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Nephrology Dialysis Transplantation

newsletter



INTERNATIONAL ADVISOR
G. Becker

Dear Colleagues,

Australia is extremely fortunate in having a high per person income and well developed programmes for universal healthcare and support for medical research, though clearly both could be improved. Balanced against this is a reasonably small population unevenly spread across an enormous continent with areas of extreme distance between patients and medical facilities, a very diverse ethnic mix including an indigenous population with high levels of renal disease yet socio-economic disadvantage, and global isolation with great distance between Australia and the leading renal centres elsewhere in the world. We feel, however, that Australia has made real contributions to global renal care and research over many decades, and continues to offer solutions potentially helpful to other countries. In these articles we hope to briefly cover some of our problems and attempts at solutions.

In the first of this 2 part series, David Harris outlines the health services and outcomes for patients with renal disease in Australia, while Wendy Hoy discusses the very troublesome issues faced by our indigenous Australian population who experience a very high disease burden and often great geographic and socio-economic pressures.

We hope these articles will encourage others to see where they can collaborate with Australia on areas of mutual concern.

EDITOR IN CHIEF
C. Zoccali, Italy



David Harris - Health Services & Outcomes



Australia and New Zealand have developed a number of valuable resources for monitoring and recommending management approaches for patients with renal disease (Table). They are fortunate in having maintained a comprehensive database of all patients commencing renal replacement therapy (RRT), the Australian and New Zealand Dialysis and Transplant Registry (ANZDATA Registry), since 1965. This has provided an invaluable resource for healthcare surveillance, clinical care planning, research into renal diseases and descriptions of outcomes of RRT. There is also a registry of living renal transplant donors (ANZOD). Both registries can be accessed via <http://www.anzdata.org.au>. Australian and New Zealand Society of Nephrology (ANZSN, <http://www.nephrology.edu.au>) and Kidney Health Australia (KHA, <http://www.kidney.org.au>, previously the Australian Kidney Foundation) combined in 1999 to set up an on-going evidence based clinical practice guideline (CPG) project titled Caring for Australasians with Renal Impairment (CARI, <http://www.cari.org.au>). Since then a large number of CPGs have been produced which can be accessed through the web-site <http://www.cari.org.au> or through the Kidney Diseases Improving Global Outcomes website <http://www.kdigo.org> where they can be compared with CPGs from other sources. A valuable resource for such CPGs is the Cochrane Renal Group which is based in Sydney, Australia and is accessible through <http://www.cochrane-renal.org>.

KHA has developed a number of other valuable initiatives and resources, such as the health professional education program Kidney Check Australia Taskforce (KCAT) which can be accessed via the KHA website. In addition, ANZSN and KHA jointly sponsor a biannual Dialysis, Nephrology and Transplantation workshop which examines important contemporary issues of nephrology practice, including the CARI CPGs.

Access to Health Care
Australia has a taxpayer-funded medical provision system (Australian Medicare) which provides healthcare to all Australians at minimal or no direct cost to the patient, as well as an active private health system underpinned by

private health insurance. However there are many areas of Australia that are sparsely populated, where strategies to deal with geographic distance (home and satellite dialysis) and to minimise cost both to Australia and the patient are an ongoing reality of nephrology practice. It is doubtful that all Australians who should have renal care are recognised and treated, a concern underscored in areas with socio-economic disadvantage by a higher incidence of RRT, yet more frequent late referral to nephrologist, suggesting less access to pre- end-stage kidney disease (ESKD) care.(1,2) New Zealand has a taxpayer funded public health system. New Zealand citizens and permanent residents are provided with free health care, including free access to all modalities of RRT.

There is a comprehensive private primary health care system substantially but not fully funded by the District Health Boards which administer most of the activity and 75% of the budget of NZ's Health System. It coordinates the management of patient care and is the first medical contact for all patients.

Renal Replacement Therapy
At the end of 2010 there were 18,971 Australians (849 patients per million population; ppm) receiving RRT; 375 ppm with a functioning renal transplant and 474 ppm on dialysis.(3) The incidence rate of Australians commencing RRT in 2010 was 101 persons ppm, lower than in most other predominantly European nations, a discrepancy possibly explained by prevalence and treatment of causes of progressive CKD and acceptance criteria for RRT. In New Zealand the prevalence of RRT was 3,820 (874 ppm) and the incidence 115 ppm.

