

Kidney disease in Aboriginal Australians: a perspective from the Northern Territory

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Abstract

This article outlines the increasing awareness, service development and research in renal disease in Aboriginal people in Australia's Northern Territory, among whom the rates of renal replacement therapy (RRT) are among the highest in the world. Kidney failure and RRT dominate the intellectual landscape and consume the most professional energy, but the underlying kidney disease has recently swung into view, with increasing awareness of its connection to other chronic diseases and to health profiles and trajectories more broadly. Albuminuria is the marker of the underlying kidney disease and the best treatment target, and glomerulomegaly and focal glomerulosclerosis are the defining histologic features. Risk factors in its multideterminant genesis reflect nutritional and developmental disadvantage and inflammatory/infectious milieu, while the major putative genetic determinants still elude detection. A culture shift of "chronic disease prevention" has been catalyzed in part by the human pain, logistic problems and great costs associated with RRT. Nowadays chronic disease management is the central focus of indigenous primary care, with defined protocols for integrated testing and management of chronic diseases and with government reimbursed service items and free medicines for people in remote areas. Blood pressure, cardiovascular risk and chronic kidney disease (CKD) are all mitigated by good treatment, which centres on renin-angiotensin system blockade and good metabolic control. RRT incidence rates appear to be stabilizing in remote Aboriginal people, and chronic disease deaths rates are falling. However, the profound levels of disadvantage in many remote settings remain appalling, and there is still much to be done, mostly beyond the direct reach of health services.

Introduction

Indigenous people have lived on the Australian continent for 40 000–60 000 years but were only recognized as Australian citizens and included in the census in 1967 [1]. Indigenous assignment is by self-report, and with more people choosing that assignment, as well as natural population growth, the reported population is now increasing with great speed, now constituting about 517 000 of Australia's broader population of 23 million [2]. 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. Traditionally, they were hunter gatherers, with no sustained agrarian tradition. Today only about 25% live in remote or very remote areas, most in the Northern Territory (NT), Western Australia and northern and western Queensland, and in a mixture of tropical, arid and desert environments which are generally hot. 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, hospitalizations and mortality.

Kidney disease came into sharp focus in the NT in the 1980s as more Aboriginal people presented with renal failure. The propensity to kidney disease in the early and middle parts of that century is unknown. 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, about 72 000 are Aboriginal [2], and most live remotely. With a national policy of universal access to renal replacement therapy (RRT), funded by the 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 [3]. From 2007 to 2011, there were annual averages of about 60 incident and 450 prevalent Aboriginal RRT patients in the NT, with *age-adjusted incidence and prevalence rates* estimated at 1600 and 10 400 pmp, compared with the general Australian rates of about 110 and 862 pmp, respectively [4].

Box 1. Some pioneers of renal services and research.



A. David Pugsley. Source: *Adelaidenow. The Advertiser*, 26 Jan 2012. Accessed: 19 Aug 2013, <http://www.adelaidenow.com.au/news/crusader-dedicated-to-kidney-research/story-e6frea6u-1226253842799>

B. Meshach Kirubakaran. Source: Richard Di Natale, *The amazing Doctor K. BNP* 14 Dec 2000. *Barkly News Pictorial*, Tennant Creek, Northern Territory. Accessed 19 Aug 2013, <http://www.artplan.com.au/BNP/BNP14text/32.htm>

C. John Mathews. Source: Menzies Foundation. Photograph of Prof J Mathews. 2013. Accessed: 19 Aug 2013, <http://www.menziesfoundation.org.au/about/directors.html>

D. Wendy Hoy. Source: The University of Queensland, Brisbane, Queensland.

Development of services and research

Development of the renal services in the Top End of the NT was led by Dr David Pugsley (Box 1), as a consultant visiting Darwin for a few weeks every 3 months from his home base in Adelaide (more than 3000 km away), and working with Dr Diane Howard, a physician and diabetologist/endocrinologist, who still practices as an esteemed clinician and teacher in Darwin. Dr Paul Snelling was appointed the first full-time renal specialist to the Top End in the mid-1990s. Dr Pugsley also pioneered services in Central Australia with intermittent consulting visits, before the full-time appointment of Dr Meshach Kirubakaran (Box 1). Today, there are five renal specialists in the Top End NT and three in Central Australia, although not all have full-time clinical roles. And, making huge contributions to policy and practice, there are at least 63 renal dialysis nurses (2014 data), and several chronic kidney disease (CKD) nurses, nurse practitioners and Aboriginal health workers.

