Maro, J. G. Callegari, and others. 2012. "Outcome of Acute Peritoneal Dialysis in Northern Tanzania." *Peritoneal Dialysis International* 32 (3): 261–66. doi:10.3747/pdi.2012.00083.

Komenda, P., T. W. Ferguson, K. Macdonald, C. Rigatto, C. Koolage, and others. 2014. "Cost-Effectiveness of Primary Screening for CKD: A Systematic Review." *American Journal of Kidney Disease* 63 (5): 789–97. doi:10.1053/j.ajkd.2013.12.012.

Kshirsagar, A. V., M. S. Joy, S. L. Hogan, R. J. Falk, and R. E. Colindres. 2000. "Effect of ACE Inhibitors in Diabetic and Nondiabetic Chronic Renal Disease: A Systematic Overview of Randomized Placebo-Controlled Trials." *American Journal of Kidney Disease* 35 (4): 695–707.

Lameire, N. H., A. Bagga, D. Cruz, J. De Maeseneer, Z. Endre, and others. 2013. "Acute Kidney Injury: An Increasing Global Concern." *The Lancet* 382 (9887): 170–79. doi:10.1016/S0140-6736(13)60647-9.

Laukkanen, A., L. Emaus, V. Pettila, and K. M. Kaukonen. 2013. "Five-Year Cost-Utility Analysis of Acute Renal Replacement Therapy: A Societal Perspective." *Intensive Care Medicine* 39 (3): 406–13. doi:10.1007/s00134-012-2760-4.

Levey, A. S., and J. Coresh. 2012. "Chronic Kidney Disease." *The Lancet* 379 (9811): 165–80. doi:10.1016/S0140-6736(11)60178-5.

Levey, A. S., J. Coresh, E. Balk, A. T. Kausz, A. Levin, and others. 2003. "National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification." *Annals of Internal Medicine* 139 (2): 137–47.

Liyanage, T., T. Ninomiya, V. Jha, B. Neal, H. M. Patrice, and others. 2015. "Worldwide Access to Treatment for End-Stage Kidney Disease: A Systematic Review." *The Lancet* 385 (9981): 1975–82. doi:10.1016/S0140-6736(14)61601-9.

Lopez, M., and B. Hoppe. 2010. "History, Epidemiology and Regional Diversities of Urolithiasis." *Pediatric Nephrology* 25 (1): 49–59. doi:10.1007/s00467-008-0960-5.

Luyckx, V. A., and S. Naicker. 2008. "Acute Kidney Injury Associated with the Use of Traditional Medicines." *Nature Clinical Practice. Nephrology* 4 (12): 664–71. doi:10.1038/ncpneph0970.

Malhotra, K. K. 2007. "Challenge of Tuberculosis in Renal Transplantation." *Transplant Proceedings* 39 (3): 756–58. doi:10.1016/j.transproceed.2007.01.062.

Mallipattu, S. K., F. Salem, and C. M. Wyatt. 2014. "The Changing Epidemiology of HIV-Related Chronic Kidney Disease in the Era of Antiretroviral Therapy." *Kidney International* 86 (2): 259–65. doi:10.1038/ki.2014.44.

Mani, M. K. 2003. "Prevention of Chronic Renal Failure at the Community Level." *Kidney International Supplements* (83): S86–89.

———. 2005. "Experience with a Program for Prevention of Chronic Renal Failure in India." *Kidney International Supplements* (94): S75–78. doi:10.1111/j.1523-1755.2005.09419.x.

———. 2010. "Treating Renal Disease in India's Poor: The Art of the Possible." *Seminars in Nephrology* 30 (1): 74–80. doi:http://dx.doi.org/10.1016/j.semnephrol.2009.10.012.

Martinez-Ramirez, H. R., B. Jalomo-Martinez, L. Cortes-Sanabria, E. Rojas-Campos, G. Barragan, and others. 2006. "Renal Function Preservation in Type 2 Diabetes Mellitus Patients with Early Nephropathy: A Comparative Prospective Cohort Study between Primary Health Care Doctors and a Nephrologist." *American Journal of Kidney Disease* 47 (1): 78–87. doi:10.1053/j.ajkd.2005.09.015.