In 2010 the median age of new patients was 62.9 years in Australia and 60.3 in NZ. In 2007-2010 the aetiology of ESKD in new RRT patients in Australia was diabetes in 35%, glomerulonephritis in 22% and hypertension in 14%; in NZ the proportions were 51%, 22% and 12% respectively. The proportion of patients receiving home HD, satellite HD and CAPD/APD were 28%, 50% and 19% in Australia, contrasting sharply with 53%, 17% and 35% in NZ. In Australia 8,382 (375 ppm) had a functioning transplant, and in NZ 1,442 (330 ppm), 22% of RRT patients in Australia and 16% in NZ were referred within 3 months of commencing RRT.

The annual mortality rate of RRT patients in 2010 was similar in Australia & NZ, at ~13.5% in dialysis patients (due mainly to cardiovascular disease and withdrawal) and ~1.2% in transplant patients (mainly cancer and infection). Transplant donors in 2010 were living in 35% in Australia and 55% in NZ. Amongst deceased donors, one fifth were non-heart beating in Australia, compared with none in NZ. Only 7% of dialysis patients received a transplant in Australia, and only 4% in NZ. One year patient and graft survival were 98% and 95-6% respectively in both countries, with five year survival about 90% and 80% respectively.

Government policy in Australia strongly encourages renal transplantation over dialysis and home dialysis over hospital dialysis because of the substantial cost savings of both (4).

Chronic Kidney Disease
The prevalence of CKD in Australia was estimated in the AusDiab Kidney Study.(5) Over 11,000 non-institutionalised Australian adults aged ≥ 25 years were interviewed in 1999-2000 and tested for proteinuria (spot urine to creatinine ratio $>0.20\text{mg/mg}$), hematuria (dipstick confirmed by microscopy) and reduced estimated creatinine clearance adjusted for body size ($<60\text{mL/min/1.73m}^2$ by Cockcroft Gault). Approximately 16% had at least one such indicator of damage, with a reduced estimated creatinine clearance in 9.7%.

Concluding**Remarks**

In summary, the small population and high GDP per capita in Australia and New Zealand has allowed development of integrated systems to provide publicly funded RRT for their citizens, as well as such resources as the ANZDATA Registry to provide data for benchmarking. An unexplained issue is the low rate of RRT when compared with USA and Canada. The low population density has encouraged a high proportion of home based therapies - both transplantation and dialysis. Unfortunately with transplantation has come a very high incidence of skin cancer.

David Harris

Valuable Australia and New Zealand websites relevant to kidney disease

Australasian Kidney Trials (AKT) Network	http://www.uq.edu.au/aktn/
Australia & New Zealand Society of Nephrology	http://www.nephrology.edu.au
Australian & NZ Dialysis & Transplant Registry (ANZDATA)	http://www.anzdata.org.au
Caring for Australasians with Renal Impairment (CARI)	http://www.cari.org.au
Cochrane Renal Group	http://www.cochrane-renal.org
Kidney Health Australia (KHA) CKD Management in General Practice booklet Kidney Check Australia Taskforce	http://www.kidney.org.au
Transplantation Society of ANZ	http://www.tsanz.com.au

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Kidney Disease in Indigenous Australians: a perspective from the Northern Territory

