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Editorial Review

Chronic kidney disease: a research and public health priority

Norberto Perico[1] and Giuseppe Remuzzi[1,2]

[1]Mario Negri Institute for Pharmacological Research, Bergamo, Italy and [2]Unit of Nephrology and Dialysis, Ospedali Riuniti Bergamo, Bergamo, Italy

Correspondence and offprint requests to: Giuseppe Remuzzi; E-mail: giuseppe.remuzzi@marionegri.it

The global burden of non-communicable diseases

The growing global burden of non-communicable diseases (NCDs) worldwide has been disregarded until recently by policy makers, major aid donors and academics. However, NCDs are the leading cause of death in the world [1–3]. In 2008, there were 57 million deaths globally, of which 63% were due to NCDs. These chronic diseases are the largest cause of death, led by cardiovascular disease (17 million deaths, mainly from ischaemic heart disease and stroke) followed by cancer (7.6 million), chronic lung disease (4.2 million, including asthma and chronic obstructive pulmonary disease) and diabetes mellitus (1.3 million deaths) [4]. They share key risk factors: tobacco use, unhealthy diets, lack of physical activity and alcohol abuse [4]. The current burden of chronic diseases reflects past exposure to these risk factors, and the future burden will be largely determined by the current exposure. Actually, worldwide the prevalence of these chronic diseases is projected to increase substantially over the next decades [5]. According to WHO, the global number of individuals with diabetes in 2000 was estimated to be 171 million (2.8% of the world's population), a figure anticipated to increase in 2030 to 366 million (6.5%), 298 million of whom will live in developing countries [6].

As a consequence, predictions for the next two decades show a near 3-fold increase in the ischaemic heart disease and stroke mortality rate in Latin America, Sub-Saharan Africa and the Middle East [4]. Countries in transition in the South-East and East Asia have also witnessed a rapid deterioration of their chronic disease risk and mortality profile [7]. India, the second most populous country, has the highest number of diabetics in the world, and in 2008, the estimates for age-standardized deaths per 100 000 population due to diabetes and cardiovascular disease were 386.3 and 283.0 in males and females, respectively [7]. In China, age-specific death rates from cardiovascular disease increased between 200 and 300% in those aged 35 through 44 years between 1986 and 1999, and by more than 100% in those aged 45–54 years [8]. Of note, the 2011 WHO report on CKD Country Profiles [7] shows that globally low- and lower-middle income countries have the highest proportion of deaths under 60 years of age from NCDs. In 2008, the proportion of these premature NCD deaths was 41% in low-income and 28% in lower-middle income countries, respectively, threefold and more than twofold as compared with the proportion in the high-income countries (13%).

Risk factors for chronic diseases are also escalating. Smoking prevalence and obesity levels among adolescents have risen considerably worldwide over the past decade and portend a rapid increase in chronic diseases [9, 10].

In all countries, the increased burden of NCDs is also leading to growing economic costs. For example, it has been anticipated that in the United States, cardiovascular diseases and diabetes together cost $750 billion annually [11]. In the next 10 years the United Kingdom will lose $33 billion in national income as a result of largely preventable heart disease, stroke and diabetes [12, 13]. Over the same period, the national income loss for NCDs in India and China will account for $237 and $558 billion, respectively [12, 13].

Thus, NCDs are among the most severe threats to global economic development, probably more detrimental than fiscal crisis, as underlined by the World Economic Forum's 2009 report.

The case of chronic kidney disease

Chronic kidney disease (CKD) is a key determinant of the poor health outcomes for major NCDs [14]. CKD is a worldwide threat to public health, but the size of the problem is probably not fully appreciated. Estimates of the global burden of the diseases report that diseases of the kidney and urinary tract contribute with ~830 000 deaths annually and 18 867 000 disability-adjusted life years (DALY), making them the 12th highest cause of death (1.4% of all deaths) and the 17th cause of disability (1% of all DALY). This ranking is similar across World Bank regions, but, among developing areas, East Asia and Pacific regions have the highest annual rate of death due to diseases of the genitourinary system [15].

National and international renal registries offer an important source of information on several aspects of CKD. In particular, they are useful in characterizing the population on renal replacement therapy (RRT) due to end-stage renal disease (ESRD), describing the prevalence and incidence of ESRD and trends in mortality and disease rates. One of the most comprehensive sources of information about the prevalence of ESRD worldwide is the United States Renal Data System (USRDS). We have implemented the USRDS dataset with ESRD data from renal registries identified after searches of web resources for registry databases, annual reports and published literature. According to this analysis, the most recent available data indicate that the prevalence of ESRD ranges from 2447 pmp in Taiwan to 10 pmp in Nigeria (Figure 1). However, there is paucity of renal registries globally with an international standard for registry data collection, especially in low- and middle-income countries, where, in addition, the use of RRT is scarce or non-existent, eventually making it difficult to compare ESRD results [16]. For these reasons, the reported prevalence rate of ESRD varies widely among countries, especially in the emerging world, which may be related more to the capacity of the health system to provide the costly RRT treatment than true difference in epidemiology of renal disease. Thus, in Latin America, the ESRD prevalence ranges from 1019 pmp in Uruguay to 34 pmp in Honduras, a difference that may also reflect the relationship with the gross national product [17]. Much less is known in Africa, with the highest ESRD prevalence in Tunisia (713 pmp) and Egypt (669 pmp) [18]. In relatively developed regions of China, especially in major cities, the prevalence of ESRD has been reported to be 102 pmp [19], whereas in Japan, it is more than 2200 pmp, one of the highest rates worldwide.

