

The global role of kidney transplantation

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World Kidney Day on 8 March 2012 provides a chance to reflect on the success of kidney transplantation as a therapy for end-stage renal disease (ESRD) that surpasses dialysis treatments for the quality and quantity of life and for cost effectiveness. An experimental, risky, and very limited treatment option 50 years ago is now routine clinical practice in more than 80 countries. What was limited to a few people in a small number of academic centers is now routinely transforming lives in most high- and medium-income countries. The largest numbers of transplantations are performed in the United States, China, Brazil, and India, while the greatest population access to transplantation is in Croatia, Portugal, Spain, Austria, the United States, and Norway, but almost all countries have growing waiting lists, and transplantation meets only 10% of the global need. Barriers to broader application include, of course, economic limitations that appropriately place transplantation at a lower priority than clean water, sanitation, and vaccination. Even in high-income countries, the technical challenges of surgery and the consequences of immunosuppression restrict the number of suitable recipients, but the major restrictions on kidney transplantation rates are the shortage of donated organs and the small size of trained medical, surgical, and nursing workforces with the required expertise.

The first successful organ transplantation occurred between identical twins in Boston on 23 December 1954. Between 1965 and 1980, patient survival progressively improved to 90%, and graft survival rose to at least 60%. Thirty years on, unsensitized recipients of first deceased- or living-donor kidney transplants can expect 1-year patient survival of 95% and transplant survival of at least 90%. Recent developments have also led to excellent results from ABO blood group-incompatible transplants in recipients with low-titer ABO antibodies. High titers of donor-specific human leukocyte antigen antibodies have also limited patients' prospects for transplantation, but better desensitization protocols and paired kidney exchange programs now afford real opportunities for those previously deemed untransplantable. Kidney transplantation provides both better qual-

ity and quantity of life than maintenance dialysis. In the United States between 1991 and 1997, mortality was 68% lower in transplant recipients than in those remaining on the transplant waiting list after more than 3 years of follow-up; 20- to 39-year-old patients with transplants were predicted to live 17 years longer than those remaining on the waiting list.

In Pakistan, Rizvi has shown that it is possible, despite the resource-poor environment, to achieve 1- and 5-year survival rates of 92% and 85%, respectively, but across the world, ethnic minorities, disadvantaged populations, and African Americans generally suffer worse outcomes when compared with white patients. Although it is possible to achieve excellent long-term results in resource-poor environments, most patients and their families are not able to afford the high-cost immunosuppressants and antiviral medications that reduce the risk of graft loss and mortality.

Worldwide, the number of potential candidates for renal replacement therapy is growing rapidly, but long-term dialysis, expensive for developed countries, is prohibitive for most emerging economies. It is critical to recognize that funding of ESRD treatment must be preceded by, and linked to, strategies to identify and prevent progressive chronic kidney diseases. The majority of patients commencing dialysis in low-income countries die or stop treatment within the first 3 months of dialysis because of cost. Transplantation, especially when preemptive of dialysis, provides a mechanism to both expand access and reduce costs for successful treatment of ESRD.

There are substantial disparities in access to transplantation across the world (Figure 1). The relationship between transplantation rate and each nation's Human Development Index (HDI) shows not only the reduced transplantation rate in the low- and middle-HDI countries but also the large spread of rates even among the richer nations. Kidney transplantation rates of more than 30 per million population (pmp) in 2010 were restricted to Western Europe, the United States, and Australia, with a slightly broader spread of countries achieving between 20 and 30 pmp. In addition to this variability, there are

Guillermo Garcia Garcia¹,
Paul N. Harden² and Jeremy
R. Chapman³

For the World Kidney Day
Steering Committee 2012⁴
¹*Nephrology Service, Hospital
Civil de Guadalajara, University
of Guadalajara Health Sciences
Center (CUCS) Hospital 278,
Guadalajara, Jalisco, Mexico;*
²*Oxford Kidney Unit and Oxford
Transplant Centre, Churchill
Hospital, Oxford, United
Kingdom; and* ³*Centre for
Transplant and Renal Research,
Westmead Millennium Institute,
Sydney University, Westmead
Hospital, Sydney, New South
Wales, Australia*

⁴*World Kidney Day is a joint
initiative of the International
Society of Nephrology and
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members: G. Abraham, P.
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Couser, T. Erk, J. Feehally, G.G.
Garcia, P.K.T. Li, M. Riella, L.
Segantini, and P. Shay.*

Correspondence: *World
Kidney Day, International
Society of Nephrology, Rue
des Fabriques 1, 1000 Brussels,
Belgium.
E-mail: smartin@theisn.org*

substantial within-country disparities in transplantation rates among women, and ethnic minorities. Even in the United States, with high overall transplantation rates, African Americans, women, and the poor fare badly compared with Caucasians, men, and the affluent.

Developing countries suffer poor transplantation rates because of a combination of low levels of infrastructure; an insufficient trained workforce; lack of a legal framework governing brain death; religious, cultural, and social constraints; patient apprehension; physician bias; commercial incentives favoring dialysis; and geographical remoteness. Poor access to transplantation is therefore almost inevitable for most of the world's population.

Both living donation and deceased-donor donation are recognized by the WHO (World Health Organization) to go hand in hand with prevention programs as critical to the capacity of nations to develop self-sufficiency for management of ESRD. No country in the world generates sufficient organs to meet the needs of its citizens. Spain, Croatia, Portugal, Austria, the United States, and Norway stand out as countries with high rates of deceased organ donors, and most countries are trying to emulate their success. A return to donation after cardiac death, instead of the now-standard donation after brain death, has enhanced the numbers of deceased organ donations in several countries. Extended-criteria donor kidneys are less successful in the long term but are accepted by patients with limited alternatives.