Wendy

Hoy

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Indigenous people have lived on the Australian continent for 40,000 to 60,000 years but were only recognised as Australian citizens and included in the census in 1967 (1). Indigenous assignment is by self-report, and with more people choosing that assignment, they now constitute about 550,000 of Australia's broader population of 23 million. The majority are mainland Aboriginal people, while about 19,000 are Torres Strait Islanders. Mainland Aboriginal people are a very heterogeneous group, which is central to informed assessment of their needs. Today only about 25% live in remote or very remote areas, most in the Northern Territory (NT), Western Australia and northern and western Queensland. For Aboriginal people, remoteness of residence is linked to pervasive disadvantage- poverty, poor nutrition and food insecurity, poor housing and infrastructure, unemployment, poor education, lack of a political voice, and impaired access to services of all kinds, while poor health is reflected in every statistic, including birth weight, hospitalisations and mortality. Kidney disease came into sharp focus in the NT in the 1980s as more Aboriginal people presented with renal failure. The NT has an area of 1.35 million square km, or 521,000 square miles, and a small population, even today, of only 233,000 people. Of these, 60-65,000 are Aboriginal, and most live remotely. With a national policy of universal access to renal replacement therapy (RRT), funded by government, and "as close to home as possible", provision of services to large numbers of remote-living Aboriginal people quickly posed financial and logistic problems. Incidence rates increased relentlessly, and in the mid-1990s were estimated to be 15-30-times that of non-Indigenous Australians (2). From 2007 to 2011 there were annual averages of about 60 incident and 450 prevalent Aboriginal RRT patients in the NT (3), with age-adjusted incidence and prevalence rate relative to the general Australian population of 1,600 and 10,400 pm respectively (3). Development of renal services in the NT was led by Drs David Pugsley and Diane Howard in the Top End and Dr Meshach Kirubakaran in Central Australia, with investigations including hundreds of biopsies. Other clinical services had already gathered traction over the previous two decades, reducing preventable infections and malnutrition and increasing survival across the life course, thus ushering in the era of chronic disease. Lower birth weight infants, previously at high risk for death, were increasingly surviving to adult life, to express the accentuated susceptibility to chronic disease predicted by the Barker hypothesis (4,5,6), while delay of death in adults continues to expand number of subjects susceptible to chronic disease on the basis of ageing.

Professor John Mathews, Founding Director of the Menzies School of Health Research in Darwin, Drs Pugsley, David McCredie and Paul van Buynder began to study renal disease in the NT in 1988, joined by the author in 1992. An early task was description of the rise of "RRT" in the NT and documentation of its great cost (2,7,8). Surveys of early and pre-terminal kidney disease were also performed in several communities. The application of quantitative tests for proteinuria or albuminuria (now commonly the albumin/creatinine ratio, or ACR) and creatinine-based eGFR estimates in those surveys, has transformed the understanding of renal disease and chronic disease more generally.

The most comprehensive community-based study, now in its 24th year, is based on the Tiwi Islands. In the late 1980s, Tiwi islanders had the highest described rates of renal failure in the world, and an age-adjusted mortality rate six times that of residents of Australia's national capital. That study shows that ACR is the central renal disease marker, while significant loss of GFR reflects very advanced disease (9). ACR increases relentlessly with age, and beyond childhood, people usually follow a consistent trajectory of relative ranking of ACR with