Therefore, overall there are ∼1.8 million people in the world who are alive simply because they have access to one form or another of RRT [20]. Ninety per cent of those live in industrialized countries, where the average gross income is in excess of US $10 000 per capita [21]. The size of this population has been expanding at a rate of 7% per year. As an example, over the last decade, the number of those requiring dialysis has increased annually by 6.1% in Canada [22], 11% in Japan [23] and 9% in Australia [24]. However, <10% of all patients with ESRD receive any form of RRT in countries such as India and Pakistan. In India, ∼100 000 patients develop ESRD each year [25]. Of these, 90% never see a nephrologist. Of the 10 000 patients who do consult a nephrologist, RRT is initiated in 90%; the remaining 10% are unable to afford any form of RRT. Of the 8900 patients who start

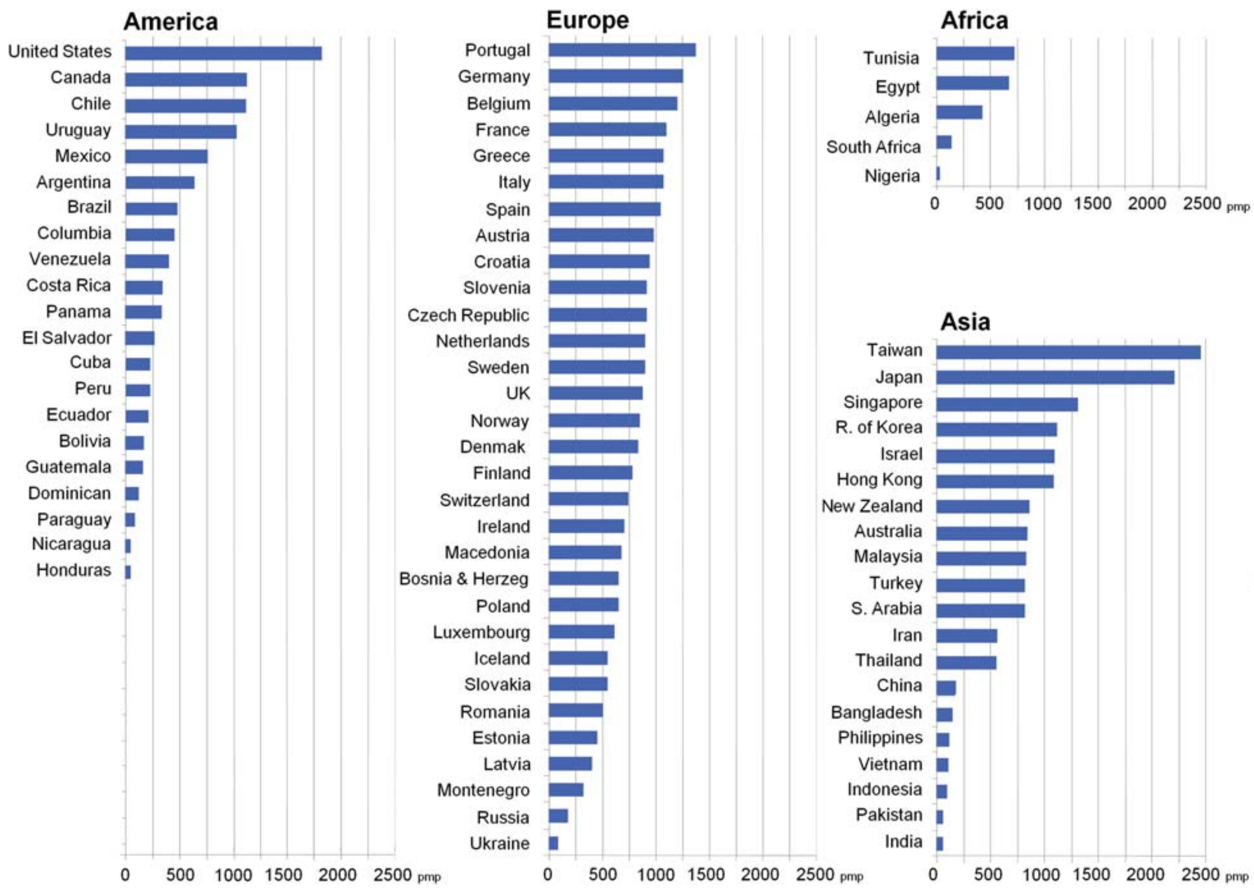

Fig. 1. Prevalence of ESRD (dialysis and transplantation) worldwide. Data are from the 2011 USRDS Annual Report and from national registry database and published literature. All rates are unadjusted and presented as prevalence rate per million population.

haemodialysis, 60% are lost to follow-up within 3 months. These patients drop out of therapy, because they realize that dialysis is not a cure and has to be performed over the long-term, ultimately causing impoverishment of their families.