A number of strategies have been implemented to reduce the disparities. The Transplantation Society has established the Global Alliance for Transplantation to collect and disseminate global information, expand education in transplantation, and develop guidelines for organ donation and transplantation. The International Society of Nephrology Global Outreach Program has catalyzed the development of kidney transplant programs across a large number of countries with targeted fellowship training and stimulation of long-term institutional links between developed and developing transplant centers. The establishment of national ESRD registries; training programs for nephrologists, transplant surgeons, nursing staff, and donor coordinators; and nationally funded organ procurement organizations providing transparent and equitable retrieval and allocation also offer an opportunity to improve access to transplantation worldwide.

The reality of the global organ-donor shortage is, however, that in general, the rich receive more transplants than the poor, either from their own country or with an organ illegally purchased from the poor or taken from an executed Chinese prisoner. Trafficking in and commercialization of human organs changed from an unusual and extremely hazardous practice in the 1980s, to a frequent but still very hazardous one in the 1990s, and then to a gruesomely burgeoning trade from the turn of the century. The WHO estimated that up to 10% of all organ transplants were of commercial origin by 2005.

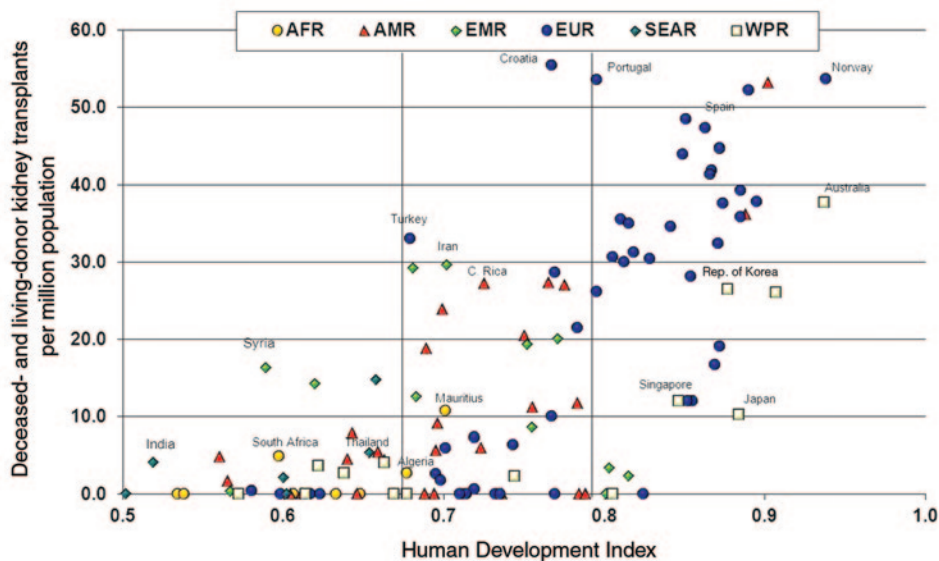


Figure 1 | Number of deceased- and living-donor kidney transplants in WHO (World Health Organization) Member States in 2010, correlated with Human Development Index. Grouped by WHO regions (AFR, Africa; AMR, Americas; EMR, Eastern Mediterranean; EUR, Europe; SEAR, South-East Asia; WPR, Western Pacific).

The first WHO Guiding Principles in this field were endorsed in 1991, making clear the decision of all national governments to ban commercialization of the human body. This principle was reaffirmed unanimously by the World Health Assembly in 2010 when the updated WHO guiding principles for human organ and tissue donation and transplantation were endorsed. Iran, alone, claims to have resolved national self-sufficiency for renal transplantation through a scheme of part government-funded, part patient-funded sale of kidneys by vendors. All other countries with transplantation programs have carried that ban on commercialism into their own legislation. It is thus illegal to buy or sell organs even in the major human-organ-trafficking countries of the world. Sadly, this has not prevented illegal continuation of the trade in countries such as China and Pakistan, nor has it prevented new entrants to this lucrative trade from taking advantage of their own or other nations' impoverished and vulnerable populations to provide kidneys and even livers for the desperate wealthy in need of transplantation.

The Transplantation Society and the International Society of Nephrology took a joint stand against the despoiling of transplantation therapy and victimization of the poor and vulnerable by doctors, brokers, and hospitals operating these illegal programs. In 2008, more than 150 representatives from across the world from different disciplines of health care, national policy development, law, and ethics produced the Declaration of Istanbul, which has now been endorsed by more than 110 professional and governmental organizations and implemented by many of these organizations with a goal to eliminate transplant tourism and enhance the ethical practice of transplantation globally.

Major challenges remain in providing optimal management of ESRD, particularly in low-income economies. There is a need to mandate more focus on community screening and implementation of simple measures to minimize progression of chronic kidney disease. The recent designation, by the United Nations High-Level Meeting, of renal disease as an important non-communicable disease is one step in the right direction.

There are transplantation solutions available that need augmentation across all economies. These include replication of the demonstrably successful models of kidney transplant programs in many developing countries; efforts to grow the availability of less expensive generic immunosuppressive agents; improved clinical training opportunities; governmental and professional guidelines legislating prohibition of commercialization and defining professional standards of ethical practice; and a framework for each nation to develop self-sufficiency in organ transplantation through focus on both living donation and nationally managed deceased organ donation programs.

The International Society of Nephrology and the Transplantation Society have pledged to work together in coordinated joint global outreach programs to help establish and grow appropriate kidney transplant programs in low- and middle-income countries utilizing their considerable joint expertise. World Kidney Day 2012 provides a focus to help spread this message to governments, health authorities, and communities across the world on 8 March 2012.

DISCLOSURE

The authors declared no competing interests.