age. Factors significantly correlated with ACR levels include adult body size, blood pressure levels, degrees of glycemia, dyslipidemia, current skin infections, remote episodes of poststreptococcal glomerulonephritis (PSGN), evidence of HPylori infection, lower birth weights, grand multiparity, and a family history of renal disease (9,10,11). These "risk factors" are all expressed through amplification of ACR in relation to adult BMI levels. The multiplicative effect of lower birth weight and PSGN history on ACR levels in young adults is especially powerful (11). Such "multideterminant" models are compatible with the multihit hypothesis of renal disease causation proposed by Brenner and colleagues (12). Albuminuria is closely linked to hypertension, diabetes and cardiovascular disease. Critically, it predicts not only all renal failure, but also most non-renal natural death (13, 14), which underpins the early observation of Dr Hedley Peach that regional renal failure rates in Aboriginal Australia reflect the "overall force of mortality" (15). Glycemia, diabetes and ACR levels are all predicted by the D allele of the angiotensin converting enzyme (ACE), but with only a 9% gene frequency, that allele accounts for only a fraction of the community burden of disease (16). Diseased Tiwi renal biopsies were remarkable only for a high frequency of glomerulomegaly and focal glomerulosclerosis (17,18). Treatment of Tiwi people with albuminuria and/or hypertension with ACE inhibitors produced striking reductions in renal failure and in non-renal deaths (18), and cost-effectiveness through dialysis avoided or delayed was demonstrated (8). Flow on effects beyond this Tiwi study have included health profiling and chronic disease capacity building programs in many Indigenous health services, input into screening and treatment protocols, and adaptations into chronic disease programs in other countries (19,20,21,22,23,24). National awareness has been heightened of the importance of early determinants of chronic disease, and association of birth weight with chronic disease confirmed in non-Indigenous people through the AUSDIAB study (25,26). Finally, the finding of glomerulomegaly in this environment, where birth weights have traditionally been low (27,28), precipitated a multiracial international autopsy of renal ultrastructure, which showed lower nephron number and larger glomerular volume in kidneys of remote-living Aboriginal Australians (29), as well as, more broadly, a direct correlation of birth weight with nephron number, and, inversely, glomerular volume (30). Some perspectives from the Tiwi study were not immediately accepted. Positioning renal disease as part of a chronic disease syndrome challenged specialty-specific paradigms. Some practitioners were reluctant to use standard renal protective medicines while the precise "causes" of kidney disease were still obscure. Some wanted Aboriginal-specific controlled clinical trials to prove efficacy of already accepted standard treatments. The propriety of offering medicine to patients living in substandard environments, and whose health behaviours and "compliance" fell short of clinicians' expectations, was challenged. Some argued, more broadly, that medical remedies to slow kidney disease progression should not be applied at all until social determinants of ill health had been remedied. There was also concern that programs for early detection would expose reservoirs of disease whose management would exceed primary health care budgets, although such interventions were ultimately vindicated by demonstration of the cost-effectiveness (8). One important question is the relevance of these findings to other Indigenous groups and locations. While the unifying label of "Indigenous Australians" has important uses for purposes of reconciliation, restitution, human rights and land rights, it is less useful in relation to some health issues. Any average statistic does little to focus strategies by region and need, when there is such vast variation in health status and access to services by region and remoteness (31,32). A major breakthrough in the renal domain was the demonstration by Cass et al of the massive gradient in Indigenous RRT rates across Australia by region and remoteness (33), confirmed years later by the Australian Institute of Health and Welfare (34), and persisting today (Figure 1). They described variation in age-standardised incidence of RRT in relation to non-Indigenous rates from 1.5 or less in Aboriginal people in major cities, to >30-fold increase in remote central and northern Australia. Cass et al also described an inverse association of RRT incidence in Aboriginal people with socioeconomic status (35), which was later demonstrated for non-Indigenous Australians as well (36). Regional profiles of renal disease and renal biopsies from a nationwide

review of 694 Indigenous biopsies confirm such variation (37). Communities in remote/very remote areas have the highest rates of albuminuria, which, as with RRT, is more common in females. Females also predominate among the great absolute and relative excess of biopsies from those remote regions (37). Fewer than half the biopsied subjects were diabetic, and even fewer had diabetic change. All common renal morphologic entities were represented in excess among those biopsies (Figure 2), but glomerulomegaly with some mesangial proliferation and glomerulosclerosis were prominent features. Those findings are compatible with nephropathy due to nephron deficiency, as we had earlier inferred from the Tiwi data (38). We suggest that such nephron deficiency, to which lower birth weights probably contribute, underlies the accentuated susceptibility of these remote populations to renal disease of all common types. In contrast, Aborigines living close to population centres have much lower rates of renal failure, which, as in other Australians, is male dominated. They had many fewer biopsies, were more often diabetic, did not have striking glomerulomegaly, and had more vascular change. In short, the high proportion of diabetics aside, their renal profile is more like that of non-Indigenous Australians. Most national focus on kidney disease still revolves around RRT. The absolute excess of incident and prevalent patients, their more youthful age, late referral, higher mortality, lower transplant rates and worse outcomes with all forms of treatment are well described (2, 39). Survival is influenced not only by limitations to optimal application of RRT, and timeliness of referral, but by multiple comorbidities and poor general health status. Problems limit widespread application of home peritoneal dialysis; it is currently not in high favour in central Australia, yet is the mandated first-line form of treatment in the vast regions of western Queensland. The first community-based hemodialysis dialysis unit in the NT was opened on the Tiwi Islands in 1999, following recommendation by consultant Dr John Mahony. Many other units have been built since, in regional centres and in remote communities nationwide, some just a single chair in a local clinic. Local funding was needed to establish some (40), variably sourced from mining companies, sale of local artwork, or bargains with governments in exchange for train track access through tribal lands. The proliferation of satellite units notwithstanding, most people from remote communities cannot access hemodialysis facilities, due to distance and poverty. Thus, many patients have to relocate to population centres. Far removed from country and family, exposed to alien therapies, multilateral communication problems, and often palpable racism (which itself has many roots) they often have a miserable existence, and sometimes decide against, or to discontinue, RRT (41,42). Creative community respite options and mobile dialysis services help alleviate the sense of social disconnection, but are additionally expensive (41,43). Governments struggle to keep up with accommodation needs, and some patients and families still need (or sometimes choose) to camp out, in the local park in Townsville for example (44), or in the dry bed of the Todd River in Alice Springs, where about 20% of the current dialysis population of more than 200 people is without stable housing (41). Squabbles occasionally erupt between adjoining states and territories about provision of RRT for people from other jurisdictions or who move among communities (45): this reflects the individual, complex and often changing health services funding agreements for each jurisdiction held with federal government, (which would be eliminated if federal government directly underwrote all RRT support). It also shows that boundaries of current jurisdictions have little relevance to the sense of identity of Aboriginal people and their concepts of homelands. The 2010 Central Australia Renal Study (41) describes many of these issues, which, with minor variations, apply more generally across remote Australia. It also proposes strategies to contain progressive disease and optimise survival and quality of life for those already on RRT. There are, of course, good news stories on RRT. These includes elimination of the Aboriginal-non-Indigenous gap in late referral for RRT in Central Australia (41), achievement in the Kimberly in Western Australia of equally good outcomes for Indigenous as non-Indigenous dialysis RRT patients (46), as well as development of renal services competency among Aboriginal people themselves and strong sense of ownership of their facilities and services. Regional and national data both suggest that Indigenous RRT incidence rates, after relentless increases