Patients on RRT can be regarded as the tip of the iceberg, whereas the number of those with CKD not yet in need of RRT is much greater. However, the exact prevalence of pre-dialysis CKD is not known and only rough estimates exist. In industrialized countries such as the USA, the Third National Health and Nutrition Evaluation Survey (NHANES III, 1999–2006) has shown a prevalence of CKD in the adult population of 11.5% (~23.2 million people) [26]. A sizeable proportion of these people will experience the progression of their disease to ESRD. In Europe, the Prevention of End-Stage Renal and Vascular End-points (PREVEND) study undertaken in the city of Groningen (the Netherlands) evaluated almost 40 000 individuals in a cross-sectional cohort study [27]. It was found that no less than 16.6% had high normal albuminuria and ~7% of those screened had microalbuminuria. If these data were to be extrapolated to the world population, the number of people with CKD could be estimated as hundreds of millions.

Although data concerning the prevalence of pre-dialysis CKD in developing countries are scarce, we would expect that there are comparable numbers of patients with CKD in poor countries as in industrialized nations. To this, the International Society of Nephrology (ISN) Global Outreach (GO) funded the Kidney Disease Data Center database to house data from sponsored programmes aimed at preventing CKD and its complications in developing nations. Some examples indicate that the overall prevalence of CKD, diagnosed based on a urinary albumin/creatinine ratio ≥30 or glomerular filtration rate (GFR) ≤60 L/min/1.73 m^2 (as Modification of Diet in Renal Disease, four variables), is 11 and 10.6% in urban areas, respectively, of Moldova [28] and Nepal [29]. Moreover, in the attempt to compare the burden of illness among centres in Nepal, China and Mongolia, in 11 394 adult subjects, it has been found that decreased estimated GFR (<60 L/min/1.73 m^2) was present in 7.3–14% of participants across centres; proteinuria (≥1+) on dipstick (2.4–10%) was also common [30]. By a recent cross-sectional survey of a nationally representative sample of Chinese adults, the overall prevalence of CKD was 10.8% [31].

Data from India also suggest that in a developing country, the prevalence rate of CKD could vary almost 5-fold between the rural and city population [32, 33]. These observations imply that CKD would affect not only very many people in the developing world, but preferentially the poor within these countries who usually have no information about disease and risk factors, and cannot have access to healthcare. Interestingly, low socioeconomic status is associated with CKD also in developed nations, as shown in Unites States by the NHANES survey, which reported people with lower income being disproportionately afflicted with a higher burden of CKD risk factors [34]. Similarly, in Sweden [35] and the UK [36], lower income and social deprivation are associated with micro- or macro-albuminuria, reduced GFR and progressive kidney function loss.

Causes of CKD vary in developed and developing nations

Diabetes and hypertension

Diabetes and hypertension are the major causes of CKD leading to kidney failure in the USA, accounting for 153 and 99 pmp, respectively [37], of incident causes of ESRD. Definitely lower is the contribution of glomerulonephritis (23.7 pmp) [37]. The proportion of people with CKD not explained by diabetes and hypertension is substantially lower in the USA (28% of stage 3–4 CKD) than in developing countries [37, 38]. Indeed, in a recent study analysing screening programs in Nepal, China and Mongolia, 43% of people with CKD did not have diabetes or hypertension [30].

Infectious diseases

There is also increasing evidence that infectious diseases, still a major health problem in low-income countries, may substantially contribute to the burden of chronic nephropathies. This mainly relates to poor environmental conditions, unsafe life habit and malnutrition. Urinary tract infections, occurring in the entire population, but with particular impact on females of all ages, especially during pregnancy, may have long-term consequences over and above the direct infectious disease morbidity and mortality these infections cause. They include chronic injury of the kidney which eventually may lead to loss of renal function, development of secondary hypertension and, for pregnant women, increased risk of maternal toxaemia, neonatal prematurity and low birth weight which is usually associated with lower-than-normal nephron number anticipating the high risk for hypertension and chronic renal injury during the life time [39]. Moreover, in several regions worldwide, tuberculosis is still an endemic infection with many cases of renal tuberculosis remaining clinically silent for years while irreversible renal destruction takes place [40]. Glomerular involvement with parasitic diseases, including malaria [41], schistosomiasis [42] and leishmaniasis [43], may also pave the way to progressive renal disease. A variety of glomerular lesions, and in particular a unique form of glomerular damage, HIV-associated nephropathy, have emerged as significant forms of renal disease in HIV-infected patients [44]. With the increasing rate of this viral infection, kidney failure in HIV-infected patients will progressively become a major public health problem, particularly in Sub-Saharan Africa. Therefore, in developing countries, infectious diseases add substantial burden to non-communicable risk factors, in enhancing the global prevalence of CKDs.