Professor John Mathews, Founding Director of the Menzies School of Health Research in Darwin (Box 1), Drs Pugsley, David McCredie and Paul van Buynder began to study renal disease in Aboriginal people in the NT in 1988 and conducted surveys of early and pre-terminal kidney disease in several communities. They were joined by the author in 1992.

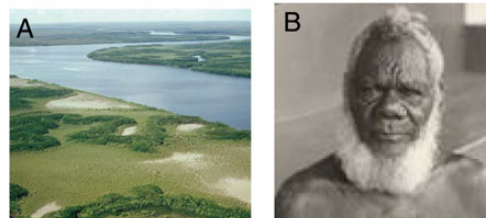
All these events were preceded and accompanied by a constantly changing background of health status, health services and circumstances of indigenous people. Other clinical services over the previous two decades were already reducing preventable infections and malnutrition and increasing survival across the life course. The very high rates of infant and childhood mortality were dropping precipitously, and survivors of low birthweight (largely related to global maternal malnutrition and disadvantage) were increasingly surviving to adult life, to express the accentuated susceptibility to chronic disease predicted by the Barker hypothesis [5–7]. Chronic non-communicable diseases were increasing, and the extending longevity of adults gave them increasing scope for expression.

Recent findings and events

One early task was the description of the rise of 'RRT' in all of the remote Aboriginal settings in NT and documentation of its great costs [3, 8, 9]. The application of quantitative tests for proteinuria (superseded by the urinary albumin/creatinine ratio, ACR), and creatinine-based estimates of glomerular filtration rate (eGFR), ushered in studies of the underlying renal disease.

The most comprehensive community-based research study, now in its 24th year, is based on the Tiwi Islands (Box 2). 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. The Tiwi study showed that ACR is the earliest renal disease marker. It increases relentlessly with age (Figure 1) and, starting at about the microalbuminuria threshold of ≥ 3.4 g/mol, is associated with progressively lower levels of eGFR [10]. 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 glycaemia, dyslipidaemia, current skin infections, remote episodes of poststreptococcal glomerulonephritis (PSGN), evidence of *Helicobacter pylori* infection, lower birth weights, grand multiparity and a family history of renal disease [10–12]. These 'risk factors' are all expressed through amplification of ACR in relation to adult body mass index levels. The multiplicative effect of lower birth weight and PSGN history on ACR levels in young adults is especially powerful [12]. Such 'multideterminant' models are compatible with the multihit hypothesis of renal disease causation proposed by Brenner and colleagues [13]. Albuminuria is closely linked to hypertension, diabetes and cardiovascular disease. Critically, it predicts not only all renal failure, but also most non-renal natural

Box 2. Tiwi Islands—images and names with explicit permission of the Tiwi Land Council.



A. Tiwi Islands, aerial photograph

B. Aloysius Puantulura

C. Former and present Tiwi Land Council members; Jimmy Tipungwuti; Cyril Rioli; Walter Kerinauia; and Matthew Woneamirri

Source: Tiwi Land Council, Tiwi Islands, Northern Territory.

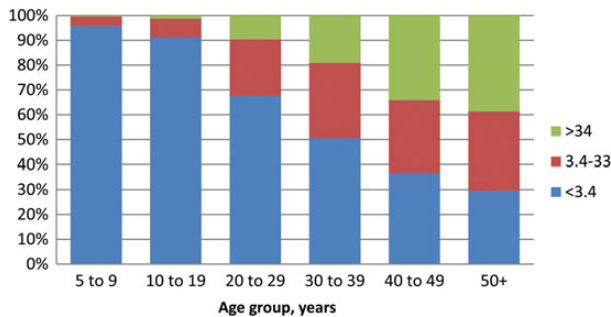


Fig. 1. ACR categories by age group in Tiwi people.

death [14, 15], which underpins the early observation of Dr Hedley Peach that regional renal failure rates in Aboriginal Australia reflected the 'overall force of mortality' [16]. Glycaemia, diabetes, ACR and diastolic blood pressure levels are all predicted by the D allele of the angiotensin-converting enzyme (ACE), but with a 9% gene frequency, that allele accounts for only a fraction of the community burden of disease [17]. There was significant heritability of ACR levels by both D allele and TP53*P72 codons, and studies in another remote indigenous community showed associations of the TP53*P72 codon with both glycaemia and ACR levels [18]. Further genetic studies are ongoing. Diseased Tiwi renal biopsies were remarkable only for a high frequency of glomerulomegaly and focal glomerulosclerosis [19–22]. Treatment of Tiwi people with albuminuria (ACR ≥ 34 g/mol) and/or hypertension ($\geq 140/\geq 90$) with ACE inhibitors over a 4-year period produced striking reductions in renal failure (by 57%), in cardiovascular deaths (49%) and in non-renal non-cardiovascular deaths (61%) [23], and cost-effectiveness was demonstrated through dialysis avoided or delayed [9].