up through the year 2000, might be stabilising (46,2). However, under all modelling scenarios, numbers of prevalent patients will increase (41); they will be further exacerbated as survival on dialysis continues to improve, and as overall Aboriginal life expectancy increases further. With limited health care budgets, it is doubtful that the burden of RRT will be supportable by 2020, as is projected for Australia generally (48), so that new approaches will be needed.

The real potential for containment of RRT lies in prevention and mitigation of CKD. Primary prevention is a lofty long-term goal, involving many programs and partners, but secondary prevention for people with evident disease is feasible and effective. Chronic disease management protocols are now embedded in primary care, where they constitute the bulk of adult Aboriginal health service delivery. Specific Medicare service items, robustly reimbursed, include the Well Person's Check for all adults (15+ yr), which can be repeated annually and incorporates integrated screening for all common diseases (49), and management streams for people with identified problems. This model supports levels of service delivery driven by the specific burden of disease in individual communities and services. For a decade now, medicines have been supplied to remote areas free of cost through the PBS S100 scheme (50), and subsidised through the QUMAX program in rural and urban settings (51), and chronic disease medicines (insulin, other hypoglycemics, RAS blockers, other antihypertensive agents and statins are now the leading medicines issued under the S100 system (52). Electronic systems have increasingly been adopted for clinical care, and there is increasing requirement for performance indicators and accountability. Many community controlled health services, now numbering about 150 nationwide, set an enviable standard of client-friendly, holistic and professional services, while their regional and national collectives drive important policy developments (53). There is a burgeoning literature on chronic disease in Aboriginal health, with a dedicated information clearing house, text books and treatment manuals (54). More Indigenous people are training in health care, and the Centres for Rural and Remote Health are further developing capacity in Indigenous health service delivery. Several major research institutions now embrace Indigenous health, and strong programs have developed around the health of indigenous people in urban and periurban settings. A multisite trial of polypill prevention of cardiovascular outcomes in high risk Indigenous people is being conducted by the Kanyini Vascular Alliance (55), and a trial of pharmacologic prevention of new onset disease in Tiwi people is under analysis. Many components of the chronic disease health care model could be adopted with benefit in mainstream Australian health services. Furthermore these concepts are applicable to "developing" countries, where good outcomes could be achieved at a fraction of the costs of the Australian model, through use of community workers, mobile vans, less frequent and more targeted screening, cheaper reagents, simplified testing algorithms and generic medicines (24).