Malnutrition

There are also factors that link early malnutrition with being overweight in adulthood, ultimately developing into diabetes and diabetic nephropathy [45]. A number of observational epidemiological studies have postulated that early (intrauterine or early postnatal) malnutrition causes an irreversible differentiation of the metabolic system, which may, in turn, increase the risk of certain chronic diseases in adulthood. For example, a fetus of an undernourished mother will respond to a reduced energy supply by switching on genes that optimize energy conservation. This survival strategy means a permanent differentiation of regulatory systems that result in an excess accumulation of energy (and consequently body fat) when the adult is exposed to an unrestricted dietary energy supply [45]. Because intrauterine growth retardation and low birth weight are common in developing countries or within minority groups, this mechanism may result in the establishment of a population in which many adults are particularly susceptible to developing obesity and CKD. These observations further imply that CKD would affect preferentially the poor within these countries.

Acute kidney injury

CKD is also linked to acute kidney injury (AKI). Thus, both the rate of progression to ESRD and all-cause mortality are increased in patients with CKD after transient increases in serum creatinine when compared with patients without CKD [46]. Moreover, up to 28% of the patients with no pre-existing kidney disease who recover from AKI develop *de novo* CKD [47]. Non-steroidal anti-inflammatory medications, several cardiovascular and diabetes drugs, as well as traditional medicines used in the primary-care setting in developing countries, may lead to the development of transient episodes of AKI. These findings emphasize the relevance of CKD detection and appropriate adjustments in management to optimal outcome in major NCDs.

CKD is a major risk factor for cardiovascular disease

It is increasingly recognized that the burden of CKD is not limited to its implication on demands for RRT but has a major impact on the health of the overall population. Indeed, patients with reduced kidney function represent a population not only at risk for the progression of kidney disease and development of ESRD, but also at even greater risk for cardiovascular diseases. CKD is a major risk factor for cardiovascular mortality, and kidney disease is a major complication of diabetes. In ∼400 000 Medicare patients with diabetes and CKD, in USA over 2 years of follow-up, the risk of death for cardiovascular diseases (32.3%) far exceeded that of the development of ESRD (6:1) [48]. Moreover, CKD has been documented as an independent risk factor for angina, myocardial infarction, heart failure, stroke, peripheral vascular disease and arrhythmias [49, 50]. The increased risk of cardiovascular disease associated with CKD has been shown in both general [37, 51, 52] and high-risk [52] populations, in young and elderly people [53], as well as in Caucasians [49], African blacks [54] and in Asian people [55].

There is also evidence that the increased cardiovascular risk in CKD patients does not just coexist with diabetes or hypertension. Indeed, an independent and progressive association between GFR and risk of cardiovascular events and death has been found in a community-based study in more than 1 million adult subjects in the USA [56]. Similarly, a recent study in more than 6000 people followed on average 7 years has shown that the risk of cardiovascular death was increased 46% in subjects with a mild-to-moderate reduction in GFR (30–60 L/min), independent of conventional risk factors such as diabetes and hypertension [57].

The reason why CKD is a risk factor for cardiovascular outcomes is not entirely clear, but it seems largely related to the excess prevalence of traditional cardiovascular risk factors, including hypertension, diabetes and dyslipidaemia associated with the renal disease. In addition, other factors such as hyperhomocystinaemia, abnormalities of mineral metabolism and parathyroid function may become more prevalent and have pathogenetic relevance as CKD progresses [58, 59]. Even patients with microalbuminuria and proteinuria, but still normal renal function, are at increased risk of cardiovascular morbidity and mortality [60]. Large studies in the general population showed that the presence of microalbuminuria or proteinuria is associated with enhanced risk of all-cause mortality at all levels of baseline kidney function [27, 49, 61–63].

Thus, through its impact on cardiovascular morbidity, CKD may directly contribute to the increasing global burden of death caused by cardiovascular disease. Therefore, these are the patients in whom efforts should be focused.

The need to raise awareness about early CKD and implement prevention programs

The major societal effect of CKD is the enormous financial cost and loss of productivity with associated advanced or ESRD. In many developed countries, treatment for ESRD accounts for more than 2–3% of their annual health-care budget, while the population with ESRD represents ∼0.02–0.03% of the total population [64]. This situation is even worse in most developing countries, where RRT is often unavailable or unaffordable, and ∼1 million people die with ESRD each year [65]. On the other hand, awareness of early and advanced CKD is low, even in developed nations, being <20% [38]. For example, in a recent survey in almost 500 000 people in Taiwan, as a part of medical screening programme, <4% of those with CKD (12%) were aware of their condition [66]. Moreover, it should be considered that CKD, even at more advanced stages, is treatable. Ample evidence from clinical trials has shown that control of hypertension and of proteinuria, especially with inhibitors of the renin–angiotensin system, are highly effective interventions for slowing the progression of diabetic and non-diabetic CKD [67, 68]. Studies have also documented that even sustained remission or regression of proteinuric CKD is achievable especially in a large proportion of non-diabetic patients [69].