Mastroianni-Kirsztajn, G., M. G. Bastos, and E. A. Burdmann. 2011. "Strategies of the Brazilian Chronic Kidney Disease Prevention Campaign (2003–2009)." *Nephron Clinical Practice* 117 (3): c259–65. doi:10.1159/000320741.

Medina-Pestana, J. O. 2006. "Organization of a High-Volume Kidney Transplant Program: The 'Assembly Line' Approach."

Transplantation 81 (11): 1510–20. doi:10.1097/01.tp.0000214934.48677.e2.

Mehta, R. L., E. A. Burdmann, J. Cerda, J. Feehally, F. Finkelstein, and others. 2016. "Current Practice for Recognition and Management of Acute Kidney Injury: The International Society of Nephrology 0by25 Global Snapshot Study: A multinational cross-sectional." *The Lancet* 387 (10032): 2017–25.

Mehta, R. L., J. Cerda, E. A. Burdmann, M. Tonelli, G. Garcia-Garcia, and others. 2015. "International Society of Nephrology's 0by25 Initiative for Acute Kidney Injury (Zero Preventable Deaths by 2025): A Human Rights Case for Nephrology." *The Lancet* 385 (9987): 2616–43. doi:10.1016/S0140-6736(15)60126-X.

Mehta, R. L., J. A. Kellum, S. V. Shah, B. A. Molitoris, C. Ronco, and others. 2007. "Acute Kidney Injury Network: Report of an Initiative to Improve Outcomes in Acute Kidney Injury." *Critical Care* 11 (2): R31. doi:10.1186/cc5713.

Mendoza, R. L. 2010. "Kidney Black Markets and Legal Transplants: Are They Opposite Sides of the Same Coin?" *Health Policy* 94 (3): 255–65. doi:10.1016/j.healthpol.2009.10.005.

Mishra, O. P., A. K. Gupta, V. Pooniya, R. Prasad, N. K. Tiwary, and others. 2012. "Peritoneal Dialysis in Children with Acute Kidney Injury: A Developing Country Experience." *Peritoneal Dialysis International* 32 (4): 431–36. doi:10.3747/pdi.2012.00118.

Moosa, M. R., and M. Kidd. 2006. "The Dangers of Rationing Dialysis Treatment: The Dilemma Facing a Developing Country." *Kidney International* 70 (6): 1107–14. doi:5001750 [pii] 10.1038/sj.ki.5001750.

Moynihan, R., R. Glassock, and J. Doust. 2013. "Chronic Kidney Disease Controversy: How Expanding Definitions Are Unnecessarily Labelling Many People as Diseased." *British Medical Journal* 347: f4298. doi:10.1136/bmj.f4298.

Murray, K. O., R. S. Fischer, D. Chavarria, C. Duttmann, M. N. Garcia, and others. 2015. "Mesoamerican Nephropathy: A Neglected Tropical Disease with an Infectious Etiology?" *Microbes and Infection* 17 (10): 671–75. doi:10.1016/j.micinf.2015.08.005.

Mushi, L., P. Marschall, and S. Flessa. 2015. "The Cost of Dialysis in Low and Middle-Income Countries: A Systematic Review." *BMC Health Services Research* 15: 506. doi:10.1186/s12913-015-1166-8.

Naicker, S., O. Aboud, and M. B. Gharbi. 2008. "Epidemiology of Acute Kidney Injury in Africa." *Seminars in Nephrology* 28 (4): 348–53. doi:10.1016/j.semnephrol.2008.04.003.

Nanayakkara, S., T. Komiya, N. Ratnatunga, S. T. Senevirathna, K. H. Harada, and others. 2012. "Tubulointerstitial Damage as the Major Pathological Lesion in Endemic Chronic Kidney Disease among Farmers in North Central Province of Sri Lanka." *Environmental Health and Preventive Medicine* 17 (3): 213–21. doi:10.1007/s12199-011-0243-9.