More recently, Aboriginal chronic disease mortality, including renal deaths, have been falling, most prominently in remote areas (56). Rates of natural death are also falling in the Tiwi community (57), and, over 10-14 years interval, children are taller, HDL levels have risen, and rates of albuminuria and e_GFR <60 ml/min/m² are lower (58). Furthermore, Aboriginal populations are growing, along with proportions of people reaching 60 years and beyond. While these trends cannot be attributed solely to advances in chronic disease care, yet they are welcome developments.

References: click [here](#).

Figures and pictures

Figure 1. Incident indigenous patients 2006-2011 by postcode (3)

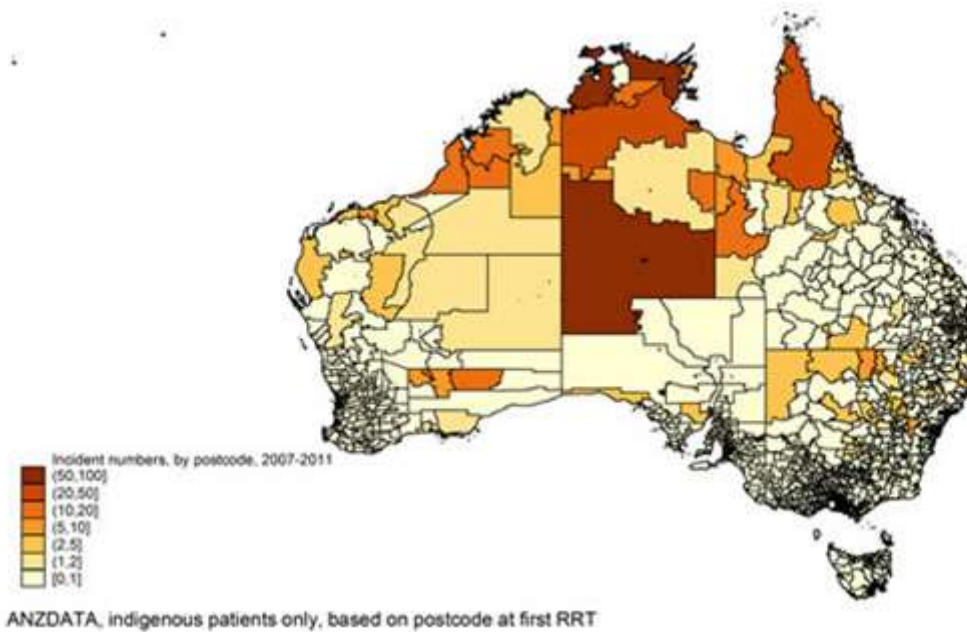


Figure 1: ANZDATA: Australia and New Zealand Dialysis and Transplant Registry, RRT: Renal replacement therapy
The data reported here have been supplied by the Australia and New Zealand Dialysis and Transplant Registry.
The interpretation and reporting of these data are the responsibility of the Editors and in no way should be seen as an official policy or interpretation of the Australia and New Zealand Dialysis and Transplant Registry.

Figure 2. Australian indigenous biopsy series' population-based frequency of morphologic findings, per million persons, by group and remoteness (37)