Together, these observations underline the urgent need for strategies to enhance awareness about CKD, especially in developing countries, where the low awareness may serve as a barrier to accessing appropriate care even when available [70] (Table 1). To this purpose, recently, the International Society of Nephrology and the International Federation of Kidney Foundation joined efforts to raise awareness regarding CKD by promoting the annual World Kidney Day (WKD). On this particular day, public activities such as free screening for CKD and its risk factors and meeting with the community population and leaders are planned and performed in numerous centres worldwide [71]. Nevertheless, the resources to implement effective early awareness, detection and prevention programmes for CKD should ultimately come from government health programmes as part of global strategy to improve public health. Some examples are the National Health Programme in Uruguay that has already incorporated CKD into their NCD prevention programmes, and the Strategic Network of Health Services against Chronic Kidney Disease in Mexico.

These programmes will help to decrease the costs of managing ESRD and cardiovascular disease and respond to public health demand. However, before these surveillance and intervention efforts are expanded, information on their sustainability and affordability to the public sector, especially in low-income countries, should be collected.

Conclusions

Medicine is developing evidence for the importance of CKD to public health and its contribution to the global burden of major NCDs, but has no equity plan [14, 72]. A more concerted, strategic and multisectorial approach, underpinned by solid research, is essential to help reverse the negative trends in the incidence of CKD and its risk factors, not just for a few beneficiaries but on a global health equity programme. Thus, a pragmatic approach to reduce the global burden of renal and cardiovascular diseases has to be adopted. For that, well-defined screening of community or high-risk populations followed by intervention programmes have to be initiated, especially in developing countries.

In recognition of the increasing burden and importance of chronic diseases, a high-level United Nations meeting with heads of governments of member states was organized last September in New York to discuss a global NCD Action Plan prepared by WHO. Although this document did provide the unique opportunity to bring attention to the pandemic of NCDs, it prioritized four chronic diseases, namely cardiovascular disease, cancer, diabetes and chronic respiratory disease [73]. Nevertheless, through intensive lobbying also by ISN, CKD has gained recognition in the final Political Declaration [73]. Indeed, a paragraph of the NCD Action Plan stated that the members of States of the UN General Assembly 'recognize that renal, oral and eye disease pose a major health burden for many countries and that diseases share

Table 1. Public health initiatives targeting CKD

Programme	Description
Surveillance/survey	
USRDS [80]	US Renal Data System collects and analyses information about prevalence/incidence of patients with end-stage renal disease on replacement therapy with dialysis or transplantation. It describes the burden of ESRD in the USA and provides international comparison.
NHANES [81]	A survey that examines a nationally representative sample of ∼5000 US civilian non-institutionalized population (aged 1 year and older). It provides data about the prevalence and incidence of earlier stages of CKD and its risk factors.
ESRD Network System [82]	It consists of 18 regional networks in the USA that collect information about treatment centre care to improve treatment and outcomes of ESRD patients.
GBD Study [14, 83]	As part of the Global Burden of Disease, Injuries and Risk Factors Study (GBD 2010), the International Society of Nephrology and the Core Team GBD study in Seattle are collecting and analysing data on prevalence, incidence of CKD stage 3 and 4 as well as ESRD on dialysis and transplantation worldwide. The survey also provides estimations of mortality and disability for CKD.
Awareness and screening	
KEEP [84]	Kidney Early Evaluation Program (KEEP) is a large screening targeting populations at high risk of CKD, such as subjects with diabetes mellitus, hypertension or first-degree relatives with diabetes mellitus, hypertension or kidney disease. KEEP provides three simple tests that determine kidney function to nearly 1500 people each month in dozens of cities across the USA. The programme, which has screened hundreds of thousands of participants, is finding kidney disease at the earliest stage possible.
ISN Global Outreach (GO) [79]	The ISN-GO programme, by making the knowledge and experience of the developed world accessible to kidney doctors and other specialists in emerging countries, is improving kidney care and prevention strategies around the globe. It improves education of nephrologists, primary care physicians and other health professionals, raises public awareness about kidney disease and its risk factors, initiates and supports research projects to demonstrate efficacy of early screening for renal disease. Together with the International Federation of Kidney Foundation, ISN-GO joins efforts to raise awareness regarding CKD by promoting the annual World Kidney Day (WKD). In this day, public activities such as free screening for CKD and its risk factors and meetings with the community populations and leaders are planned and performed in numerous centres worldwide.

common risk factors and can benefit from common responses to non-communicable diseases' [73]. However, NCD advocacy groups, such as ISN [74], as well as the editors of *The Lancet* and *The British Medical Journal* have underlined their disappointment over the insufficient emphasis on action to be taken by governments [75, 76]. In addition, they pointed out that a major opportunity to advance global health was in danger of being lost since the Political Declaration did not set substantive targets or timelines in the need for member states to activate policies in their public health programmes to address NCD issues [74–77].