O'Hare, A. M., J. R. Hotchkiss, M. Kurella Tamura, E. B. Larson, B. R. Hemmelgarn, and others. 2014. "Interpreting Treatment Effects from Clinical Trials in the Context of Real-World Risk Information: End-Stage Renal Disease Prevention in Older Adults." *JAMA Internal Medicine* 174 (3): 391–97. doi:10.1001/jamainternmed.2013.13328.

Oliveira, M. B., J. E. Romao, Jr., and R. Zatz. 2005. "End-Stage Renal Disease in Brazil: Epidemiology, Prevention, and Treatment." *Kidney International Supplements* (97): S82–86. doi:10.1111/j.1523-1755.2005.09714.x.

Palevsky, P. M., K. D. Liu, P. D. Brophy, L. S. Chawla, C. R. Parikh, and others. 2013. "KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for Acute Kidney Injury." *American Journal of Kidney Disease* 61 (5): 649–72. doi:10.1053/j.ajkd.2013.02.349.

Pecoits-Filho, R., H. Abensur, A. M. Cueto-Manzano, J. Dominguez, J. C. Divino Filho, and others. 2007. "Overview of Peritoneal Dialysis in Latin America." *Peritoneal Dialysis International* 27 (3): 316–21. doi:27/3/316 [pii].

Plata, R., C. Silva, J. Yahuita, L. Perez, A. Schieppati, and others. 1998. "The First Clinical and Epidemiological Programme on Renal Disease in Bolivia: A Model for Prevention and Early Diagnosis of Renal Diseases in the Developing Countries." *Nephrology Dialysis Transplantation* 13 (12): 3034–36.

Poggio, E. D., and A. D. Rule. 2009. "A Critical Evaluation of Chronic Kidney Disease: Should Isolated Reduced Estimated Glomerular Filtration Rate Be Considered a 'Disease'?" *Nephrology Dialysis Transplantation* 24 (3): 698–700. doi:10.1093/ndt/gfn704.

Ponce, D., J. T. Caramori, P. Barretti, and A. L. Balbi. 2012. "Peritoneal Dialysis in Acute Kidney Injury: Brazilian Experience." *Peritoneal Dialysis International* 32 (3): 242–46. doi:0.3747/pdi.2012.00089.

Prakash, J., T. Gupta, S. Prakash, S. S. Rathore, Usha, and others. 2015. "Acute Kidney Injury in Patients with Human Immunodeficiency Virus Infection." *Indian Journal of Nephrology* 25 (2): 86–90. doi:10.4103/0971-4065.138696.

Remuzzi, G., and R. Horton. 2013. "Acute Renal Failure: An Unacceptable Death Sentence Globally." *The Lancet* 382 (9910): 2041–42. doi:10.1016/S0140-6736(13)62193-5.

Rewa, O., and S. M. Bagshaw. 2014. "Acute Kidney Injury: Epidemiology, Outcomes and Economics." *Nature Reviews Nephrology* 10 (4): 193–207. doi:10.1038/nrneph.2013.282.

Riella, M. C., and A. J. Locatelli. 2007. "History of Peritoneal Dialysis in Latin America." *Peritoneal Dialysis International* 27 (3): 322–72. doi:27/3/322 [pii].

Rizvi, S. A., S. A. Naqvi, Z. Hussain, A. Hashmi, F. Akhtar, and others. 2003. "Renal Transplantation in Developing Countries." *Kidney International Supplements* (83): S96–100.

Rizvi, S. A., S. A. Naqvi, M. N. Zafar, Z. Hussain, A. Hashmi, and others. 2011. "A Renal Transplantation Model for Developing Countries." *American Journal of Transplantation* 11 (11): 2302–7. doi:10.1111/j.1600-6143.2011.03712.x.