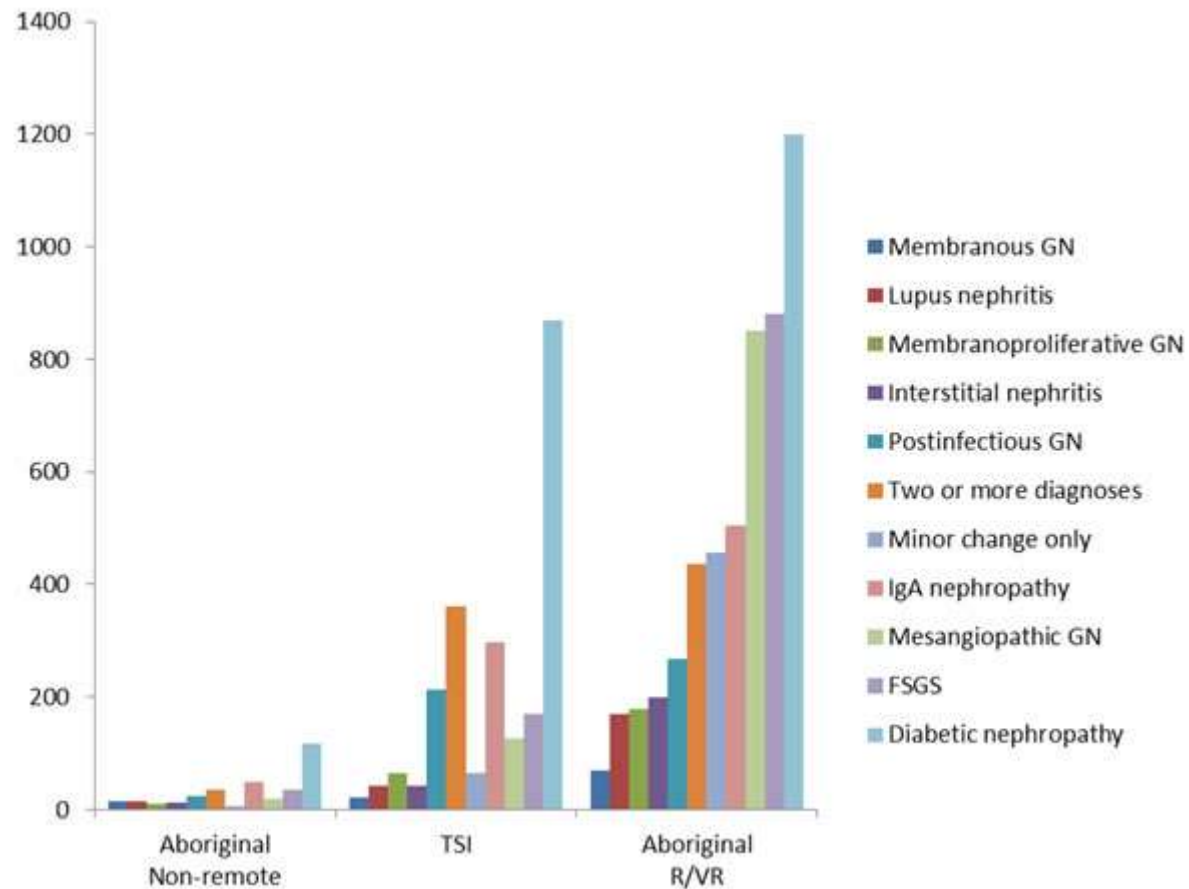


Figure 2: FSGS: focal segmental glomerulosclerosis; GN: glomerulonephritis; R/VR: remote or very remote living; TSI: Torres Strait Islander. Source of denominator, Australian Bureau of Statistics. 2006 Census of Population and Housing. Commonwealth of Australia 2007. CData online. <http://www.abs.gov.au/CDataOnline> (accessed 4 April 2012).

Some of the team a-d



Tiwi Islands e-g



Central Australia h-j



Some of the team

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3. John Mathews Source: Menzies Foundation. Photograph of Prof J Mathews. 2013. Accessed: 19 Aug 2013, <http://www.menziesfoundation.org.au/about/directors.html>
4. Wendy Hoy Source: The University of Queensland, Brisbane, Queensland

Tiwi Islands

1. Tiwi Islands, aerial photograph Source: Tiwi Land Council, Tiwi Islands, Northern Territory.
2. Aloysius Puantulura Source: Tiwi Land Council, Tiwi Islands, Northern Territory.
3. Former and present Tiwi Land Council members; Jimmy Tipungwuti; Cyril Rioli; Walter Kerinauia; Matthew Woneamirri Source: Tiwi Land Council, Tiwi Islands, Northern Territory

Central Australia

1. Central Australia, aerial photograph Source: Cepolina. Alice Springs Australia. Cepolina 2012. Accessed: 19 Aug 2013, <http://www.cepolina.com/s/Alice-Springs.htm>
2. The Purple Truck dialysis unit, Western Desert Source: Brown S. The Purple Truck dialysis unit. Western Desert Nganampa Walytja Palyantjaku Tjutaku Aboriginal Corporation (WDNGWPT), Northern Territory.
3. Maurice Gibson, Kintore dialysis unit Source: Brown S., Western Desert Nganampa Walytja Palyantjaku Tjutaku Aboriginal Corporation (WDNGWPT), Northern Territory.