In developing nations, there must also be a commitment to create in-country capacity, notably a human capacity that can determine for itself locally specific problems dealing with kidney diseases to be addressed through clinical research programmes. However, this implies greater efforts by the developed nations to limit the brain drain of scientists and health personnel from low- and middle-income countries [78]. The North-South capacity gap in health science, including nephrology, continues to narrow, but it has by no means disappeared. At the same time, a new gap in capacity has emerged between scientifically proficient and scientifically lagging developing countries, the so-called South–South gap. This divide has surfaced because the number of developing countries making significant strides in building scientific capacity remains small (Brazil, Argentina, Mexico, Chile, South Africa, India, China and Malaysia). There are examples of increasing South–South cooperation that are helping to close this gap. However, even developing countries that have successfully strengthened their scientific capacity have proven more adept at building their knowledge base than applying the know-how, scientists/physicians acquire to address societal concerns. Along these lines, ISN through its Global Outreach programmes, especially the Research and Prevention programme, has developed several initiatives for emerging countries that can be implemented according to the peculiar needs and organization facilities of the given nation [79]. Overall, the emphasis is on models to promote and foster autonomous programmes in regions where they are most needed.

The hope is that all these efforts will assist to make a major advance in addressing the neglected aspect of the renal health of people worldwide.

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References

1. *Preventing Chronic Diseases: A Vital Investment*. Geneva: World Health Organization, 2005.
2. Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: systematic review. *BMC Public Health* 2008; 8: 117.
3. El Nahas M. The global challenge of chronic kidney disease. *Kidney Int* 2005; 68: 2918–2929.
4. *Global Status Report on Noncommunicable Diseases 2010*. Geneva: World Health Organization, 2011.
5. Murray C, Lopez A. *The Global Burden of Disease*. Boston, MA: Harvard School of Public Health, 1996.
6. Wild S, Roglic G, Green A *et al*. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004; 27: 1047–1053.
7. *Noncommunicable Diseases Country Profiles*. Geneva: World Health Organization, 2011.
8. Bumgarner R. China: non-communicable disease issues and options revisited. *Soc Prev Med* 2004; 38: 202–210.
9. Jha P, Chaloupka F. *Curbing the Epidemic: Governments and the Economics of Tobacco Control*. Washington, DC: International Bank for Reconstruction and Development/World Bank, 1999.
10. Popkin BM, Doak CM. The obesity epidemic is a worldwide phenomenon. *Nutr Rev* 1998; 56: 106–114.
11. Narayan KM, Ali MK, Koplan JP. Global noncommunicable diseases—where worlds meet. *N Engl J Med* 2010; 363: 1196–1198.
12. Daar AS, Singer PA, Persad DL *et al*. Grand challenges in chronic non-communicable diseases. *Nature* 2007; 450: 494–496.
13. Yach D, Hawkes C, Gould CL *et al*. The global burden of chronic diseases: overcoming impediments to prevention and control. *J Am Med Assoc* 2004; 291: 2616–2622.
14. Couser WG, Remuzzi G, Mendis S *et al*. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. *Kidney Int* 2011; 80: 1258–1270.
15. Fogarty International Center. *Global Burden of Disease for the Year 2001. By World Bank Region for Use in Disease Control. Priorities in Developing Countries*, 2nd edn, 2004. http://www.pic.nih.gov/dcpp/gbd.html.
16. Barsoum RS. Overview: end-stage renal disease in the developing world. *Artif Organs* 2002; 26: 737–746.
17. Zatz R, Romao JE, Jr, Noronha IL. Nephrology in Latin America, with special emphasis on Brazil. *Kidney Int Suppl* 2003; 63: S131–S134.
18. Naicker S. End-stage renal disease in sub-Saharan and South Africa. *Kidney Int Suppl* 2003; 63: S119–S122.
19. Li L. End-stage renal disease in China. *Kidney Int* 1996; 49: 287–301.
20. Remuzzi G, Weening JJ. Albuminuria as early test for vascular disease. *Lancet* 2005; 365: 556–557.
21. Xue JL, Ma JZ, Louis TA *et al*. Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. *J Am Soc Nephrol* 2001; 12: 2753–2758.
22. Canadian Institute for Health Information. Dialysis and renal transplantation, Canadian Organ Replacement Register, Canadian Institute for Health Information, Report V. Ottawa, Ontario, 2001.
23. Usami T, Koyama K, Takeuchi O *et al*. Regional variations in the incidence of end-stage renal failure in Japan. *J Am Med Assoc* 2000; 284: 2622–2624.
24. Disney AP. Some trends in chronic renal replacement therapy in Australia and New Zealand, 1997. *Nephrol Dial Transplant* 1998; 13: 854–859.
25. Kher V. End-stage renal disease in developing countries. *Kidney Int* 2002; 62: 350–362.
26. Levey AS, Stevens LA, Schmid CH *et al*., for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150: 604–612.
27. Hillege HL, Fidler V, Diercks GF *et al*. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation* 2002; 106: 1777–1782.
28. Codreanu I, Tanase A, Sali V *et al*. Preliminary results of a program for detection and management of chronic kidney disease, hypertension, diabetes and cardiovascular disease in the Republic of Moldova. World Congress of Nephrology, Rio de Janeiro, Brazil, 21–25 April 2007, 419.
29. Sharma S, Karki P, Bartal N *et al*. A community screening for chronic kidney disease, hypertension, diabetes and their management in Dharan, Nepal. World Congress of Neprology, Rio de Janeiro, Brazil, 21–25 April 2007, 415.
30. Sharma SK, Zou H, Togtokh A *et al*. Burden of CKD, proteinuria, and cardiovascular risk among Chinese, Mongolian, and Nepalese participants in the International Society of Nephrology screening programs. *Am J Kidney Dis* 2010; 56: 915–927.