Roncal Jimenez, C. A., T. Ishimoto, M. A. Lanaspa, C. J. Rivard, T. Nakagawa, and others. 2013. "Fructokinase Activity Mediates Dehydration-Induced Renal Injury." *Kidney International* 86 (2): 294–302. doi:10.1038/ki.2013.492.

Sakuma, Y., A. Glassman, and C. Vacca. 2017. "Priority-Setting Processes for Expensive Treatments for Chronic Diseases." In *Disease Control Priorities* (third edition): Volume 5, *Cardiovascular, Respiratory, and Related Diseases,* edited by D. Prabhakaran, S. Anand, T. A. Gaziano, J.-C. Mbanya, Y. Wu, and R. Nugent. Washington, DC: World Bank.

Schwedt, E., L. Sola, P. G. Rios, N. Mazzuchi, and National Renal Healthcare Program. 2010. "Improving the Management of Chronic Kidney Disease in Uruguay: A National Renal Healthcare Program." *Nephron Clinical Practice* 114 (1): c47–59. doi:10.1159/000245069.

Sesso Rde, C., A. A. Lopes, F. S. Thome, J. R. Lugon, Y. Watanabe, and others. 2012. "[Chronic Dialysis in Brazil: Report of the Brazilian Dialysis Census, 2011]." *Brazilian Journal of Nephrology* 34 (3): 272–77.

Sharma, S. K., A. Ghimire, S. Carminati, G. Remuzzi, and N. Perico. 2014. "Management of Chronic Kidney Disease and Its Risk Factors in Eastern Nepal." *The Lancet Global Health* 2 (9): e506–7. doi:10.1016/S2214-109X(14)70281-5.

Soderland, P., S. Lovekar, D. E. Weiner, D. R. Brooks, and J. S. Kaufman. 2010. "Chronic Kidney Disease Associated with Environmental Toxins and Exposures." *Advances in Chronic Kidney Disease* 17 (3): 254–64. doi:10.1053/j.ackd.2010.03.011.

Stone, J. H., P. A. Merkel, R. Spiera, P. Seo, C. A. Langford, and others, for the Rave-ITN Research Group. 2010. "Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis." *New England Journal of Medicine* 363 (3): 221–32. doi:10.1056/NEJMoa0909905.

Susantitaphong, P., D. N. Cruz, J. Cerda, M. Abulfaraj, F. Alqahtani, and others. 2013. "World Incidence of AKI: A Meta-Analysis." *Clinical Journal of the American Society of Nephrology* 8 (9): 1482–93. doi:10.2215/CJN.00710113.

Talabani, B., S. Zouwail, R. D. Pyart, S. Meran, S. G. Riley, and others. 2014. "Epidemiology and Outcome of Community-Acquired Acute Kidney Injury." *Nephrology (Carlton)* 19 (5): 282–87. doi:10.1111/nep.12221.

Thomas, B., M. van Pelt, R. Mehrotra, C. Robinson-Cohen, and J. LoGerfo. 2014. "An Estimation of the Prevalence and Progression of Chronic Kidney Disease in a Rural Diabetic Cambodian Population." *PLoS One* 9 (1): e86123. doi:10.1371/journal.pone.0086123.

Thomas, B., S. Wulf, B. Bikbov, N. Perico, M. Cortinovis, and others. 2015. "Maintenance Dialysis throughout the World in Years 1990 and 2010." *Journal of the American Society of Nephrology* 26 (11): 2621–33. doi:10.1681/ASN.2014101017.

Trang, T. T., N. H. Phu, H. Vinh, T. T. Hien, B. M. Cuong, and others. 1992. "Acute Renal Failure in Patients with Severe *Falciparum* Malaria." *Clinical Infectious Diseases* 15 (5): 874–80.

U.S. Renal Data System. 2013. *2013 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*. Bethesda, MD: National Institutes of Health, NIDDK.

van Dijk, P. C., K. J. Jager, F. de Charro, F. Collart, R. Cornet, and others. 2001. "Renal Replacement Therapy in Europe: The Results of a Collaborative Effort by the ERA-EDTA Registry and Six National or Regional Registries." *Nephrology Dialysis Transplantation* 16 (6): 1120–09.