The early studies in Tiwi were followed by health profiling and chronic disease capacity building programs in many other indigenous health services, with development of screening and treatment protocols, and adaptations into chronic disease programs in other countries [24–28]. Awareness of the importance of early determinants of chronic disease was heightened nationwide, and association of low birth weight with chronic disease was confirmed in non-indigenous people through the AUSDIAB study [29, 30]. Biopsy findings prompted a nationwide indigenous renal biopsy survey [31]. Finally, the finding of glomerulomegaly in this environment, where birth weights have traditionally been low, precipitated a multi-racial international autopsy of renal ultrastructure, which showed lower nephron number and larger glomerular volume in kidneys of remote-living Aboriginal Australians [32], as well as, more broadly, a direct correlation of birth weight with nephron number, and, inversely, glomerular volume [33].

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 thought that Aboriginal-specific controlled clinical trials were required 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 parties 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 programmes for early detection would expose reservoirs of disease whose management would exceed primary healthcare budgets, although such interventions were ultimately vindicated by demonstration of the cost-effectiveness [9].

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 helps 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 [34, 35]. 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 [36], confirmed years later by the Australian Institute of Health and Welfare [37], and persisting today (Figure 2). They described variation in age-standardized 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.* [38] also described an inverse association of RRT incidence in Aboriginal people with socioeconomic status, which was later demonstrated for non-indigenous Australians as well [39]. Moreover, while all remote communities studied to date show an excess of albuminuria, hypertension and diabetes, absolute rates differ markedly among them [26]. The previously cited nationwide indigenous biopsy review showed great regional variation [30]: remote areas had the highest biopsy rates, a female predominance and striking glomerulomegaly with glomerulosclerosis, findings compatible with nephropathy due to nephron deficiency [40], as we had earlier inferred from the Tiwi data. Fewer than half the biopsied subjects in remote areas were diabetic, and even fewer had morphologic diabetic change. In contrast, Aborigines living close to population centres had many fewer biopsies, were more often diabetic, more often males, did not have striking glomerulomegaly and had more vascular change. In short, their renal profile was more like that of non-indigenous Australians.

Most national focus on indigenous 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 [3, 41]. 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 haemodialysis 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 then, in regional centres and in remote communities nationwide, some just a single chair in a local clinic. Local funding was needed to establish some [42], variably sourced from mining companies, sale of local