31. Zhang L, Wang F, Wang L *et al*. Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet* 2012; 379: 815–22.
32. Mani MK. Experience with a program for prevention of chronic renal failure in India. *Kidney Int Suppl* 2005; 67: S75–S78.
33. Dash SC, Agarwal SK. Incidence of chronic kidney disease in India. *Nephrol Dial Transplant* 2006; 21: 232–233.
34. Martins D, Tareen N, Zadshir A *et al*. The association of poverty with the prevalence of albuminuria: data from the Third National Health and Nutrition Examination Survey (NHANES III). *Am J Kidney Dis* 2006; 47: 965–971.
35. Fored CM, Ejerblad E, Fryzek JP *et al*. Socio-economic status and chronic renal failure: a population-based case–control study in Sweden. *Nephrol Dial Transplant* 2003; 18: 82–88.
36. Bello AK, Peters J, Rigby J *et al*. Socioeconomic status and chronic kidney disease at presentation to a renal service in the United Kingdom. *Clin J Am Soc Nephrol* 2008; 3: 1316–1323.
37. Collins AJ, Foley RN, Herzog C *et al*. United States Renal Data System 2008 Annual Data Report. *Am J Kidney Dis* 2009; 53: S1–S374.
38. Vassalotti JA, Li S, McCullough PA *et al*. Kidney early evaluation program: a community-based screening approach to address disparities in chronic kidney disease. *Semin Nephrol* 2010; 30: 66–73.
39. Reyes L, Manalich R. Long-term consequences of low birth weight. *Kidney Int Suppl* 2005; 68: S107–S111.
40. Eastwood JB, Corbishley CM, Grange JM. Tuberculosis and the kidney. *J Am Soc Nephrol* 2001; 12: 1307–1314.
41. Bhamarapravati N, Boonpucknavig S, Boonpucknavig V *et al*. Glomerular changes in acute plasmodium falciparum infection. An immunopathologic study. *Arch Pathol* 1973; 96: 289–293.
42. Barsoum RS. Schistosomiasis and the kidney. *Semin Nephrol* 2003; 23: 34–41.
43. Dutra M, Martinelli R, de Carvalho EM *et al*. Renal involvement in visceral leishmaniasis. *Am J Kidney Dis* 1985; 6: 22–27.
44. Rao TK, Filippone EJ, Nicastri AD *et al*. Associated focal and segmental glomerulosclerosis in the acquired immunodeficiency syndrome. *N Engl J Med* 1984; 310: 669–673.
45. Caballero B. A nutrition paradox—underweight and obesity in developing countries. *N Engl J Med* 2005; 352: 1514–1516.
46. Lafrance JP, Djurdjev O, Levin A. Incidence and outcomes of acute kidney injury in a referred chronic kidney disease cohort. *Nephrol Dial Transplant* 2010; 25: 2203–2209.
47. Levin A, Stevens PE. Early detection of CKD: the benefits, limitations and effects on prognosis. *Nat Rev Nephrol* 2011; 7: 446–457.
48. Collins AJ, Li S, Gilbertson DT *et al*. Chronic kidney disease and cardiovascular disease in the Medicare population. *Kidney Int Suppl* 2003; 64: S24–S31.
49. Matsushita K, van der Velde M, Astor BC *et al*. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010; 375: 2073–2081.
50. Tonelli M, Wiebe N, Culleton B *et al*. Chronic kidney disease and mortality risk: a systematic review. *J Am Soc Nephrol* 2006; 17: 2034–2047.
51. McCullough PA, Jurkovitz CT, Pergola PE *et al*. Independent components of chronic kidney disease as a cardiovascular risk state: results from the Kidney Early Evaluation Program (KEEP). *Arch Intern Med* 2007; 167: 1122–1129.
52. McCullough PA, Li S, Jurkovitz CT *et al*. CKD and cardiovascular disease in screened high-risk volunteer and general populations: the Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) 1999–2004. *Am J Kidney Dis* 2008; 51: S38–S45.
53. McCullough PA, Li S, Jurkovitz CT *et al*. Chronic kidney disease, prevalence of premature cardiovascular disease, and relationship to short-term mortality. *Am Heart J* 2008; 156: 277–283.
54. Mehrotra R, Kermah D, Fried L *et al*. Racial differences in mortality among those with CKD. *J Am Soc Nephrol* 2008; 19: 1403–1410.
55. Barbour SJ, Er L, Djurdjev O *et al*. Differences in progression of CKD and mortality amongst Caucasian, Oriental Asian and South Asian CKD patients. *Nephrol Dial Transplant* 2010; 25: 3663–3672.
56. Go AS, Chertow GM, Fan D *et al*. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; 351: 1296–1305.