Waikar, S. S., G. C. Curhan, R. Wald, E. P. McCarthy, and G. M. Chertow. 2006. "Declining Mortality in Patients with Acute Renal Failure, 1988 to 2002." *Journal of the American Society of Nephrology* 17 (4): 1143–50. doi:10.1681/ASN.2005091017.

Weiner, D. E., M. D. McClean, J. S. Kaufman, and D. R. Brooks. 2013. "The Central American Epidemic of CKD." *Clinical Journal of the American Society of Nephrology* 8 (3): 504–11. doi:10.2215/CJN.05050512.

Wesseling, C., J. Crowe, C. Hogstedt, K. Jakobsson, R. Lucas, and others. 2013. "The Epidemic of Chronic Kidney Disease of Unknown Etiology in Mesoamerica: A Call for Interdisciplinary Research and Action." *American Journal of Public Health* 103 (11): 1927–30. doi:10.2105/AJPH.2013.301594.

Wetzels, J. F., L. A. Kiemeney, D. W. Swinkels, H. L. Willems, and M. den Heijer. 2007. "Age- and Gender-Specific Reference Values of Estimated GFR in Caucasians: The Nijmegen Biomedical Study." *Kidney International* 72 (5): 632–37. doi:10.1038/sj.ki.5002374.

Wijkstrom, J., R. Leiva, C. G. Elinder, S. Leiva, Z. Trujillo, and others. 2013. "Clinical and Pathological Characterization of Mesoamerican Nephropathy: A New Kidney Disease in Central America." *American Journal of Kidney Disease* 62 (5): 908–18. doi:10.1053/j.ajkd.2013.05.019.

Wilkie, M. 2014. "The Role of Peritoneal Dialysis in Saving Young Lives from Acute Kidney Injury." *Peritoneal Dialysis International* 34 (5): 476–77. doi:10.3747/pdi.2014.00185.

Winkelmayer, W. C., M. C. Weinstein, M. A. Mittleman, R. J. Glynn, and J. S. Pliskin. 2002. "Health Economic Evaluations: The Special Case of End-Stage Renal Disease Treatment." *Medical Decision Making* 22 (5): 417–30.

Wolfe, R. A., V. B. Ashby, E. L. Milford, A. O. Ojo, R. E. Ettenger, L. Y. Agodoa, and others. 1999. "Comparison of Mortality in All Patients on Dialysis, Patients on Dialysis Awaiting Transplantation, and Recipients of a First Cadaveric Transplant." *New England Journal of Medicine* 341 (23): 1725–30. doi:10.1056/NEJM199912023412303.

Wong, F. K., S. K. Chow, and T. M. Chan. 2010. "Evaluation of a Nurse-Led Disease Management Programme for Chronic Kidney Disease: A Randomized Controlled Trial." *International Journal of Nursing Studies* 47 (3): 268–78. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/848/CN-00743848/frame.html.

Wright, J. T., Jr., G. Bakris, T. Greene, L. Y. Agodoa, L. J. Appel, and others. 2002. "Effect of Blood Pressure Lowering and Antihypertensive Drug Class on Progression of Hypertensive Kidney Disease: Results from the AASK Trial." *Journal of the American Medical Association* 288 (19): 2421–31.

Wyatt, C., V. Konduri, J. Eng, and R. Rohatgi. 2007. "Reporting of Estimated GFR in the Primary Care Clinic." *American Journal of Kidney Diseases* 49 (5): 634–41.

Zhang, A. H., H. Zhong, W. Tang, S. Y. Chen, L. He, and others. 2008. "Establishing a Renal Management Clinic in China: Initiative, Challenges, and Opportunities." *International Urology and Nephrology* 40 (4): 1053–58. doi:10.1007/s11255-008-9450-8.