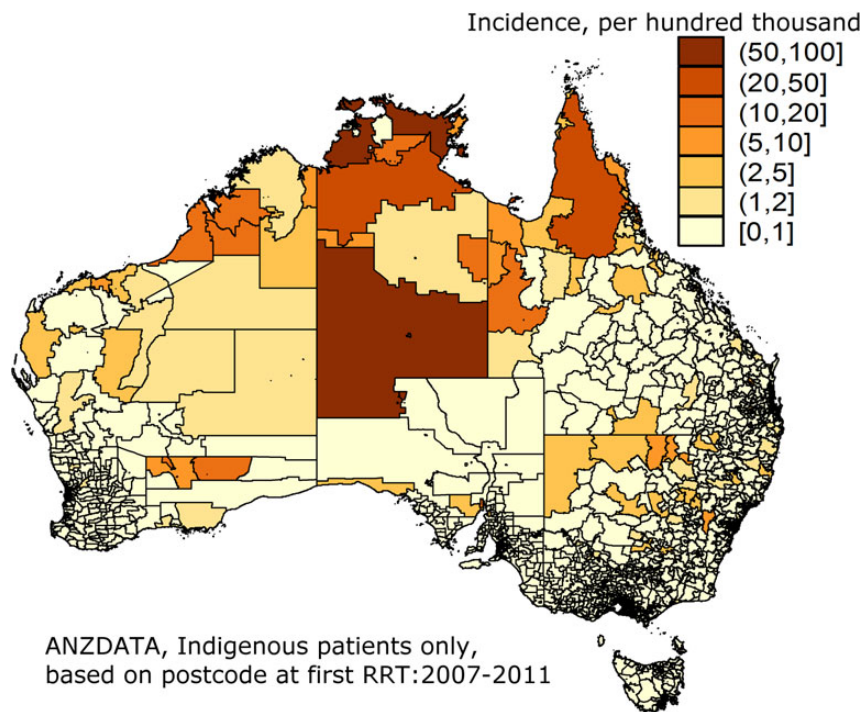


Fig. 2. Incident indigenous patients 2007–2011 by postcode (3). The data reported here have been supplied by the Australia and New Zealand Dialysis and Transplant Registry. The interpretation and reporting of these data are the responsibility of the Editors and in no way should be seen as an official policy or interpretation of the Australia and New Zealand Dialysis and Transplant Registry. ANZDATA, Australia and New Zealand Dialysis & Transplant Registry; RRT, renal replacement therapy.

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 haemodialysis 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 RRT, or to discontinue RRT [42, 43]. Creative community respite options and mobile dialysis services (Box 3) help alleviate the sense of social disconnection, but are additionally expensive [43–45]. 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, or in the usually dry bed of the Todd River in Alice Springs, where about 20% of the current dialysis population of more than 200 people are without stable housing [45, 46]. Squabbles occasionally erupt between adjoining states and territories about provision of RRT for people who come from other jurisdictions or who move among communities [47]. These tensions reflect the individual, complex and often changing health service funding agreements each jurisdiction has with federal government, and would be eliminated if federal government directly underwrote all RRT support directly. These issues also show that boundaries of current jurisdictions have little relevance to Aboriginal people and their concepts of homelands, belonging and identity. The 2010 Central Australia Renal Study [43] describes many of these issues, which, with minor variations, apply more generally across remote Australia. It also

Box 3. Central Australia—with permission.



A. Central Australia, aerial photograph. *Source:* Cepolina. Alice Springs Australia. Cepolina 2012. Accessed: 19 Aug 2013, <http://www.cepolina.com/s/Alice-Springs.htm>

B. The Purple Truck dialysis unit. *Source:* Brown S. The Purple Truck dialysis unit

Western Desert Nganampa Walytja Palyantjaku Tjutaku Aboriginal Corporation (WDNGWPT), Northern Territory
C. Maurice Gibson, Kintore Dialysis Unit. *Source:* Brown S. Western Desert Nganampa Walytja Palyantjaku Tjutaku Aboriginal Corporation (WDNGWPT), Northern Territory.

proposes strategies to contain progressive disease and optimize survival and quality of life for those already on RRT.

There is, of course, some good news concerning RRT. This includes elimination of the Aboriginal-non-Indigenous gap in late referral for RRT in Central Australia [43], achievement in the Kimberly in Western Australia of equally good outcomes for Indigenous as non-Indigenous dialysis patients [48] and the development of renal services competency among Aboriginal people themselves, together with a strong sense of ownership of their facilities and

services. Furthermore, both regional and national data suggest that the rate of increase of indigenous RRT incidence might be slowing [3, 49]. However, under all modelling scenarios, the numbers of prevalent patients will increase [42]; they will be further exacerbated as survival on dialysis continues to improve and as overall Aboriginal life expectancy increases further. With limited healthcare budgets, it is doubtful that the burden of RRT will be supportable by 2020, as is projected for Australia generally [50], 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 and involves many programmes 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+ years), which can be repeated annually and incorporates integrated screening for all common diseases [51] 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 [52] and subsidized through the QUMAX program in rural and urban settings [53], and chronic disease medicines (insulin, other hypoglycemics, RAS blockers, other antihypertensive agents and statins) are now the leading medicines issued under the S100 system [54]. 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 [55]. There is a burgeoning literature on chronic disease in Aboriginal health, with a dedicated information clearing house, text books and treatment manuals [56]. More indigenous people are training in healthcare, 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 programmes 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 [57], and a trial of pharmacologic prevention of new onset disease in Tiwi people is under analysis.

Many components of the chronic disease healthcare 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 [28].

More recently, Aboriginal chronic disease mortality, including renal deaths, have been falling, most prominently in remote areas [58]. Rates of natural death are also falling in the Tiwi community [59], and, on a repeat community screen over a 10–14 year interval, children are taller, high density lipoprotein levels have risen and rates of albuminuria and eGFR < 60 mL/min/m² are lower [60]. 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, they are welcome developments.

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Conflict of interest statement. None declared.

(See related article by Martin-Cleary and Ortiz. CKD hotspots around the world: where, why and what the lessons are. A CKJ review series. *Clin Kidney J* (2014) 7: 519–523.)

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