57. Fox CS, Muntner P, Chen AY *et al*. Use of evidence-based therapies in short-term outcomes of ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction in patients with chronic kidney disease: a report from the National Cardiovascular Data Acute Coronary Treatment and Intervention Outcomes Network registry. *Circulation* 2010; 121: 357–365.
58. Kaysen GA. The microinflammatory state in uremia: causes and potential consequences. *J Am Soc Nephrol* 2001; 12: 1549–1557.
59. von Eckardstein A. Is there a need for novel cardiovascular risk factors? *Nephrol Dial Transplant* 2004; 19: 761–765.
60. de Jong PE, Hillege HL, Pinto-Sietsma SJ *et al*. Screening for microalbuminuria in the general population: a tool to detect subjects at risk for progressive renal failure in an early phase? *Nephrol Dial Transplant* 2003; 18: 10–13.
61. Hemmelgarn BR, Manns BJ, Lloyd A *et al*. Relation between kidney function, proteinuria, and adverse outcomes. *J Am Med Assoc* 2010; 303: 423–429.
62. Bello AK, Hemmelgarn B, Lloyd A *et al*. Associations among estimated glomerular filtration rate, proteinuria, and adverse cardiovascular outcomes. *Clin J Am Soc Nephrol* 2011; 6: 1418–1426.
63. van der Velde M, Matsushita K, Coresh J *et al*. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. *Kidney Int* 2011; 79: 1341–1352.
64. Levey AS, Atkins R, Coresh J *et al*. Chronic kidney disease as a global public health problem: approaches and initiatives—a position statement from Kidney Disease Improving Global Outcomes. *Kidney Int* 2007; 72: 247–259.
65. Barsoum RS. Chronic kidney disease in the developing world. *N Engl J Med* 2006; 354: 997–999.
66. Wen CP, Cheng TY, Tsai MK *et al*. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. *Lancet* 2008; 371: 2173–2182.
67. Remuzzi G, Ruggenenti P, Perico N. Chronic renal diseases: renoprotective benefits of renin-angiotensin system inhibition. *Ann Intern Med* 2002; 136: 604–615.
68. Ruggenenti P, Schieppati A, Remuzzi G. Progression, remission, regression of chronic renal diseases. *Lancet* 2001; 357: 1601–1608.
69. Ruggenenti P, Perticucci E, Cravedi P *et al*. Role of remission clinics in the longitudinal treatment of CKD. *J Am Soc Nephrol* 2008; 19: 1213–1224.
70. Obrador GT, Garcia-Garcia G, Villa AR *et al*. Prevalence of chronic kidney disease in the Kidney Early Evaluation Program (KEEP) Mexico and comparison with KEEP US. *Kidney Int Suppl* 2010; 77: S2–S8.
71. Atkins RC, Zimmet P. World Kidney Day 2010: diabetic kidney disease—act now or pay later. *Am J Kidney Dis* 2010; 55: 205–208.
72. The International Society of Nephrology. A briefing on the global impact of kidney disease [online], 2011. http://cdn.theisn.org/images/stories/WHO_CKD_Brochure_LR.pdf.
73. The UN General Assembly. Political declaration of the high-level meeting of the General Assembly on the prevention and control of non-communicable diseases [online], 2011. http://www.un.org/ga/search/view_doc.asp?symbol=A/66/L.1.
74. Feehally J. Health burden of kidney disease recognized by UN. *Nat Rev Nephrol* 2012; 8: 12–13.
75. Time for action in New York on non-communicable diseases. *Lancet* 2011; 378: 961.
76. UN meeting for non-communicable diseases. *Br Med J* 2011; 343: 545–546.
77. Reardon S, U.N. Summit on Noncommunicable Diseases. Meeting brings attention but little action on chronic diseases. *Science* 2011; 333: 1561.

78. Taylor AL, Hwenda L, Larsen BI *et al*. Stemming the brain drain—a WHO global code of practice on international recruitment of health personnel. *N Engl J Med* 2011; 365: 2348–2351.
79. ISN Global Outreach program at http://www.theisn.org/.
80. US Renal Data System. USRDS 2011 Annual Data Report. The National Institutes of Health, National Institute of Diabetes, and Digestive and Kidney Diseases, Bethesda, MS, 2011. www.usrds.org.
81. National Heath and Nutrition Examination Survey (NHANES). http://www.cdc.gov/nchs/nhanes.htm.
82. The ESRD Network Coordinating Center. http:www.esrdncc.org.
83. The Global Burden of Diseases, Injuries, and Risk Factor Study (the GBD 2010 Study). http://www.globalburden.org.
84. National Kidney Foundation. Kidney Early Evaluation Program (KEEP). http://www.kidney.org.

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